BMJ Open

Proposing Ethical Principles for Participant-Led Research: A Qualitative Case Study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-025633
Article Type:	Research
Date Submitted by the Author:	06-Aug-2018
Complete List of Authors:	Grant, Azure; University of California, Berkeley, Neuroscience; Quantified Self Labs Wolf, Gary; Quantified Self Labs Nebeker, Camille; University of California, San Diego, Family Medicine and Public Health
Keywords:	Public Involvement, Research Ethics, Informed Consent, Self-Tracking, Citizen Science

Title: Proposing Ethical Principles for Participant-Led Research: A Qualitative Case Study

Authors: Azure Grant[1,2*], Gary Wolf[1], Camille Nebeker[3]

[1] Quantified Self Labs, Berkeley, California

[2] Helen Wills Neuroscience Institute, University of California, Berkeley

[3.] Department of Family Medicine and Public Health, School of Medicine, University of California, San Diego

Running Head: Ethical Principles for Participant-Led Research

Word Count: 4247

Figures: 1

Tables: 2

Keywords: Participant-Led Research, Informed Consent, Research Ethics, Public Involvement

Acknowledgements: We would like to thank all participants in Blood Testers for their excellent work in shaping this PLR. We would also like to thank Dr. Sunita Vohra and Dr. Martijn de Groot for their careful readings and commentary on the manuscript.

Funding: Funding for the project was provided by a grant from Amgen Inc. to Quantified Self Labs. The company did not contribute to the research question(s), methods, analysis or interpretation. Amgen Inc. did not have access to data obtained via this project and has not had the opportunity to review this paper prior to its submission for peer-reviewed publication.

Conflict of Interest: The authors declare no conflict of interest.

Submitted on: 08/02/2018

***Address correspondence to:**

Azure Grant, B.A., Helen Wills Neuroscience Institute, University of California, Berkeley, California, 94720. Email: azuredominique@berkeley.edu

Phone: 1 (530) 592 9174

Fax: 510-642-5293

Data Sharing Statement: As interview transcripts contain personally identifying information that can not easily be removed while preserving the content of the interview (e.g., discussion of individuals' health condition in the context of their experiments, discussion of death of a family member's impact on trying to complete a project, descriptions of other participants in the context of their projects), transcripts will not be shared.

Abstract

Objectives: Participant-led research (PLR) is a rapidly developing form of citizen science in which individuals can create personal and generalizable knowledge. Although PLR lacks a formal framework for ethical review, participants should not be excused from considering the ethical implications of their work. Therefore, a PLR cohort consisting of 24 self-trackers aimed to 1) substitute IRB procedures with engagement in ethical reflection before and throughout the study, and 2) draft principles to encourage further development of ethical review frameworks for PLR.

Methods: A qualitative case study method was used to analyze the ethical reflection process. Participants discussed study risks, risk management strategies and benefits pre-project, during a series of weekly webinars, via individual meetings with the participant-organizers, and during semi-structured interviews at project completion. Themes arising from discussions and interviews were used to draft ethical principles for PLR.

Results: Data control, aggregation and identifiability were the most common risks identified. These were addressed by a commitment to transparency among all participants, and by establishing participant control via self-collection and self-management of data. Group discussions and resources (e.g., assistance with experimental design and data analysis) were the most commonly referenced benefits of participation. Additional benefits included greater understanding of one's physiology and greater ability to structure an experiment. Nine principles were constructed to encourage further development of ethical PLR practices. All participants expressed interest in participating in future PLR.

Conclusions: Projects involving a small number of participants can sustain engagement in ethical reflection among participants and participant-organizers. PLR that prioritizes transparency, participant control of data, and ongoing risk-to-benefit evaluation is compatible

with the principles that underlie traditional ethical review of health research, while being appropriate for a context in which citizen scientists play the central role.

Strengths and limitations of this study:

- A case study is traditionally considered a qualitative strategy to study a program, activity or process in-depth (1), allowing for what (2) calls a holistic investigation of group behavior and processes useful for describing interventions in real-life contexts, like the one presented here.
- Qualitative case studies also have the benefit of "intensive study of a single unit for the purpose of understanding a larger class of (similar) units" (p. 342) (3); our case is a small Participant-Led Research project, and our results may benefit development of general ethical frameworks for future PLR.
- The discussions and interviews that comprised the data set for this manuscript occurred naturally in the project as part of the ethical review process, and therefore did not create an extra burden on participants.
- This study is limited by the composition of this relatively small and self-selected group; it was not designed to balance sex, age, educational background or socioeconomic status.

Introduction

This paper explores a case of Participant-Led Research (PLR), which is defined as:

> "An activity that characteristically aims at the socially valued goal of producing generalizable health knowledge… It is distinctive as being initiated and conducted by the participants themselves. PLR includes individuals interested in acquiring health information, whether about themselves or more generally (4)."

This practice builds on over a decade of initiatives supporting public participation in the research process (5–8). Members of these initiatives, including community health workers (9), crowdsourced researchers (7), and "bio-citizens" (10), align to the common goal of increasing the participation of everyday individuals in science for the mutual benefit of citizens and researchers. For example, in community-based participatory research (11) and patient-centered outcomes research (12), community members or patients, respectively, work with professional scientists to shape the research questions most relevant to those participants. Relatedly, on citizen science platforms like Zooniverse (8,13,14) and Citizen Science Alliance (15), individuals may contribute to hypothesis development, study design, data collection, data analysis or dissemination of results (6,16–20). PLR combines characteristics of these initiatives in that it facilitates participant direction of all parts of the research process (4,21). Common reasons for engaging in PLR include: improving one's health via self-observation (22), gaining knowledge and support from others dealing with a common health condition (23), and contributing to the creation of useful tools (24). Despite its potential to contribute to the scientific literature, PLR publication is infrequent, even within the family of citizen science (17,25).

A significant challenge to extending the impact of PLR is that research led by participants presents challenges to traditional methods of ethical review (11,26–29). Indeed, existing methods for ethical review may not be well suited to the new challenges introduced by participant-led initiatives (28,30–32). For instance, in PLR, involvement of an academic institution may be peripheral or entirely absent (4,21,33). Normally, the ethical and regulatory dimensions of scientific research are addressed by the Institutional Review Board (IRB), whose role is to ensure that study risks are identified and managed, that benefits are appropriate in relation to risks and that people are given the information needed to provide informed consent to volunteer (34). Though this review process was developed to protect research participants, the

IRB, as its name clearly states, is an institutional process that developed for use in an academic research context.

Given the novelty of PLR and the well-known history of harm caused by unethical experimentation in science, a PLR conducted in a self-tracking community believed it was necessary to develop a framework for ethical evaluation of their research plan, and to document their procedures so that they could be critically reviewed and, if proven useful, be replicated or extended. Although an IRB was not utilized, participant-organizers were able to take advantage of the fact that IRBs have been well described in an extensive literature on research ethics.

One such example is a guidance manual that was published in 2011 by the World Health Organization (WHO) (35). Because ethical review and oversight for research involving human participants can vary globally, the WHO developed this manual to standardize guidelines such that research taking place internationally would share expectations of competencies needed by a research ethics committee (36). The key criteria articulated in this document focus on the following: that research must be designed in accordance with valid scientific methods; that risks are minimized to the extent that they are reasonable in relation to the possible benefits; that participants represent those most likely to gain from resulting knowledge; that conflicts of interest have been evaluated; that participant privacy and data confidentiality have been carefully considered; that respect for persons is demonstrated via an informed consent process; and that the greater community is actively involved in the design and conduct of the research (36). Our ethical review process aimed to satisfy the high-level requirements outlined by the WHO (35) in a situation where the formal procedures of an IRB were not applied.

Case: Ethical Reflection in the Blood Testers Project

The idea for a PLR, “Blood Testers” in which participants would frequently measure their own blood lipid levels emerged from discussions at Quantified Self Meetups and conferences. Quantified Self (QS) (22) is a global community united by an interest in what can be learned

from self-collected data. Those affiliated with the QS community may be researchers, engineers, or technologists, but formal research training is not required – only an interest in self-tracking. Quantified Self Labs, a California based limited liability corporation, provides administrative support, logistics, and project leadership to the community. Quantified Self does not have an academic affiliation nor does it receive government funding to support research.

Project equipment was lent to participants by Quantified Self Labs; guidance on methods for ethical review was provided by participant CN, a research ethicist, and several participants with prior academic research training agreed to share expertise. While this was a group activity with a general, collective goal of learning about natural variability in blood lipid levels, each participant also developed an individual research question. That is, each participant in Blood Testers conducted a single-subject experiment based on an hypothesis of personal interest related to cholesterol and triglycerides. All participants and participant-organizers subsequently collected and analyzed their own blood cholesterol and triglycerides as often as once per hour using a commercially available blood lipid testing system.

Participants engaged in active discussion of risks and benefits of participation throughout the project. Participants and participant-organizers met to identify study risks and benefits; discuss what constitutes responsible conduct of PLR, including what information is needed to inform willingness to volunteer; and to engage with media created for the project. At the project's conclusion, participants were interviewed about their experience in order to carefully assess perception of the project's ethical review process, allow participants to make final suggestions for improvement, and to record any additional risks and benefits of participation. A step-by-step description of the process follows.

Recruitment

People affiliated with the QS community were provided with information about the project either through direct contact with the participant-organizers or via a session at the Quantified Self 2017 Global Conference. An example of information conveyed during recruitment follows:

> *Cardiovascular disease (CVD) is the number 1 killer in the world. CVD risk is commonly assessed via annual point measurement of blood cholesterol and triglycerides. However, there is evidence to suggest that these outputs can be vary significantly on short timescales. The Blood Testers project will explore whether collaborative self-tracking of cholesterol and triglycerides using a finger prick assay could lead to actionable, personal knowledge.*

Following the session, potential participants communicated their interest via response to a survey and confirmed their intent to participate via email or phone call with the participant-organizers. Participants were then sent experimental equipment. **Figure 1 Recruitment.**

Training and Data Integrity

All participants were trained to conduct a finger-prick lipid assay with the CLIA-waived CardioChek Plus (PTS Diagnostics, Indianapolis, Indiana) according to manufacturer's instructions. Training was delivered by participant-organizer AG via: 1) video tutorial 2) live-webcast tutorial 3) one-on-one Skype coaching or 4) in person training. Each participant had access to one-on-one conversations with a participant-organizer throughout the project for any further training needed. Training efficacy was assessed first by the participant meeting or exceeding manufacturer's standards for accuracy and precision of cholesterol and triglyceride levels in a set of test samples. Training was considered complete if the participant met these standards and verbally expressed readiness to move on to experimental data collection.

Methods:

Patient and Public Involvement:

As described below, participants co-led the recruitment, development and execution of this project. As one of the main goals of the study was to crowdsource participants' opinions and experiences to generate a list of risks and benefits, and another was to have each participant conduct their experiments based on personally relevant questions, participant leadership was central. The study was designed with many available channels of communication for participants to exchange ideas before and throughout the study, as well as structured group discussions through which to do so. All participants were given the opportunity to read and comment on this manuscript prior to its publication. This manuscript will be disseminated open access such that all participants can view and share the work.

Phase Zero: Blood Testers Pilot

Prior to the beginning of the Blood Tester project, a pilot phase was conducted during which lipid measurement instrumentation was evaluated, equipment was purchased and potential research protocols were piloted. Preparation for the ethical review process included the recruitment of a research ethicist into the group as a participant.

Phase One: Pre-Participation Ethical Reflection

At the official commencement of the project, a webinar was held during which participant-organizers and eight prospective participants generated a list of risks, risk mitigation strategies, and potential benefits of participation. A presentation by the participating research ethicist, CN, summarized the principles of ethical research: autonomy, beneficence and justice (37) with an emphasis on the purpose of informed consent. This session was repeated so those who were not able to attend the initial session could contribute. Other webinar training sessions were recorded and transcribed to maintain a running list of risks, benefits and attendance. Videos of these meetings remained available as a reference for participants throughout the project.

Phase Two: Engagement via Online and In-Person Group Sessions:

As this project took place across six countries, and among participants from diverse backgrounds, it was decided that participants would be most likely to reflect seriously on the risks and benefits of participation if given multiple opportunities, described below, to do so.

