Patient Participation and Empowerment in Precision Medicine

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Abstract
Precision medicine functions by grouping or stratifying patients along genetic, molecular, and other related '-omics' factors. This stratification relies on large, growing databases of patient-volunteered information. Both private companies and government bodies incentivize patients to volunteer this genetic data appealing to the creation of *patient partnerships* and *empowerment*. This paper aims to answer two questions: (1) what is the actual nature of the partnership created by participating in precision medicine? And (2) is this participation really that empowering to individual patients? I contend that firstly, the nature of this participation is merely *contributory*. Contributory participation, as it will be shown, requires little to no additional input or collaboration from patients after giving their biological data. With that in mind, I secondly contend that there are caveats to claims that patient participation in precision medicine is empowering. Empowerment here is hindered by the type of participation, the practical use or actionability of the data that patient participants receive, genetic literacy, the cost of precision drugs for patients that qualify, and bioethical issues of data autonomy.

Keywords: precision medicine; participatory research; empowerment; genetic testing; autonomy.

1. Introduction

Precision medicine (PM) or stratified medicine functions by grouping and sub-grouping patients based on genetic, molecular, and other '-omics' factors. In PM a patient gives their genetic material – usually samples of blood, saliva, or buccal swabs – to databases containing the genetic information of up to millions of other patients. The patient is then identified in some genetic group, and ideally, there then exists a gene-guided drug for the patient's illness. The mantra of PM is the 'right drug at the right time for the right patient,' echoed by health authorities like the US Food and Drug Administration (FDA).[1] PM's successes have been mostly in oncology, e.g., imatinib for chronic myelogenous leukemia and trastuzumab for breast cancer. However, more generally, and even within oncology, PM has fallen short of expectations (Hayes et al. 2013; Hey & Barsanti-Innes 2016). The success of PM as a revolutionary medical model is uncertain and remains promissory (Kuch et al. 2020). The millions of dollars spent on experimental precision drugs might be better used to save lives via preventative public health interventions (Tabery 2023). Either way, the continuing practice of PM and any of its future successes hinge on large, growing databases of publicly volunteered data. The more genetic data

[1] https://www.fda.gov/medical-devices/in-vitro-diagnostics/precision-medicine. Accessed Jan. 2024.

researchers have, the better they can identify, develop, and test gene-guided treatments – at least in theory. With that in mind, PM institutions incentivize the donation of this data.

Private direct-to-consumer (DTC) companies that engage in PM like '23andMe'[2] and government bodies like the US National Institutes of Health (NIH) 'All of Us' program – formed from the 2015 Precision Medicine Initiative – incentivize donation appealing to *empowerment*. Empowerment is one of the guiding principles of 'All of Us'[3] and is explicit in the marketing materials for private companies.[4] This empowerment is supposed to be partly due to the creation of patient partnerships where volunteers go beyond being mere patients. Francis Collins and Harold Varmus – former directors of the NIH and leads on the Precision Medicine Initiative – lauded PM in the *New England Journal of Medicine* in 2015 as even *pioneering* this sort of collaborative partnership (Collins & Varmus 2015). However, as some have rightly pointed out, the methods of PM are far from personal. A common synonym for PM one sees is 'personalized' medicine, though this is infelicitous. Personalized medicine looks at individuals holistically and stresses shared decision making; PM's methods hold no such commitments (Vegter 2018; El-Alti et al. 2019; Cesario et al. 2021; Valent et al. 2021). The primacy that PM places on diagnoses based on genetic biomarkers runs against non-reductionist person-centric medicine.[5] In other words, PM is lauded as collaborative and empowering, but given its methodology two questions naturally arise: (1) what is the actual nature of patient participation in PM, i.e., does this partnership really amount to collaboration? And (2) how is participating in PM empowering to individual patients, if at all? This paper aims to answer both questions.

Answering question (1) requires looking at the different functions and goals of public or patient participation in medicine and science. After briefly surveying work in philosophy, sociology, and ecology on taxonomizing participatory projects in section 2, I argue that – overwhelmingly – the type

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[2] Since 2013, '23andMe' does not offer medical advice due to a FDA missive. However, they still sell data to pharmaceutical companies and have invested millions in precision drug research (Van Dijck & Poell 2016).

[3] https://allofus.nih.gov/protecting-data-and-privacy/precision-medicine-initiative-privacy-and-trust-principles. Accessed