One-on-One Meetings

If participants were unable to join a group meeting, then a one-on-one meeting was scheduled with a participant-organizer. The same material was covered in these meetings, and any new risks or benefits uncovered were recorded. These sessions were continued or repeated as requested by participants and required an approximate total of 20 hours of conversation throughout the project.

Written and Video Materials

Discussions were summarized in a blog post to quantifiedself.com. A brief literature review providing background on the project was also available to participants on a shared google drive. Based on participants' most common questions, two animations were created by AG to explain concepts in lipid physiology and biological timeseries.

Data Management

Lipid data collected by each participant was controlled by that participant at all times. Participants could document their data privately on personal computers or notebooks or publicly via upload to a group google sheet. Alternately, some participants opted to share their data privately with a participant-organizer who assisted with data analysis, without sharing publicly. At the conclusion of the project, data was removed from the public google sheet unless participants explicitly asked to keep it online. Similarly, participants could opt-in to have their data de-identified and aggregated as part of a scientific manuscript. The manuscript was

circulated prior to submission such that all participants could see how their data were represented and give feedback.

Phase Three: Semi-Structured Interviews

At the culmination of the testing period, semi-structured interviews were conducted with all finishing participants (n=18), excluding the authors. The primary goal of the interviews was to better understand participants' risk benefit evaluation, what factors they considered important for ethical review in PLR and what elements would be most useful to them in future PLR. For the complete list of interview questions see **supplemental table 1**. Interviews took place over private webcast or phone and were recorded and transcribed verbatim. Participants were introduced to the purpose of the interview and were asked for permission to audio record the conversation. The interview protocol was developed by CN, GW and AG, and AG conducted all interviews. As is common with qualitative methods, participants were encouraged to speak freely and not prohibited from sharing additional anecdotes about their experience with the project.

Data Analysis

A case study methodology was chosen to examine the ethical review process of this PLR. The case study method is a form of empirical inquiry that can be used to study real-life phenomena (e.g., decisions, programs, implementation process, organizational change, etc.) at an individual or group level (1,2). The case study method allows for a holistic investigation of group behavior and processes and is useful in describing an intervention in real-life context, in this case the substitution of typical IRB procedures with a discussion-based ethical review process. Data collected specifically during dedicated discussions in phases one and three were analyzed using content analysis techniques commonly used in qualitative research (39). The notes taken during the initial discussion focusing on ethical research practices as well as transcripts containing responses to the semi-structured interview questions were read line-by-line and then

coded to identify themes and patterns independently by CN and AG. Upon completion of independent review, the researchers discussed themes and patterns and any disagreements in observations about the data were discussed until agreement was reached. Lipid data analysis for individual projects that occurred within the phase two period is not a focus of this paper and is not reported here.

Results

Participant Demographics:

The final group consisted of 24 participants, six women and 18 men, ages 22-70 years (median 36 years, standard deviation 12 years). Twenty-one out of 24 (88%) of participants completed the project. Participants lived in six countries: The United States, The Netherlands, Denmark, England, Ireland and Austria; and were of white European, Middle Eastern, or Indian descent. Sixty-one percent of interviewed participants had no formal research experience, 23% had professional (e.g., Master's Degree or higher in a scientific field) training but were not career researchers, and 14% were actively pursuing a research career.

Phase One.

A total of 11 participants contributed to the initial discussion about ethical dimensions of the project. See **Tables 1 and 2** for brainstormed risks & risk mitigation strategies and benefits, respectively.

Phase Two.

Documentation and results of this phase have been submitted separately for publication (38).

Participant Hypotheses

Topics of investigation included daily rhythms in lipids, cholesterol fluctuation across the menstrual cycle, and the effects of switching to a plant-based diet on within-a-day and across-days variability of cholesterol and triglycerides.

Risks and Benefits of Participation

Risks regarding data management, including sharing of their personal health data, and privacy expectations dominated participant responses**.** Even participants who were willing to share their data in this project expressed that privacy was a main concern that would need to be addressed as PLR expanded. No participant proposed that the project posed a risk to their physical well-being. Although the risk of infection from finger prick device and risk of pain from testing was raised as an hypothetical concern, it was rejected by all participants as negligible.

Using Transparency to Mitigate Risk in Participant-Led Research

When talking about how to reduce risks, participants referred frequently to "transparency" regarding the nature of the sponsorship for the project; how data are stored, aggregated and shared; and data ownership. Maintaining transparency via frequent communication thus became a key principle that helped build trust between participants and participant-organizers. Communication occurred through several formats, including large-group webinars, one-on-one meetings with a participant-organizer, Slack chat window, and written/video material.

Phase Three.

Group Communication

During the semi-structured interviews, participants were asked about their preferences for receiving study information. As noted, several methods were used to share information and promote discussion, in order to ensure that all participants engaged in reflection on risks and benefits of participation. Direct one-on-one communications with the participant-organizers was preferred by 57% of participants. Thirty-five percent preferred the group webinar format, and 8% preferred to reflect on their own by referencing written materials. All participants reported that ethical reflection was an important component of the project, despite its low-risk design.

Additionally, several participants mentioned that familiarity with the other members of the group contributed to their positive assessment of risks and benefits of participation. One participant said:

"It gave me comfort walking into a study knowing that people that I knew were participating as well. It gave me comfort in what I was doing was useful, because I trust these people… If you were to take any sort of subject or any test and say, "X, Y and Z are all involved in this, would you consider joining?" The answer is that I'm probably biased towards joining because they are part of it. I know those people, and I know that they are very rational and calculated thinkers…"

While this interaction appears strongly positive, it also sets the stage for the possibility of peer-pressure or coercion in PLR. That being said, 88% of our cohort said that they would have felt comfortable halting their participation at any time. The remaining 12% reported "self-pressure" during their experiments, reflecting: "It's not in any way the kind of pressure that has been put on by the group, but it is more responsibilities I have taken on for myself.", or "It was my own pressure. I said I would do it." While this is a highly self-motivated cohort, there is no doubt that peer pressure could play a role in participants taking experimentation further than if they were on their own.

Benefits of Participation - Participant Learning

The key benefit expressed by participants in this PLR was the assistance they received from one another in answering their own research questions. Even individuals well-versed in data analysis sometimes struggled with defining precise experimental questions, and individuals with a background in medicine or biology were not often familiar with statistical analysis. A common outcome was that once data were plotted with the aid of another participant, a discussion between the two yielded the most valuable insights of the project. In answer to a question about what would aid them in their future personal experiments, participants mentioned a number of features of the Blood Testers PLR. These included help with design of experimental questions

and protocols, statistical analysis, data visualization, and short educational videos to explain physiology behind commonly measured outputs. Finally, all participants expressed interest in joining future PLR. See **table 2** for a complete list of participant-generated benefits.

Guiding Principles for PLR

Nine themes emerged from discussions and interviews as prospective ethical principles for PLR. As this PLR was driven by people with different backgrounds asking personal questions in diverse locations, we found that ethical reflection needed to be tailored to the individual rather than standardized. For this reason, guiding principles were drafted rather than codified rules.

1. **Transparency**: All relevant information about the project should be actively shared among participants and participant-organizers, including the source of research funding, equipment selection, data management protocols, risks and benefits, and conflicts of interest.
2. **Access to Expertise**: PLR requires access to experts (e.g., in experimental design, data analysis, research ethics) so that participants can rigorously carry out single-subject experiments (40).
3. **Data Access & Control:** The participant has the right and ability to manage their own data, and has the final say in what they collect about themselves.
4. **Right to Withdraw:** Participants have a right to reduce or withdraw their participation at any time.
5. **Relevance**: PLR addresses questions of relevance to the participants.
6. **Beneficence:** The participant actively reflects on the balance of benefits and risks of participation and freely choose whether to participate.
7. **Responsibility:** PLR requires that the participant actively consider the potential benefits and harms of the project to both themselves and others. The responsibility to stay informed is an ongoing process, not a one-time decision.
8. **Flexibility:** Ethical reflection in PLR should be tailored to individual needs and to the specific context, rather than be handled with “one size fits all” rules.
9. **Inclusivity:** If a prospective participant is willing and able to uphold these principles, they are welcome to participate.

Discussion

In this PLR, a global cohort of self-trackers collaboratively generated risks, risk mitigation strategies and benefits of participation in a study of blood lipids. Participants and participant-organizers mainly identified risks associated with data aggregation and identifiability and proposed individual data management and ownership as risk mitigations. Participant benefits centered on personal learning, and access to data and diverse experimental expertise. Guiding principles were created to capture essential ethical components of the project.

All participants expressed interest in joining future PLR, yet we lack formal guidelines to inform ethical review PLR for those not bound by the federal regulations protecting human research participants. For instance, in the United States, these regulations apply specifically to research funded by the Department of Health and Human Services (34). This means that PLR organizers outside this mandate must decide whether or not to obtain IRB review. It is important to note that the IRB was designed for clinical research led by professional researchers. This may be very different from a collaboratively-led international cohort of everyday individuals, who may lack academic research training or exposure to research ethics, and professional researchers (30,41). As such, IRB involvement may lead decisions specific to data ownership, data management and informed consent that directly conflict with the aims of research that is explicitly *participant-led*. For instance, IRBs often require that a Principal Investigator take complete responsibility for and ownership of study-generated data, which may oppose participants' expectation to own the data they collect about themselves (42). Together, the challenges of systematizing ethical review, and the lack of clear precedents for divisions of leadership and ownership have led many to conclude that current ethical review guidelines must be adapted or substituted to suit participant-led initiatives (11).

Recognizing that PLR is a rapidly evolving form of investigation, integrating ethical review requires a commitment to addressing challenges in the unknown future. In projects directed by a group of researchers from within an academic institution, study risks and benefits are conveyed to participants by researchers. By contrast, in PLR, participants and participant-organizers seek to uncover project risks and benefits collaboratively. The very concept of risk and benefit is altered when experimental questions are determined by participants rather than by a Principal Investigator. For example, PLR participants may alter their course of investigation at any point. This allows the risk to benefit calculation made by the participant at the study outset to be dynamically during the study period (e.g., if the individual's experimental question evolves in a way that changes their risk and benefit evaluation). However, this also means that it is not possible to anticipate every experiment to be conducted prior to the start of the study, to determine whether or not the participant understands the risks and benefits of those experiments, and to ensure that the participant consents to carry them out. As noted in our proposed principles, this permission to dynamically reevaluate risks and benefits is central to participant control.

Although formal ethical guidelines for non-governmentally funded PLR are yet to be put in place, this does not exempt PLR from ethical review in principle. This ethical review in PLR requires a common stake among all participants. This common stake means that all who take part in the project share an investment in the conduct and outcomes of the research. While best practices continue to be developed for specific use in higher-risk projects, low-risk, observational PLR may not need to wait for governmental guidelines to formalize its methods and contribute its findings to the scientific literature. Our experience suggests that encouraging ethical reflection among a small group while asking research questions that can be answered using low-risk procedures can safely generate participant benefits.

Limitations

As is often the case with new research methodologies, our learning is biased by our narrow context, intentional minimal-risk design and unique community of self-trackers. Larger, more diverse cohorts, and other distinctive communities may find discussion based ethical-review less applicable to their context

Conclusions

PLR is an emerging form of investigation in which responsibility is shared more equally between participants and participant-organizers. The PLR described in this paper is novel in two ways. It is the first PLR, to our knowledge, in which all participants formed unique research questions to explore and collected and managed all data individually. Second, the cohort engaged in ethical reflection before, during and upon conclusion of the project and used documentation of these discussions to create guiding principles for future PLR. This PLR retained 88% participation through its conclusion and 100% satisfaction among finishing participants. We conclude that low-risk PLR involving single-subject study in a small group may be conducted safely by incorporating an ethical reflection process. It is our hope that the principles generated during this PLR may encourage discussion and development of ethical PLR practices.

References:

1. Creswell JW. Research Design: Qualitative, Quantitative, and Mixed Methods Approaches. SAGE Publications; 2009. 297 p.

2. Aberdeen T. Yin, R. K. (2009). Case study research: Design and methods (4th Ed.). Thousand Oaks, CA: Sage. Can J Action Res. 2013;14(1):69–71.

3. Gerring J. What Is a Case Study and What Is It Good for? Am Polit Sci Rev. 2004;98(2):341–54.

4. Vayena E, Brownsword R, Edwards SJ, Greshake B, Kahn JP, Ladher N, et al. Research led by participants: a new social contract for a new kind of research. J Med Ethics. 2016;42(4):216–9.

5. Mikesell L, Bromley E, Khodyakov D. Ethical community-engaged research: a literature review. Am J Public Health. 2013 Dec;103(12): e7–14.

6. Bonney R, Shirk JL, Phillips TB, Wiggins A, Ballard HL, Miller-Rushing AJ, et al. Citizen science: Next steps for citizen science. Science. 2014;343(6178):1436–7.

7. Swan M. Crowdsourced Health Research Studies: An Important Emerging Complement to Clinical Trials in the Public Health Research Ecosystem. J Med Internet Res [Internet]. 2012 Mar 7;14(2). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3376509/

8. Pettibone L, Vohland K, Ziegler D. Understanding the (inter)disciplinary and institutional diversity of citizen science: A survey of current practice in Germany and Austria. PLoS ONE [Internet]. 2017 Jun 27;12(6). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5487260/

9. Nebeker C, López-Arenas A. Building Research Integrity and Capacity (BRIC): An Educational Initiative to Increase Research Literacy among Community Health Workers and Promotores. J Microbiol Biol Educ. 2016 Mar 1;17(1):41–5.

10. The Rise of the New Bio-Citizen [Internet]. Wilson Center. 2018 [cited 2018 Jun 20]. Available from: https://www.wilsoncenter.org/article/the-rise-the-new-bio-citizen

11. Banks S, Armstrong A, Carter K, Graham H, Hayward P, Henry A, et al. Everyday ethics in community-based participatory research. Vol. 8, Contemporary Social Science. 2013. p. 263–77.

12. Fleurence R, Whicher D, Dunham K, Gerson J, Newhouse R, Luce B. The Patient-centered Outcomes Research Institute's Role in Advancing Methods for Patient-centered Outcomes Research. Med Care. 2015 Jan;53(1):2–8.

13. Jones FM, Allen C, Arteta C, Arthur J, Black C, Emmerson LM, et al. Time-lapse imagery and volunteer classifications from the Zooniverse Penguin Watch project. Sci Data. 2018 Jun 26;5:180124.

14. Swanson A, Kosmala M, Lintott C, Packer C. A generalized approach for producing, quantifying, and validating citizen science data from wildlife images. Conserv Biol J Soc Conserv Biol. 2016;30(3):520–31.

15. Citizen Science Alliance [Internet]. Available from: https://www.citizensciencealliance.org/

16. Bonney R, Cooper C, Ballard H. The Theory and Practice of Citizen Science: Launching a New Journal. Citiz Sci Theory Pract. 2016 May;1(1):1–1.

17. Follett R, Strezov V. An Analysis of Citizen Science Based Research: Usage and Publication Patterns. PloS One. 2015;10(11):e0143687.

18. Gura T. Citizen science: amateur experts. Nature. 2013;496(7444):259–61.

19. Cohn JP. Citizen Science: Can Volunteers Do Real Research? BioScience. 2008;58(3):192–7.

20. Hand E. Citizen science: People power. Nature. 2010;466(7307):685–7.

21. Vayena E, Tasioulas J. Adapting Standards: Ethical Oversight of Participant-Led Health Research. PLOS Med. 2013 Mar 12;10(3): e1001402.

22. Wolf G, Ramirez E. Quantified Self/Public Health Symposium. 2014;

23. Wicks P, Vaughan TE, Massagli MP, Heywood J. Accelerated clinical discovery using self-reported patient data collected online and a patient-matching algorithm. Nat Biotechnol. 2011 May 24;29(5):411–4.

24. Dana Lewis. Setting Expectations for Successful Artificial Pancreas/Hybrid Closed Loop/Automated Insulin Delivery Adoption. J Diabetes Sci Technol. 2018;12(2):533–4.

25. Godlee F. Towards the patient revolution. BMJ. 2014 Jan 29;348:g1209.

26. Doerr M, Maguire Truong A, Bot BM, Wilbanks J, Suver C, Mangravite LM. Formative Evaluation of Participant Experience with Mobile eConsent in the App-Mediated Parkinson mPower Study: A Mixed Methods Study. JMIR MHealth UHealth. 2017 Feb 16;5(2):e14.

27. Grady C, Cummings SR, Rowbotham MC, McConnell M V., Ashley EA, Kang G. Informed Consent. Drazen JM, Harrington DP, McMurray JJV, Ware JH, Woodcock J, editors. N Engl J Med. 2017 Mar 2;376(9):856–67.

28. Rothstein MA, Wilbanks JT, Brothers KB. Citizen Science on Your Smartphone: An ELSI Research Agenda. J Law Med Ethics. 2015;43(4):897–903.

29. Sugarman J. Examining Provisions Related to Consent in the Revised Common Rule. Am J Bioeth. 2017;17(7):22–6.

30. Bloss C, Nebeker C, Bietz M, Bae D, Bigby B, Devereaux M, et al. Reimagining Human Research Protections for 21st Century Science. J Med Internet Res. 2016 Dec 22;18(12):e329.

31. Thorogood A, Bobe J, Prainsack B, Middleton A, Scott E, Nelson S, et al. APPLaUD: access for patients and participants to individual level uninterpreted genomic data. Hum Genomics. 2018 Feb 17;12(1):7.

32. Weissman JS, Campbell EG, Cohen IG, Lynch HF, Largent EA, Gupta A, et al. IRB Oversight of Patient-Centered Outcomes Research: A National Survey of IRB Chairpersons , IRB Oversight of Patient-Centered Outcomes Research: A National Survey of IRB Chairpersons. J Empir Res Hum Res Ethics. 2018 Jun 14;1556264618779785.

33. Vayena E, Tasioulas J. The ethics of participant-led biomedical research. Nat Biotechnol. 2013 Sep 1;31(9):786–7.

34. 45 CFR 46 Protection of Human Subjects. U.S. Department of Health and Human Services 2009.

35. Bouesseau M-C, Coleman C, Kass N, Laothavorn J, Saxena A, Vanderpoel S. Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants. World Health Organ [Internet]. 2011; Available from: http://apps.who.int/iris/bitstream/handle/10665/44783/9789241502948_eng.pdf;jsessionid=5E488F141667C3CEA6FED5BE49301ED4?sequence=1

36. Bouesseau M-C, Coleman C, Kass N, Laothavorn J, Saxena A, Vanderpoel S. Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants. World Health Organ. 2011;

37. Department of Health, Education, and Welfare, National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report. Ethical principles and guidelines for the protection of human subjects of research. J Am Coll Dent. 2014;81(3):4–13.

38. Patton MQ. Qualitative research & evaluation methods: integrating theory and practice. 806 p.

39. Azure Grant, Gary Wolf. Cholesterol and Triglycerides Traverse Risk Categories on Short Timescales: A Participant-Led Study. PLOS Med. *Submitted 2018 Jul 20*;

40. Choe EK, Lee NB, Lee B, Pratt W, Kientz JA. Understanding quantified-selfers' practices in collecting and exploring personal data. In: Proceedings of the 32nd annual ACM conference on Human factors in computing systems. 2014. p. 1143–52.

41. Nebeker C, Harlow J, Espinoza Giacinto R, Orozco-Linares R, Bloss CS, Weibel N. Ethical and regulatory challenges of research using pervasive sensing and other emerging technologies: IRB perspectives. AJOB Empir Bioeth. 2017 Oct 2;8(4):266–76.

42. Gliklich RE, Dreyer NA, Leavy MB. Principles of Registry Ethics, Data Ownership, and Privacy [Internet]. Agency for Healthcare Research and Quality (US); 2014 [cited 2018 Jun 4]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK208620/

43. Wiggins A, Crowston K. From conservation to crowdsourcing: A typology of citizen science. In: Proceedings of the Annual Hawaii International Conference on System Sciences. 2011.

44. Hudson KL, Collins FS. Bringing the Common Rule into the 21st Century. N Engl J Med. 2015 Oct 28;373(24):2293–6.

45. Sharon T. Self-Tracking for Health and the Quantified Self: Re-Articulating Autonomy, Solidarity, and Authenticity in an Age of Personalized Healthcare. Philos Technol. 2017 Mar 18;30(1):93–121.

46. Shore N, Brazauskas R, Drew E, Wong KA, Moy L, Baden AC, et al. Understanding community-based processes for research ethics review: a national study. Am J Public Health. 2011 Dec;101 Suppl 1(Suppl 1): S359-64.

Table 1. Participant-Generated Risks and Risk Mitigation Strategies

Risk	Risk Mitigation
Engagement with ethical issues of participation was perceived as difficult, which could limit engagement.	Our challenge is to test if collaborative discussion of risks and benefits will be more enjoyable and engaging.
Participants could learn something unpleasant (e.g., results that require medical attention).	Participants were made aware of this risk in the initial project discussion, before taking any lipid tests.
Frequent testing can cause some people anxiety.	After some discussion, and polling of participants, we agreed that this risk is minimal in our group.
Participants could be disappointed by learning the actual bounds of uncertainty of the data, even if these bounds are comparable to that of professional tests.	This topic was discussed at length in the beginning of the project and was also considered a benefit. Consumers often do not realize the extent to which data from at-home testing can be uncertain.
Reputation risk to participant-organizers if ethical concerns are not well understood.	Participant-organizers convened all participants to engage in discussion of risks and benefits.
Reputation risk to participant-organizers if training on how to use the test system is not effective.	Participants were thoroughly trained, and training materials and expertise were made available for the entire duration of the project.
Participants could feel peer-pressure to carry out an experiment.	Participants were encouraged to only carry out testing that was personally interesting and productive.
Reputation risk to all project participants if data-quality is questionable.	Participants were incentivized to collect good data because they conducted personally-relevant experiments.
Conflict of interest concern by participants regarding funding.	Goals and funding were clearly stated to all before joining the project, and funders did not view the manuscript or advise on project content.
Demands on Participants' time.	There was no minimal required time commitment Our goal was to be as supportive as possible- and to understand reasons for halted projects as they arrived.
Minor pain and bruising.	Participants were trained with techniques to minimize discomfort. Participants chose how frequently to sample and could stop at any point.
Almost negligible risk of infection.	Participants were given sterile supplies and trained to use equipment safely.
Risk of being penalized in the future based on data being read by others and associated with a sanction by insurance companies.	All participants could keep their data private and offline. Data was removed from group-spreadsheet post-project unless participant expressed interest in keeping the data public.
Risk that Quantified Self as a movement puts itself at risk by stumbling across legal and/or social liabilities.	Transparency was maintained about risks and benefits, and multiple opportunities were provided for participants to reflect.

Table 2. Participant-Generated Benefits of Participation

Benefit
Sharing the method of small group, collaborative self-discovery. Uncovering challenges therein is necessary for revising the process of participant-led research.
Proposing a new method for more engaging ethical review in participant-led research.
Greater community ability and motivation to validate new self-tracking tools before use.
Educating ourselves, to the best of our ability, about the current literature in cholesterol and triglyceride research.
Learning the extent to which individuals' lipids vary throughout the day as measured.
Learning the extent to which a single measurement at the doctor's office is representative of one's "regular" lipid levels.
Increased ability to engage with one's physician in a conversation about the health-relevance of one's cholesterol and triglyceride levels.
Increased ability to conduct an experiment, and empowerment to interrogate future personal questions using scientific tools.
Access to costly blood-testing equipment, and the data generated by it.
Encouragement from respected fellow participants.
Access to advice from individuals experienced in experimental design.
Access to help with data analysis.
Opportunity to share learnings at a Quantified Self symposium or conference.

Figure Legend

Figure 1: Phase II Recruitment Flowchart

Recruitment Flowchart for the Quantified Self "Blood Testers" Participant-Led Research project. Four employees of Quantified Self Labs and thirty-five prospective participants met at the Quantified Self 2017 Global Conference to propose and discuss the project. Emails were collected and follow-up surveys were sent to gauge interest. Responders confirmed their interest in participation and their goal for the project with an organizer from QS Labs. These individuals received a equipment, and subsequently attended online discussions to brainstorm risks and benefits of participation. In total, twenty-one participants completed a project.

Supplemental Tables:

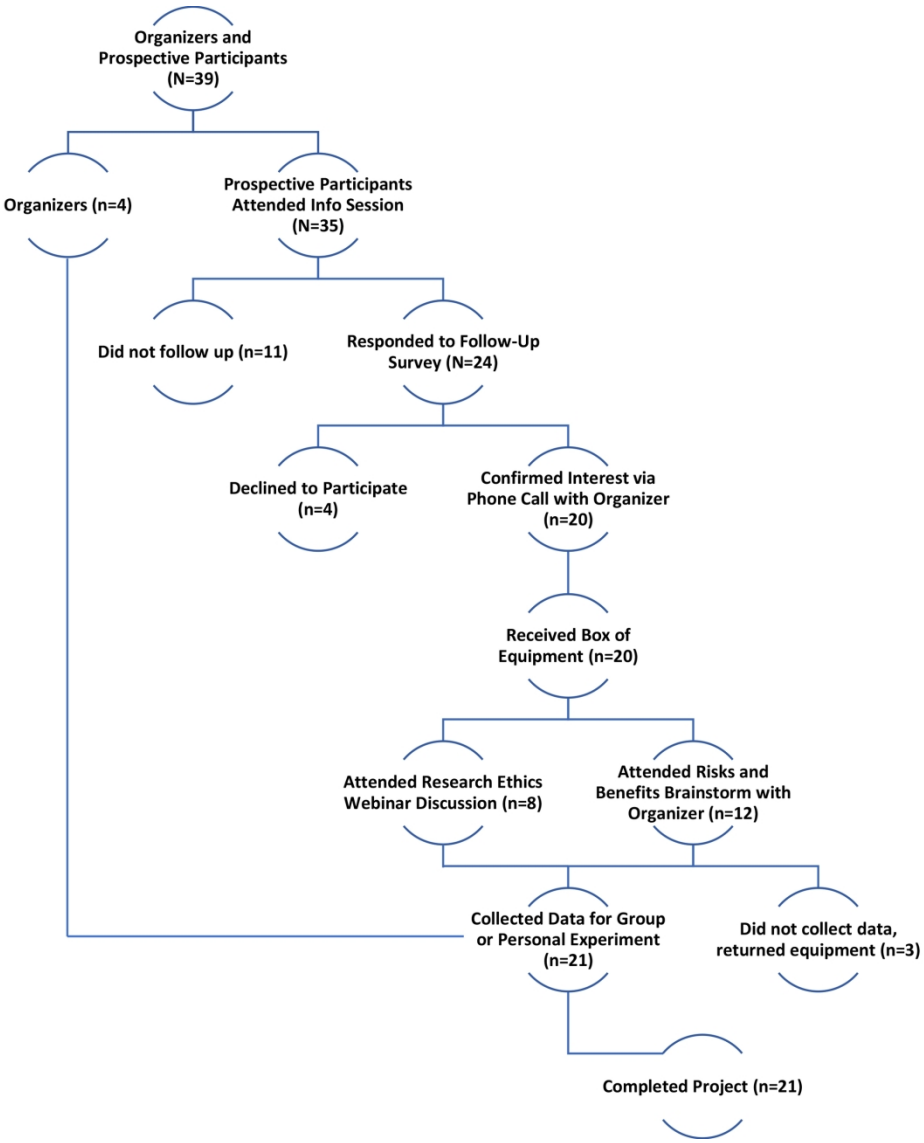
Supplemental Table 1: Semi-Structured Interview Questions

Authorship Contributor Statement:

AG led the writing and editing of the manuscript, led the project which is the case under analysis in this manuscript, conducted all interviews, and carried out qualitative analysis of the interviews with CN.

CN provided guidance and recommendations on the ethical review process of the project and contributed to the writing and editing of the manuscript and carried out qualitative analysis of the interviews with AG.

GW contributed extensively to conception and the organization of the project, and to writing and editing of the manuscript.



Recruitment Flowchart for the Quantified Self "Blood Testers" Participant-Led Research project. Four employees of Quantified Self Labs and thirty-five prospective participants met at the Quantified Self 2017 Global Conference to propose and discuss the project. Emails were collected and follow-up surveys were sent to gauge interest. Responders confirmed their interest in participation and their goal for the project with an organizer from QS Labs. These individuals received a equipment, and subsequently attended online discussions to brainstorm risks and benefits of participation. In total, twenty-one participants completed a project.

190x215mm (300 x 300 DPI)

Supplementary Table 1. Semi-Structured Interview Questions

Question Number	Question Text
1	How long have you been doing self-tracking experiments?
2	How did you become involved with the Blood Testers project?
3	Do you have any formal or informal research training?
4	Have you ever been part of a participant-led research project?
5	Whose responsibility is it to determine that a participant-led research project is conducted ethically?
6	What are the factors which should be considered for participant-led research to be conducted ethically?
7	Do you feel this project put you at any risk? Why or why not?
8	Was there anything in the project that surprised you, or that you wished you had known in advance?
9	Would your assessment of the project's risk change if you were with a group of people that you didn't know?
10	Did you feel that it was important to discuss the benefits and risks in the Blood Testers project?
11	I am going to ask you to rank three different things that we did in the project, from most useful to least useful, in terms of informing you about risks and benefits. Those things are, written materials about the project, a webinar where we met and talked about ethical ramifications in the project. The third one is one-on-one communication.
12	Would you have felt comfortable halting your participation at any time?
13	In the future, are there any kinds of research training materials that would be useful to you for personal or participatory research projects?
14	Would you be interested in joining another round of participant-led research in the future?
15	Given that in this project participants can halt their participation at any time, do you think there is any way for a participant to be coerced into participation or continuation?
16	Do you rate yourself completely confident, somewhat confident, or not at all confident with your understanding of risks and benefits of participation?

BMJ Open

Approaches to Governance of Participant-Led Research: A Qualitative Case Study

Journal:	*BMJ Open*
Manuscript ID	bmjopen-2018-025633.R1
Article Type:	Research
Date Submitted by the Author:	18-Dec-2018
Complete List of Authors:	Grant, Azure; University of California, Berkeley, Neuroscience; Quantified Self Labs Wolf, Gary; Quantified Self Labs Nebeker, Camille; University of California, San Diego, Family Medicine and Public Health
Primary Subject Heading:	Ethics
Secondary Subject Heading:	Health policy, Patient-centred medicine, Public health, Qualitative research, Research methods
Keywords:	Public Involvement, Research Ethics, Informed Consent, Citizen Science, Participant-Led Research

Title: Approaches to Governance of Participant-Led Research: A Qualitative Case Study

Authors: Azure Grant[1,2*], Gary Wolf[1], Camille Nebeker[3]

[1] Quantified Self Labs, Berkeley, California

[2] Helen Wills Neuroscience Institute, University of California, Berkeley

[3.] Department of Family Medicine and Public Health, School of Medicine, University of California, San Diego

Running Head: Ethical Principles for Participant-Led Research

Word Count: 5032

Figures: 2

Tables: 2

Keywords: Participant-Led Research, Informed Consent, Research Ethics, Governance, Public Involvement

Acknowledgements: We would like to thank all participants in Blood Testers for their excellent work in shaping this PLR. We would also like to thank Dr. Sunita Vohra and Dr. Martijn de Groot for their careful reading and commentary on the manuscript.

Funding: Funding for the project was provided by a grant from Amgen Inc. to Quantified Self Labs. The company did not contribute to the research question(s), methods, analysis or interpretation. Amgen Inc. did not have access to data obtained via this project and has not had the opportunity to review this paper prior to its submission for peer-reviewed publication.

Conflict of Interest: The authors declare no conflict of interest.

Submitted on: 08/02/2018

Revision Submitted on: 12/14/2018

***Address correspondence to:**

Camille Nebeker, EdD, MS, Department of Family Medicine and Public Health, School of Medicine, University of California, San Diego, California, 92093.

Email: nebeker@eng.ucsd.edu

Phone: 1 (858) 534-7786

Fax: 1- (858) 534-0377

Data Sharing Statement: As interview transcripts contain personally identifying information that cannot easily be removed while preserving the content of the interview (e.g., discussion of individuals' health condition in the context of their experiments, discussion of the death of a family member's impact on trying to complete a project, descriptions of other participants in the context of their projects), transcripts will not be shared.

Abstract

Objectives: Participant-led research (PLR) is a rapidly developing form of citizen science in which individuals can create personal and generalizable knowledge. Although PLR lacks a formal framework for ethical review, participants should not be excused from considering the ethical implications of their work. Therefore, a PLR cohort consisting of 24 self-trackers aimed to: 1) substitute research ethics board procedures with engagement in ethical reflection before and throughout the study, and 2) draft principles to encourage further development of the governance and ethical review of PLR.

Methods: A qualitative case study method was used to analyze the ethical reflection process. Participants discussed study risks, risk management strategies and benefits pre-project, during a series of weekly webinars, via individual meetings with the participant-organizers, and during semi-structured interviews at project completion. Themes arising from discussions and interviews were used to draft prospective principles to guide PLR.

Results: Data control, aggregation and identifiability were the most common risks identified. These were addressed by a commitment to transparency among all participants, and by establishing participant control via self-collection and self-management of data. Group discussions and resources (e.g., assistance with experimental design and data analysis) were the most commonly referenced benefits of participation. Additional benefits included greater understanding of one's physiology and greater ability to structure an experiment. Nine principles were constructed to encourage further development of ethical PLR practices. All participants expressed interest in participating in future PLR.

Conclusions: Projects involving a small number of participants can sustain engagement in ethical reflection among participants and participant-organizers. PLR that prioritizes transparency, participant control of data, and ongoing risk-to-benefit evaluation is compatible with the principles that underlie

traditional ethical review of health research, while being appropriate for a context in which citizen scientists play the central role.

Strengths and limitations of this study:

- A case study is traditionally considered a qualitative strategy to study a program, activity or process in-depth, permitting description of processes or groups responses to interventions in real-life contexts, like the one presented here.
- Qualitative case studies also have the benefit of deeply analyzing a single unit with the intension of understanding how future iterations of similar units may function. We applied this methodology to study to a Participant-Led Research project, and anticipate our results may contribute to the development of governance structures and ethical frameworks for future PLR.
- The discussions and interviews that comprised the data set for this manuscript occurred naturally as part of our ethical review process, and therefore did not introduce additional burden to participants.
- This study is limited by the composition of this relatively small and self-selected group; it was not designed to balance sex, age, educational background nor socioeconomic status.
- Although the authors have attempted to generalize across Institutional Review Boards/Research Ethics Committees whenever possible, the introduction to this study focuses primarily on research regulation in the United States. As several participants in the case are from the European Union, this is a limitation.

Introduction

This paper explores a case of Participant-Led Research (PLR), which is defined as:

> "An activity that characteristically aims at the socially valued goal of producing generalizable health knowledge… It is distinctive as being initiated and conducted by the participants themselves. PLR includes individuals interested in acquiring health information, whether about themselves or more generally (1)."

This practice builds on over a decade of initiatives supporting public participation in the research process (2–5). Members of these initiatives, including community health workers (6), crowdsourced researchers (4), and "bio-citizens" (7), align to the mutually beneficial goal of increasing the participation of everyday individuals in science (8). For example, in community-based participatory research (9) and patient-centered outcomes research (10), community members or patients, respectively, work with professional scientists to shape the research questions most relevant to those participants. Relatedly, on citizen science platforms like Zooniverse (5,11,12) and Citizen Science Alliance (13), individuals may contribute to hypothesis development, study design, data collection, data analysis or dissemination of results, while enabling greater scale and reducing costs for researchers (3,14–18). PLR combines characteristics of these initiatives in that it facilitates participant direction of all parts of the research process (1,19). Common reasons for engaging in PLR include: improving one's health via self-observation (20), gaining knowledge and support from others dealing with a common health condition (21), and contributing to the creation of useful tools (22). Despite its potential to contribute to the scientific literature, PLR publication is infrequent, even within the family of citizen science (15,23).

A significant challenge to extending the impact of PLR is that research led by participants presents challenges to traditional methods of ethical review (9,24–27). Indeed, existing methods for ethical review may not be well suited to the new challenges introduced by participant-led initiatives (26,28–30). For instance, in PLR the involvement of an academic institution may be peripheral or entirely absent (1,19,31). Normally, the ethical and regulatory dimensions of scientific research are addressed by a regulatory body (i.e., the Institutional Review Board (IRB) in the US; the Research Ethics Committee

(REC) in the UK, Canada and EU), whose role is to ensure that study risks are identified and managed, that benefits are appropriate in relation to risks and that people are given the information needed to provide informed consent to volunteer (32). Though this review process was developed to protect research participants, the IRB (US), as its name clearly states, is an institutional process that developed for use in an academic research context.

Given the novelty of PLR and the well-known history of harm caused by unethical experimentation in science, a PLR conducted in a self-tracking community believed it was necessary to develop a process for ethical evaluation of their research plan, and to document procedures so that they could be critically reviewed and, if proven useful, be replicated or extended. Although an IRB was not utilized, participant-organizers were able to take advantage of the fact that IRBs/RECs have been well described in an extensive literature on research ethics.

One such example is a guidance manual that was published in 2011 by the World Health Organization (WHO) (33). Because ethical review and oversight for research involving human participants can vary globally, the WHO developed this manual to standardize guidelines such that research taking place internationally would share expectations of competencies needed by a research ethics committee (34). The key criteria articulated in this document are the following: research must be designed in accordance with valid scientific methods; risks are minimized to the extent that they are reasonable in relation to the possible benefits; participants represent those most likely to gain from resulting knowledge; conflicts of interest have been evaluated; participant privacy and data confidentiality have been carefully considered; respect for persons is demonstrated via an informed consent process; and the greater community is actively involved in the design and conduct of the research (34). Our ethical review process aimed to satisfy the high-level global requirements outlined by the WHO (33) in a situation where the formal procedures of an IRB/REC were not applied.

Case: Ethical Reflection in the Blood Testers Project

The idea for a PLR, "Blood Testers", in which participants would frequently measure their own blood lipid levels emerged from discussions at Quantified Self Meetups and conferences. Quantified Self (QS) (20) is a global community united by an interest in what can be learned from self-collected data. Those affiliated with the QS community may be researchers, engineers, or technologists, but formal research training is not required – only an interest in self-tracking. Quantified Self Labs, a California-based limited liability corporation, provides administrative support, logistics, and project leadership to the community. Quantified Self does not have an academic affiliation nor does it receive government funding to support research.

Project equipment was lent to participants by Quantified Self Labs; guidance on methods for ethical review was provided by participant CN, a research ethicist. Additionally, several participants with prior academic research training agreed to share expertise. Although this was a group activity with a general, collective goal of learning about natural variability in blood lipid levels, each participant also developed an individual research question. That is, each participant in Blood Testers conducted a single-subject experiment based on an hypothesis of personal interest related to cholesterol and triglycerides. All participants and participant-organizers subsequently collected and analyzed their own blood as often as once per hour using a commercially available blood lipid testing system.

Participants engaged in active discussion of risks and benefits of participation throughout the project. Participants and participant-organizers met to identify study risks and benefits; discuss what constitutes responsible conduct of PLR, including what information is needed to inform willingness to volunteer; and to engage with media created for the project. At the project's conclusion, participants were interviewed about their experience in order to carefully assess perception of the project's ethical review process, allow participants to make final suggestions for improvement, and to record any additional risks and benefits of participation. A step-by-step description of the process follows.

Recruitment

People affiliated with the QS community were provided with information about the project either through direct contact with the participant-organizers or via a session at the Quantified Self 2017 Global Conference. An example of information conveyed during recruitment follows:

> *Cardiovascular disease (CVD) is the number 1 killer in the world. CVD risk is commonly assessed via annual point measurement of blood cholesterol and triglycerides. However, there is evidence to suggest that these outputs can vary significantly on short timescales. The Blood Testers project will explore whether collaborative self-tracking of cholesterol and triglycerides using a finger prick assay leads to actionable, personal knowledge.*

Following the session, potential participants communicated their interest via response to a survey and confirmed their intent to participate via email or phone call with the participant-organizers. Participants were then sent experimental equipment. **(Figure 1 Recruitment). (Place Figure 1 here).**

Training and Data Integrity

All participants were trained to conduct a finger-prick lipid assay with the CLIA-waived CardioChek Plus (PTS Diagnostics, Indianapolis, Indiana) according to manufacturer's instructions. Training was delivered by participant-organizer AG via: 1) video tutorial, 2) live-webcast tutorial, 3) one-on-one Skype coaching or 4) in-person training. Each participant had access to one-on-one conversations with a participant-organizer throughout the project for any further training needed. Training efficacy was assessed first by the participant meeting or exceeding manufacturer's standards for accuracy and precision of cholesterol and triglyceride levels in a set of test samples. Training was considered complete if the participant met these standards and verbally expressed readiness to move on to experimental data collection.

Methods:

Patient and Public Involvement:

As described below, participants co-led the recruitment, development and execution of this project. As one of the main goals of the study was to crowdsource participants' opinions and experiences to generate a list of risks and benefits, and another was to have each participant conduct their experiments based on personally relevant questions, participant leadership was central. The study was designed with many available channels of communication for participants to exchange ideas before and throughout the study, as well as structured group discussions through which to do so. All participants were given the opportunity to read and comment on this manuscript prior to its publication. This manuscript will be disseminated open access such that all participants can view and share the work.

Researcher Characteristics:

In PLR, the "researchers" also participate in data collection, and the "citizen" participants also take on research duties (e.g., contribute to ideas for data analysis, share software). Although only the authors met the standards for academic authorship, nearly all participants took on some type of organizational role or shared expertise, as described further below. In this manuscript, we refer to the authors/researchers as "participant-organizers" rather than researchers, and acknowledge that although these individuals oversaw the project, participants acted as co-researchers. The authors were a leader in the Quantified Self community, GW, the leader of the project, AG, and the ethical review adviser/participant in the project, CN. These individuals have past academic research experience in physiology & data science (AG), history and single-subject research (GW), and research ethics (CN). In this case, the authors were acquainted with most of those who decided to join the PLR through prior meeting at Quantified Self conferences. The fact that the participant-organizers were integrated into the community that conducted the project, and that several of the participants were long time community members, undoubtedly added some familiarity and ease to the project that would not have otherwise existed.

Phase Zero: Blood Testers Pilot

Prior to the beginning of the Blood Tester project, a pilot phase was conducted during which lipid measurement instrumentation was evaluated, equipment was purchased and potential research protocols were piloted. The group involved also initiated communications on a Slack, a project communication platform, to share questions, protocol drafts and updates on equipment selection and use. In preparation for the ethical review process, a research ethicist known by GW was invited to join the group as a participant.

Phase One: Pre-Participation Ethical Reflection

At the official commencement of the project, a webinar was held during which participant-organizers and eleven prospective participants generated a list of risks, risk mitigation strategies, and potential benefits of participation. A presentation by the participating research ethicist, CN, summarized the principles of ethical research, including autonomy, beneficence and justice (35), with an emphasis on the purpose of informed consent. This session was repeated so that those who were not able to attend the initial session could contribute. Webinar training sessions were recorded and transcribed to maintain a running list of potential risks, benefits and attendance. Video recordings of webinar meetings remained available as a reference for participants throughout the project.

Phase Two: Engagement via Online and In-Person Group Sessions:

As this project took place across six countries, and among participants from diverse educational and occupational backgrounds, it was decided that participants would be most likely to reflect seriously on the risks and benefits of participation if given multiple opportunities, described below, to do so.

One-on-One Meetings

If participants were unable to join a group meeting, then a one-on-one meeting was scheduled with a participant-organizer. The same material was covered in these meetings, and any new risks or benefits

uncovered were recorded. These sessions were continued or repeated as requested by participants and required an approximate total of 20 hours of conversation throughout the project.

Written and Video Materials

Discussions were summarized in a blog post to quantifiedself.com. A brief literature review providing background on the project was also available to participants on a shared google drive and Slack channel. Based on participants' most common questions, two educational animations (36,37) were created by AG to explain concepts in lipid physiology and biological timeseries.

Data Management

Lipid data collected by each participant was controlled by that participant at all times. Participants could document their data privately on personal computers or notebooks or publicly via upload to a group google sheet. Alternately, some participants opted to share their data privately with AG, who led data analysis, without sharing publicly. At the conclusion of the project, data was removed from the public google sheet unless participants explicitly asked to keep it online. Similarly, participants could opt-in to have their data de-identified and aggregated as part of a scientific manuscript. The manuscript was circulated prior to submission such that all participants could see how their data were represented and give feedback.

Phase Three: Semi-Structured Interviews

At the culmination of the data collection period, semi-structured interviews were conducted with all finishing participants (n=18), excluding the authors and non-finishing participants. The primary goal of the interviews was to better understand participants' risk and benefit evaluation, what factors they considered important for ethical review in PLR and what elements would be most useful to them in future PLR. For the complete list of interview questions see **Supplemental Table 1**. Interviews took place over private webcast or phone and were recorded and transcribed verbatim. Participants were

introduced to the purpose of the interview and were asked for permission to audio record the conversation. The interview protocol was developed by CN, GW and AG, and AG conducted all interviews. As is common with qualitative methods, participants were encouraged to speak freely and not prohibited from sharing additional anecdotes about their experience with the project.

Research Design and Analysis

A case study methodology was chosen to examine the ethical review process of this PLR. The case study method is a form of empirical inquiry that can be used to study real-life phenomena (e.g., decisions, programs, implementation process, organizational change, etc.) at an individual or group level (38–40). The case study method allows for a holistic investigation of group behavior and processes and is useful in describing an intervention in real-life context, in this case the substitution of typical IRB procedures with a discussion-based ethical review process. Data collected specifically during dedicated discussions in phases one and three were analyzed using content analysis techniques commonly used in qualitative research (41). The notes taken during the initial discussion focusing on ethical research practices as well as transcripts containing responses to the semi-structured interview questions were read line-by-line and then coded to identify themes and patterns independently by CN and AG. Upon completion of independent review, the researchers discussed themes and patterns and any disagreements in observations about the data were discussed until agreement was reached. Lipid data analysis for individual projects that occurred within the phase two period is not a focus of this paper and is not reported here. **Figure 2: Timeline**

Results

Participant Demographics:

The final group consisted of 24 participants, six women and 18 men, ages 22-70 years (median 36 years, standard deviation 12 years). Twenty-one out of 24 (88%) of participants completed the project.

Participants lived in six countries: The United States, The Netherlands, Denmark, England, Ireland and Austria; and were of white European, Middle Eastern, or Indian descent. Sixty-one percent of interviewed participants had no formal research experience, 23% had professional (e.g., Master's Degree or higher in a scientific field) training, but were not career researchers, and 14% were actively pursuing a research career.

Phase One.

A total of 11 participants contributed to the initial discussion about ethical dimensions of the project. See **Tables 1 and 2** for brainstormed risks & risk mitigation strategies and benefits, respectively. **(Place Table 1 here).**

Phase Two.

Documentation and results of this phase have been submitted separately for publication (42).

Participant Hypotheses

Topics of investigation included daily rhythms in lipids, cholesterol fluctuation across the menstrual cycle, and the effects of switching to a plant-based diet on within-a-day and across-days variability of cholesterol and triglycerides.

Reflections on Ethical Dimensions: Risks and Benefits of Participation

Risks regarding data management, including sharing of their personal health data, and privacy expectations dominated participant responses**.** Even participants who were willing to share their data in this project expressed that privacy was a main concern that would need to be addressed as PLR expanded. No participant proposed that the project posed a risk to their physical well-being. Although the risk of infection from finger prick device and risk of pain from testing was raised as an hypothetical concern, it was rejected by all participants as negligible.

Using Transparency to Mitigate Risk in Participant-Led Research

When talking about how to reduce risks, participants referred frequently to "transparency" regarding the nature of the sponsorship for the project; how data are stored, aggregated and shared; and data ownership. Maintaining transparency via frequent communication thus became a key principle that helped build trust between participants and participant-organizers. Communication occurred through several formats, including group webinars, one-on-one meetings with a participant-organizer, Slack chat window, and written/video material.

Phase Three.

Group Communication to Enable Ongoing Ethical Reflection

During the semi-structured interviews, participants were asked about their preferences for receiving study information. As noted, several methods were used to share information and promote discussion, in order to ensure that all participants engaged in reflection on risks and benefits of participation. Direct one-on-one communications with the participant-organizers was preferred by the majority (57%) of participants, as evidenced by the following comments: "I learned a ton of background [in one-on-one meetings]," (P07) and, "I really valued getting to ask direct questions." (P11). These one-on-one meetings incorporated discussion of potential risks and benefits into the construction of the individual research protocols, which participants said helped put the project in context. For example, P17 said: "The conversation was really good because I was more engaged with the idea of the experiment… Planning an experiment was deep work that was hard to do by myself and another person to bounce ideas off of was valuable. Instead of feeling like I just wanted to do an experiment and turn something in, I felt that my question was very interesting and I'm doing something new [sic]. It felt transparent and comfortable."

Others (35%) engaged most during the webinars due to a preference for listening to a group's conversation, stating: "Having a group chat let me see other types of questions people had, I think it helped me get an understanding of the process [of the study]" (P16), and "Because of the type of learner I am, the webinar was more helpful because I could listen and follow along" (P09). The practice of thinking alongside other participants appeared to help some to compare and contrast their assumptions with others, thereby reflecting more critically on the PLR process. For the remaining 8%, webinar recordings and written material were an absolute necessity. One participant (P01) opted to watch recorded webinars and post comments for the group, saying that "I was very busy with working and caring [for a relative], but the webinars were the most informative, along with our written correspondence." Most participants moved fluidly between different types of communication; and discussion of risks and benefits naturally came up in conversation as a part of experimental planning sessions. All participants reported that ethical reflection was an important component of the project.

Factors Influencing Informed Consent.

Additionally, several participants mentioned that familiarity with the other members of the group contributed to their positive assessment of risks in relation to benefits. One participant (P05) said: "It gave me comfort walking into a study knowing that people that I knew were participating as well. It gave me comfort in what I was doing was useful, because I trust these people… If you were to take any sort of subject or any test and say, "X, Y and Z are all involved in this, would you consider joining?" The answer is that I'm probably biased towards joining because they are part of it. I know those people, and I know that they are very rational and calculated thinkers…"

While this interaction appears strongly positive, it also sets the stage for the possibility of peer-pressure or coercion in PLR. That being said, almost all of our cohort said that they would have felt comfortable halting their participation at any time. Two individuals reported "self-pressure" during their experiments, reflecting: "It's not in any way the kind of pressure that has been put on by the group, but

it is more responsibilities I have taken on for myself." (P11) or "It was my own pressure. I said I would do it." (P08). One participant (P03), brought up that it can be very challenging to avoid the possibility of coercion, thereby giving inherently low-risk PLR an advantage: "One can say 'yes, it's ok, I chose to do this [experiment]', but that might be irrelevant. There is a history of people like physicians getting patients to make choices against their own interests…" Although this is a highly self-motivated cohort, there is no doubt that peer pressure could play a role in participants taking experimentation further than if they were on their own. For this reason, PLR that minimizes potential risk of harm (for example, collection of wearable data) may be most appropriate while standards for PLR governance are developed.

Benefits of Participation - Participant Learning

The key benefit expressed by participants was the assistance they received from one another in forming and interrogating their own research questions. Even individuals well-versed in data analysis sometimes struggled with defining precise experimental questions, and individuals with a background in medicine or biology were not often familiar with statistical analysis. A common outcome was that once data were plotted, with the aid of another participant, a discussion between the two yielded the most valuable insights of the project. Participants even expressed pride in their experimental outcomes, one saying "I was going around telling people that I collected 24-hour cholesterol readings, which hadn't been published before. And now I've done it… I feel like a pioneer!" (P17). In answer to a question about what would aid them in future personal experiments, participants mentioned a number of features of the Blood Testers PLR. These included help with forming research questions and protocols, statistical analysis, and data visualization. A bonus for this PLR was the creation of two short and accessible educational videos developed to explain physiological functions and patterns in the measured lipid outputs (39,40). Finally, all participants expressed interest in joining future PLR. See **Table 2** for a complete list of participant-generated benefits. **(Place Table 2 here).**

Prospective Consent and Governance Principles for PLR

Nine themes emerged from discussions and interviews relating to informed consent in and governance of PLR. As this PLR was driven by people with different backgrounds asking personal questions, we found that ethical reflection needed to be ongoing and tailored to the individual. For this reason, prospective governance principles were drafted rather than codified rules. Many of the themes were expressed over the course of our PLR as an ongoing informed consent. The process, fostered via frequent communication, helped to reinforce trust among participants and organizers (43,44).

1. **Transparency**: All relevant information about the project should be actively shared among participants and participant-organizers, including the source of research funding, equipment selection, data management protocols, risks and benefits, and conflicts of interest.

2. **Access to Expertise**: PLR requires access to experts (e.g., in experimental design, data analysis, research ethics) so that participants can rigorously carry out single-subject experiments (45).

3. **Data Access & Control:** The participant has the right and ability to manage their own data, and has the final say in what they collect about themselves.

4. **Right to Withdraw:** Participants have a right to reduce or withdraw their participation at any time.

5. **Relevance**: PLR addresses questions of relevance to the participants.

6. **Beneficence:** The participant actively reflects on the balance of benefits and risks of participation and freely choose whether to participate.

7. **Responsibility:** PLR requires that the participant actively consider the potential benefits and harms of the project to both themselves and others. The responsibility to stay informed is an ongoing process, not a one-time decision.

8. **Flexibility:** Ethical reflection in PLR should be tailored to individual needs and to the specific context, rather than be handled with "one size fits all" rules. The needs of an individual are dynamic, and a lack of rigidity can reinforce trust between participants and organizers (46,47).

9. **Inclusivity:** If a prospective participant is willing and able to uphold these principles, they are welcome to participate.

Discussion

In this PLR, a global cohort of self-trackers collaboratively identified risks, risk mitigation strategies and benefits of participation in a study of blood lipids. Participants and participant-organizers mainly identified risks associated with data aggregation and identifiability and proposed individual data management, ownership and control as risk mitigation strategies. Participant benefits centered on personal learning, and access to data and diverse experimental expertise. Prospective principles were created to capture essential ethical components of the project. These principles may aid the development of governance and informed consent practices in future PLR, but leave an important question: how can PLR grow as a rigorous and ethical research practice before official governance standards are established? Further acknowledgement of the differences between PLR and traditional research, flexibility in addressing 'unknown unknowns' and commitment to crafting examples of low-risk PLR may be useful next steps.

All participants expressed interest in joining future PLR, yet we lack formal guidelines to inform ethical review for PLR not bound by the federal regulations protecting human research participants. For instance, in the United States, these regulations apply specifically to research funded by the Department of Health and Human Services (35). This means that PLR organizers not bound by this mandate must decide whether or not to obtain review by an IRB or REB. It is important to note that the IRBs and RECs were designed for research led by professional researchers affiliated with organizations that receive government funding for biomedical and behavioral research studies involving human participants. This traditional paradigm of ethical review is obviously very different from a collaboratively-led international cohort of individuals, who may lack academic research training or exposure to research ethics, and professional researchers (28,48). As such, IRB/REB involvement may promote decisions specific to data ownership, data management and informed consent that directly conflict with the aims of research that

is explicitly *participant-led*. For instance, IRBs often require that a Principal Investigator take complete responsibility for and ownership of study-generated data, which may oppose participants' expectation to own the data they collect about themselves (49). Together, the challenges of systematizing ethical review, and the lack of clear precedents for divisions of leadership and ownership have led many to conclude that current ethical review guidelines must be adapted or substituted to suit participant-led initiatives (12).

Recognizing that PLR is a rapidly evolving form of investigation, integrating ethical review requires a commitment to addressing challenges in the unknown future. In projects directed by a group of researchers from within an academic institution, study risks and benefits are conveyed to participants by researchers. By contrast, in PLR, participants and participant-organizers seek to uncover project risks and benefits collaboratively. The very concept of risk and benefit is altered when experimental questions are determined by participants rather than by a Principal Investigator (50). For example, PLR participants may alter their course of investigation at any point (see principle 8). This allows the risk to benefit calculation made by the participant at the study outset to be dynamically adjusted during the study period (e.g., if the individual's experimental question evolves in a way that changes their risk and benefit evaluation). However, this also means that it is not possible to anticipate every experiment to be conducted prior to the start of the study, to determine whether or not the participant understands the risks and benefits of those experiments, and to ensure that the participant consents to carry them out. As noted in our proposed principles, this permission to dynamically reevaluate risks and benefits is central to participant control.

Although formal ethical guidelines for non-governmentally funded PLR are yet to be put in place, this does not exempt PLR from ethical review in principle. This ethical review in PLR requires a common stake among all participants. This common stake means that all who take part in the project share an investment in the conduct and outcomes of the research. This stake even extends to those in traditional

research conditions, in which greater attention to the participant experience stands to benefit not just the participant, but the ultimate quality of the research in terms of improved data annotation, participant retention (8,42). While best practices continue to be developed for specific use in higher-risk projects, low-risk, observational PLR may not need to wait for governmental guidelines to formalize its methods and contribute its findings to the scientific literature. Our experience suggests that encouraging ethical reflection among a small group while asking research questions that can be answered using low-risk procedures can safely generate participant benefits.

Limitations

As is often the case with new research methodologies, our learning is biased by our narrow context, intentional minimal-risk design and unique community of self-trackers. Larger, more diverse cohorts, and other distinctive communities may find discussion based ethical-review less applicable to their context. Additionally, this project and writing of this manuscript took place prior to and during the adoption of changing ethical regulations across national borders (i.e., the General Data Protection Regulation or GDPR). We chose to limit our introduction largely to ethical regulatory frameworks in the United States, acknowledging that the UK and EU regulations are relatively similar in content and implementation practices.

Conclusions

PLR is an emerging form of investigation in which responsibility is shared more equally between participants and participant-organizers. The PLR described in this paper is novel in two ways. First, it is the first PLR, to the authors' knowledge, in which all participants formed unique research questions to explore and collected and managed all data individually. Second, the cohort engaged in ethical reflection before, during and upon conclusion of the project and used documentation of these discussions to create guiding principles for future PLR. This PLR retained 88% participation through its conclusion and

100% satisfaction among finishing participants. We conclude that low-risk PLR involving single-subject study in a small group may be conducted responsibly and ethically by incorporating an ethical reflection process at onset and throughout the study duration. It is our hope that the principles generated during this PLR may encourage discussion and development of ethical PLR practices.

References:

1. Vayena E, Brownsword R, Edwards SJ, Greshake B, Kahn JP, Ladher N, et al. Research led by participants: a new social contract for a new kind of research. J Med Ethics. 2016;42(4):216–9.

2. Mikesell L, Bromley E, Khodyakov D. Ethical community-engaged research: a literature review. Am J Public Health. 2013 Dec;103(12):e7–14.

3. Bonney R, Shirk JL, Phillips TB, Wiggins A, Ballard HL, Miller-Rushing AJ, et al. Citizen science: Next steps for citizen science. Science. 2014;343(6178):1436–7.

4. Swan M. Crowdsourced Health Research Studies: An Important Emerging Complement to Clinical Trials in the Public Health Research Ecosystem. J Med Internet Res [Internet]. 2012 Mar 7;14(2). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3376509/

5. Pettibone L, Vohland K, Ziegler D. Understanding the (inter)disciplinary and institutional diversity of citizen science: A survey of current practice in Germany and Austria. PLoS ONE [Internet]. 2017 Jun 27;12(6). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5487260/

6. Nebeker C, López-Arenas A. Building Research Integrity and Capacity (BRIC): An Educational Initiative to Increase Research Literacy among Community Health Workers and Promotores. J Microbiol Biol Educ. 2016 Mar 1;17(1):41–5.

7. The Rise of the New Bio-Citizen [Internet]. Wilson Center. 2018 [cited 2018 Jun 20]. Available from: https://www.wilsoncenter.org/article/the-rise-the-new-bio-citizen

8. Cox SM, McDonald M. Ethics is for human subjects too: participant perspectives on responsibility in health research. Soc Sci Med 1982. 2013 Dec;98:224–31.

9. Banks S, Armstrong A, Carter K, Graham H, Hayward P, Henry A, et al. Everyday ethics in community-based participatory research. Vol. 8, Contemporary Social Science. 2013. p. 263–77.

10. Fleurence R, Whicher D, Dunham K, Gerson J, Newhouse R, Luce B. The Patient-centered Outcomes Research Institute's Role in Advancing Methods for Patient-centered Outcomes Research. Med Care. 2015 Jan;53(1):2–8.

11. Jones FM, Allen C, Arteta C, Arthur J, Black C, Emmerson LM, et al. Time-lapse imagery and volunteer classifications from the Zooniverse Penguin Watch project. Sci Data. 2018 Jun 26;5:180124.

12. Swanson A, Kosmala M, Lintott C, Packer C. A generalized approach for producing, quantifying, and validating citizen science data from wildlife images. Conserv Biol J Soc Conserv Biol. 2016;30(3):520–31.

13. Citizen Science Alliance [Internet]. Available from: https://www.citizensciencealliance.org/

14. Bonney R, Cooper C, Ballard H. The Theory and Practice of Citizen Science: Launching a New Journal. Citiz Sci Theory Pract. 2016 May;1(1):1–1.

15. Follett R, Strezov V. An Analysis of Citizen Science Based Research: Usage and Publication Patterns. PloS One. 2015;10(11):e0143687.

16. Gura T. Citizen science: amateur experts. Nature. 2013;496(7444):259–61.

17. Cohn JP. Citizen Science: Can Volunteers Do Real Research? BioScience. 2008;58(3):192–7.

18. Hand E. Citizen science: People power. Nature. 2010;466(7307):685–7.

19. Vayena E, Tasioulas J. Adapting Standards: Ethical Oversight of Participant-Led Health Research. PLOS Med. 2013 Mar 12;10(3):e1001402.

20. Wolf G, Ramirez E. Quantified Self/Public Health Symposium. 2014;

21. Wicks P, Vaughan TE, Massagli MP, Heywood J. Accelerated clinical discovery using self-reported patient data collected online and a patient-matching algorithm. Nat Biotechnol. 2011 May 24;29(5):411–4.

22. Dana Lewis. Setting Expectations for Successful Artificial Pancreas/Hybrid Closed Loop/Automated Insulin Delivery Adoption. J Diabetes Sci Technol. 2018;12(2):533–4.

23. Godlee F. Towards the patient revolution. BMJ. 2014 Jan 29;348:g1209.

24. Doerr M, Maguire Truong A, Bot BM, Wilbanks J, Suver C, Mangravite LM. Formative Evaluation of Participant Experience With Mobile eConsent in the App-Mediated Parkinson mPower Study: A Mixed Methods Study. JMIR MHealth UHealth. 2017 Feb 16;5(2):e14.

25. Grady C, Cummings SR, Rowbotham MC, McConnell M V., Ashley EA, Kang G. Informed Consent. Drazen JM, Harrington DP, McMurray JJV, Ware JH, Woodcock J, editors. N Engl J Med. 2017 Mar 2;376(9):856–67.

26. Rothstein MA, Wilbanks JT, Brothers KB. Citizen Science on Your Smartphone: An ELSI Research Agenda. J Law Med Ethics. 2015;43(4):897–903.

27. Sugarman J. Examining Provisions Related to Consent in the Revised Common Rule. Am J Bioeth. 2017;17(7):22–6.

28. Bloss C, Nebeker C, Bietz M, Bae D, Bigby B, Devereaux M, et al. Reimagining Human Research Protections for 21st Century Science. J Med Internet Res. 2016 Dec 22;18(12):e329.

29. Thorogood A, Bobe J, Prainsack B, Middleton A, Scott E, Nelson S, et al. APPLaUD: access for patients and participants to individual level uninterpreted genomic data. Hum Genomics. 2018 Feb 17;12(1):7.

30. Weissman JS, Campbell EG, Cohen IG, Lynch HF, Largent EA, Gupta A, et al. IRB Oversight of Patient-Centered Outcomes Research: A National Survey of IRB Chairpersons , IRB Oversight of Patient-Centered Outcomes Research: A National Survey of IRB Chairpersons. J Empir Res Hum Res Ethics. 2018 Jun 14;1556264618779785.

31. Vayena E, Tasioulas J. The ethics of participant-led biomedical research. Nat Biotechnol. 2013 Sep 1;31(9):786–7.

32. 45 CFR 46 Protection of Human Subjects. U.S. Department of Health and Human Services 2009.

33. Bouesseau M-C, Coleman C, Kass N, Laothavorn J, Saxena A, Vanderpoel S. Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants. World Health Organ [Internet]. 2011; Available from: http://apps.who.int/iris/bitstream/handle/10665/44783/9789241502948_eng.pdf;jsessionid=5E488F141667C3CEA6FED5BE49301ED4?sequence=1

34. Bouesseau M-C, Coleman C, Kass N, Laothavorn J, Saxena A, Vanderpoel S. Standards and Operational Guidance for Ethics Review of Health-Related Research with Human Participants. World Health Organ. 2011;

35. Department of Health, Education, and Welfare, National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Belmont Report. Ethical principles and guidelines for the protection of human subjects of research. J Am Coll Dent. 2014;81(3):4–13.

36. An Introduction to Lipids on Vimeo [Internet]. [cited 2018 Dec 10]. Available from: https://vimeo.com/237116970

37. Biological Rhythms on Vimeo [Internet]. [cited 2018 Dec 10]. Available from: https://vimeo.com/239682398

38. Aberdeen T. Yin, R. K. (2009). Case study research: Design and methods (4th Ed.). Thousand Oaks, CA: Sage. Can J Action Res. 2013;14(1):69–71.

39. Creswell JW. Research Design: Qualitative, Quantitative, and Mixed Methods Approaches. SAGE Publications; 2009. 297 p.

40. Gerring J. What Is a Case Study and What Is It Good for? Am Polit Sci Rev. 2004;98(2):341–54.

41. Patton MQ. Qualitative research & evaluation methods : integrating theory and practice. 806 p.

42. Azure Grant, Gary Wolf. Cholesterol and Triglycerides Traverse Risk Categories on Short Timescales: A Participant-Led Study. PLOS Med. 2018 Jul 20;

43. Kerasidou A. Trust me, I'm a researcher!: The role of trust in biomedical research. Med Health Care Philos. 2017 Mar;20(1):43–50.

44. Guillemin M, Gillam L, Barnard E, Stewart P, Walker H, Rosenthal D. "We're checking them out": Indigenous and non-Indigenous research participants' accounts of deciding to be involved in research. Int J Equity Health. 2016 Jan 16;15:8.

45. Choe EK, Lee NB, Lee B, Pratt W, Kientz JA. Understanding quantified-selfers' practices in collecting and exploring personal data. In: Proceedings of the 32nd annual ACM conference on Human factors in computing systems. 2014. p. 1143–52.

46. McDonald M, Townsend A, Cox SM, Paterson ND, Lafrenière D. Trust in Health Research Relationships: Accounts of Human Subjects. J Empir Res Hum Res Ethics. 2008 Dec 1;3(4):35–47.

47. Guillemin M, Barnard E, Allen A, Stewart P, Walker H, Rosenthal D, et al. Do Research Participants Trust Researchers or Their Institution? J Empir Res Hum Res Ethics. 2018 Jul 1;13(3):285–94.

48. Nebeker C, Harlow J, Espinoza Giacinto R, Orozco-Linares R, Bloss CS, Weibel N. Ethical and regulatory challenges of research using pervasive sensing and other emerging technologies: IRB perspectives. AJOB Empir Bioeth. 2017 Oct 2;8(4):266–76.

49. Gliklich RE, Dreyer NA, Leavy MB. Principles of Registry Ethics, Data Ownership, and Privacy [Internet]. Agency for Healthcare Research and Quality (US); 2014 [cited 2018 Jun 4]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK208620/

50. Townsend A, Taylor K, Cox S. Conceptions of Risk Regarding a Chronic Illness Survey: Perspectives of Participants, Researchers, and Ethics Review Board Members. IRB. 2014 Oct;36(5):13–20.

Table 1. Participant-Generated Risks and Risk Mitigation Strategies

Risk	Risk Mitigation
Engagement with ethical issues of participation was perceived as difficult, which could limit engagement.	Our challenge is to test if collaborative discussion of risks and benefits will be more enjoyable and engaging.
Participants could learn something unpleasant (e.g., results that require medical attention).	Participants were made aware of this risk in the initial project discussion, before taking any lipid tests.
Frequent testing can cause some people anxiety.	After some discussion, and polling of participants, we agreed that this risk is minimal in our group.
Participants could be disappointed by learning the actual bounds of uncertainty of the data, even if these bounds are comparable to that of professional tests.	This topic was discussed at length in the beginning of the project and was also considered a benefit. Consumers often do not realize the extent to which data from at-home testing can be uncertain.
Reputation risk to participant-organizers if ethical concerns are not well understood.	Participant-organizers convened all participants to engage in discussion of risks and benefits.
Reputation risk to participant-organizers if training on how to use the test system is not effective.	Participants were thoroughly trained, and training materials and expertise were made available for the entire duration of the project.
Participants could feel peer-pressure to carry out an experiment.	Participants were encouraged to only carry out testing that was personally interesting and productive.
Reputation risk to all project participants if data-quality is questionable.	Participants were incentivized to collect good data because they conducted personally-relevant experiments.
Conflict of interest concern by participants regarding funding.	Goals and funding were clearly stated to all before joining the project, and funders did not view the manuscript or advise on project content.
Demands on Participants' time.	There was no minimal required time commitment Our goal was to be as supportive as possible- and to understand reasons for halted projects as they arrived.
Minor pain and bruising.	Participants were trained with techniques to minimize discomfort. Participants chose how frequently to sample and could stop at any point.
Almost negligible risk of infection.	Participants were given sterile supplies and trained to use equipment safely.
Risk of being penalized in the future based on data being read by others and associated with a sanction by insurance companies.	All participants could keep their data private and offline. Data was removed from group-spreadsheet post-project unless participant expressed interest in keeping the data public.
Risk that Quantified Self as a movement puts itself at risk by stumbling across legal and/or social liabilities.	Transparency was maintained about risks and benefits, and multiple opportunities were provided for participants to reflect.

Table 2. Participant-Generated Benefits of Participation

Benefit
Sharing the method of small group, collaborative self-discovery. Uncovering challenges therein is necessary for revising the process of participant-led research.
Proposing a new method for more engaging ethical review in participant-led research.
Greater community ability and motivation to validate new self-tracking tools before use.
Educating ourselves, to the best of our ability, about the current literature in cholesterol and triglyceride research.
Learning the extent to which individuals' lipids vary throughout the day as measured.
Learning the extent to which a single measurement at the doctor's office is representative of one's "regular" lipid levels.
Increased ability to engage with one's physician in a conversation about the health-relevance of one's cholesterol and triglyceride levels.
Increased ability to conduct an experiment, and empowerment to interrogate future personal questions using scientific tools.
Access to costly blood-testing equipment, and the data generated by it.
Encouragement from respected fellow participants.
Access to advice from individuals experienced in experimental design.
Access to help with data analysis.
Opportunity to share learnings at a Quantified Self symposium or conference.

Figure Legends

Figure 1: Phase II Recruitment Flowchart

Recruitment Flowchart for the Quantified Self "Blood Testers" Participant-Led Research project. Four employees of Quantified Self Labs and thirty-five prospective participants met at the Quantified Self 2017 Global Conference to propose and discuss the project. Emails were collected and follow-up surveys were sent to gauge interest. Responders confirmed their interest in participation and their goal for the project with an organizer from QS Labs. These individuals received a equipment, and subsequently attended online discussions to brainstorm risks and benefits of participation. In total, twenty-one participants completed a project.

Figure 2: Timeline of Ethical Reflection in the Blood Testers PLR.

Phase Zero: Participant-organizers prepared for the project by gathering supplies and piloting protocols. Phase One: A research ethicist was recruited as a participant to lead a webinar/brainstorming session on research ethics, focusing on informed consent. Documentation of this discussion was shared in the common project google drive. Recruitment was held at a Quantified Self Global Conference, followed by an online summary of potential risks and benefits of participation. A large group webinar then shared the material of the first ethical reflection meetings with the full group of participants. This phase overlaps slightly with Phase 2, as some participants joined later than others. Phase 2: Participants kept ongoing communications with one another and participant-organizers while conducting personal experiments and data analysis. Experiment planning meetings/check-ins often included "updates" to assessment of risks and benefits. Phase 3: Following project completion, participants were interviewed about their experience in the project. Projects were shared at the QS Public Health Symposium.

Supplemental Tables:

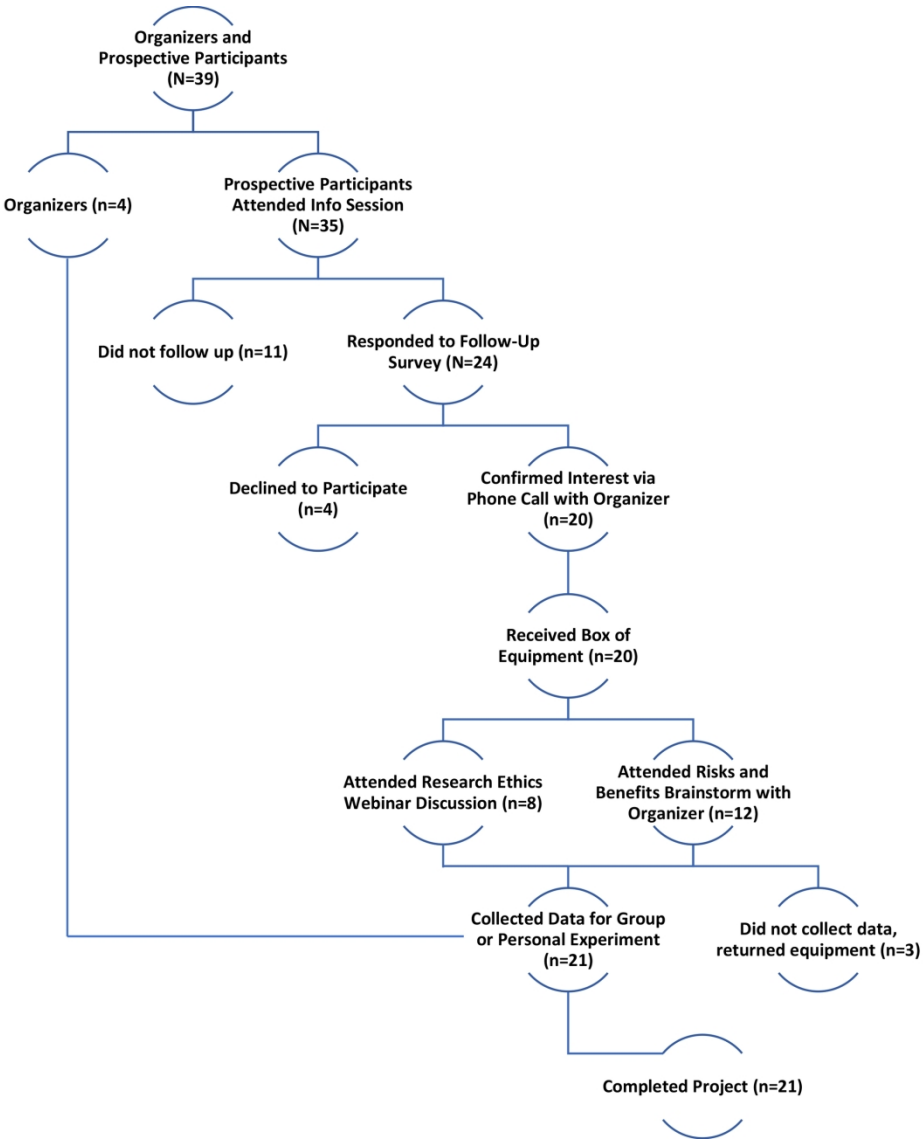
Supplemental Table 1: Semi-Structured Interview Questions

Authorship Contributor Statement:

AG led the writing and editing of the manuscript, led the project which is the case under analysis in this manuscript, conducted all interviews, and carried out qualitative analysis of the interviews with CN.

CN provided guidance and recommendations on the ethical review process of the project and contributed to the writing and editing of the manuscript and carried out qualitative analysis of the interviews with AG.

GW contributed extensively to conception and the organization of the project, and to writing and editing of the manuscript.



Recruitment Flowchart for the Quantified Self "Blood Testers" Participant-Led Research project. Four employees of Quantified Self Labs and thirty-five prospective participants met at the Quantified Self 2017 Global Conference to propose and discuss the project. Emails were collected and follow-up surveys were sent to gauge interest. Responders confirmed their interest in participation and their goal for the project with an organizer from QS Labs. These individuals received a equipment, and subsequently attended online discussions to brainstorm risks and benefits of participation. In total, twenty-one participants completed a project.

190x215mm (300 x 300 DPI)

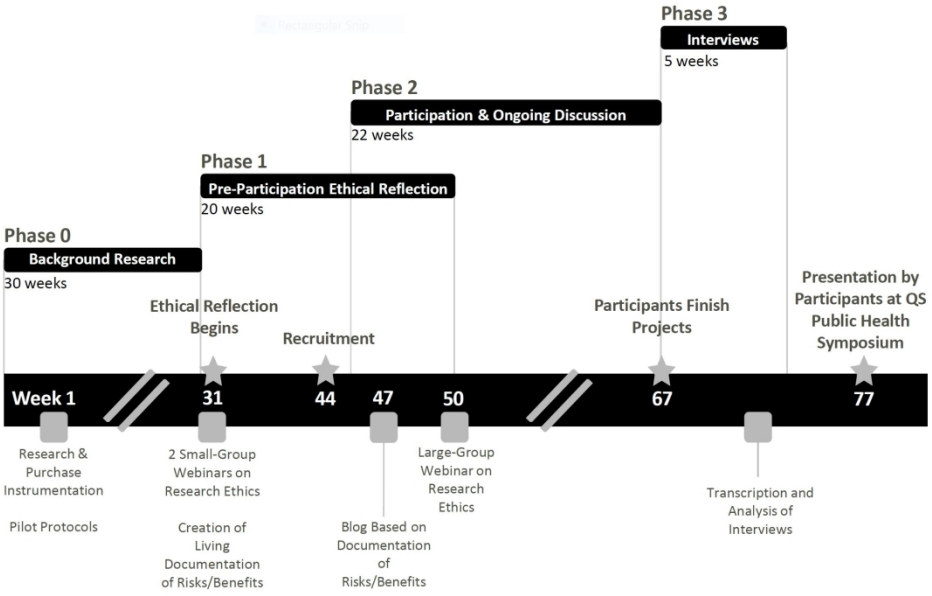


Figure 2: Timeline of Ethical Reflection in the Blood Testers PLR.
Phase Zero: Participant-organizers prepared for the project by gathering supplies and piloting protocols. Phase One: A research ethicist was recruited as a participant to lead a webinar/brainstorming session on research ethics, focusing on informed consent. Documentation of this discussion was shared in the common project google drive. Recruitment was held at a Quantified Self Global Conference, followed by an online summary of potential risks and benefits of participation. A large group webinar then shared the material of the first ethical reflection meetings with the full group of participants. This phase overlaps slightly with Phase 2, as some participants joined later than others. Phase 2: Participants kept ongoing communications with one another and participant-organizers while conducting personal experiments and data analysis. Experiment planning meetings/check-ins often included "updates" to assessment of risks and benefits. Phase 3: Following project completion, participants were interviewed about their experience in the project. Projects were shared at the QS Public Health Symposium.

258x160mm (240 x 240 DPI)

Supplementary Table 1. Semi-Structured Interview Questions

Question Number	Question Text
1	How long have you been doing self-tracking experiments?
2	How did you become involved with the Blood Testers project?
3	Do you have any formal or informal research training?
4	Have you ever been part of a participant-led research project?
5	Whose responsibility is it to determine that a participant-led research project is conducted ethically?
6	What are the factors which should be considered for participant-led research to be conducted ethically?
7	Do you feel this project put you at any risk? Why or why not?
8	Was there anything in the project that surprised you, or that you wished you had known in advance?
9	Would your assessment of the project's risk change if you were with a group of people that you didn't know?
10	Did you feel that it was important to discuss the benefits and risks in the Blood Testers project?
11	I am going to ask you to rank three different things that we did in the project, from most useful to least useful, in terms of informing you about risks and benefits. Those things are, written materials about the project, a webinar where we met and talked about ethical ramifications in the project. The third one is one-on-one communication.
12	Would you have felt comfortable halting your participation at any time?
13	In the future, are there any kinds of research training materials that would be useful to you for personal or participatory research projects?
14	Would you be interested in joining another round of participant-led research in the future?
15	Given that in this project participants can halt their participation at any time, do you think there is any way for a participant to be coerced into participation or continuation?
16	Do you rate yourself completely confident, somewhat confident, or not at all confident with your understanding of risks and benefits of participation?

Standards for Reporting Qualitative Research (SRQR)*

http://www.equator-network.org/reporting-guidelines/srqr/

	Page/line no(s).
Title and abstract	
Title - Concise description of the nature and topic of the study Identifying the study as qualitative or indicating the approach (e.g., ethnography, grounded theory) or data collection methods (e.g., interview, focus group) is recommended	1
Abstract - Summary of key elements of the study using the abstract format of the intended publication; typically includes background, purpose, methods, results, and conclusions	3
Introduction	
Problem formulation - Description and significance of the problem/phenomenon studied; review of relevant theory and empirical work; problem statement	4-6
Purpose or research question - Purpose of the study and specific objectives or questions	3,5
Methods	
Qualitative approach and research paradigm - Qualitative approach (e.g., ethnography, grounded theory, case study, phenomenology, narrative research) and guiding theory if appropriate; identifying the research paradigm (e.g., postpositivist, constructivist/ interpretivist) is also recommended; rationale**	5,8-11
Researcher characteristics and reflexivity - Researchers' characteristics that may influence the research, including personal attributes, qualifications/experience, relationship with participants, assumptions, and/or presuppositions; potential or actual interaction between researchers' characteristics and the research questions, approach, methods, results, and/or transferability	9
Context - Setting/site and salient contextual factors; rationale**	8-11
Sampling strategy - How and why research participants, documents, or events were selected; criteria for deciding when no further sampling was necessary (e.g., sampling saturation); rationale**	8-12
Ethical issues pertaining to human subjects - Documentation of approval by an appropriate ethics review board and participant consent, or explanation for lack thereof; other confidentiality and data security issues	9-10
Data collection methods - Types of data collected; details of data collection procedures including (as appropriate) start and stop dates of data collection and analysis, iterative process, triangulation of sources/methods, and modification of procedures in response to evolving study findings; rationale**	8-10

Data collection instruments and technologies - Description of instruments (e.g., interview guides, questionnaires) and devices (e.g., audio recorders) used for data collection; if/how the instrument(s) changed over the course of the study	8-10
Units of study - Number and relevant characteristics of participants, documents, or events included in the study; level of participation (could be reported in results)	12
Data processing - Methods for processing data prior to and during analysis, including transcription, data entry, data management and security, verification of data integrity, data coding, and anonymization/de-identification of excerpts	10-12
Data analysis - Process by which inferences, themes, etc., were identified and developed, including the researchers involved in data analysis; usually references a specific paradigm or approach; rationale**	11-12
Techniques to enhance trustworthiness - Techniques to enhance trustworthiness and credibility of data analysis (e.g., member checking, audit trail, triangulation); rationale**	11-12

Results/findings

Synthesis and interpretation - Main findings (e.g., interpretations, inferences, and themes); might include development of a theory or model, or integration with prior research or theory	12-17
Links to empirical data - Evidence (e.g., quotes, field notes, text excerpts, photographs) to substantiate analytic findings	12-17

Discussion

Integration with prior work, implications, transferability, and contribution(s) to the field - Short summary of main findings; explanation of how findings and conclusions connect to, support, elaborate on, or challenge conclusions of earlier scholarship; discussion of scope of application/generalizability; identification of unique contribution(s) to scholarship in a discipline or field	17-20
Limitations - Trustworthiness and limitations of findings	20

Other

Conflicts of interest - Potential sources of influence or perceived influence on study conduct and conclusions; how these were managed	1
Funding - Sources of funding and other support; role of funders in data collection, interpretation, and reporting	1

*The authors created the SRQR by searching the literature to identify guidelines, reporting standards, and critical appraisal criteria for qualitative research; reviewing the reference lists of retrieved sources; and contacting experts to gain feedback. The SRQR aims to improve the transparency of all aspects of qualitative research by providing clear standards for reporting qualitative research.

**The rationale should briefly discuss the justification for choosing that theory, approach, method, or technique rather than other options available, the assumptions and limitations implicit in those choices, and how those choices influence study conclusions and transferability. As appropriate, the rationale for several items might be discussed together.

Reference:

O'Brien BC, Harris IB, Beckman TJ, Reed DA, Cook DA. **Standards for reporting qualitative research: a synthesis of recommendations.** *Academic Medicine*, Vol. 89, No. 9 / Sept 2014
DOI: 10.1097/ACM.0000000000000388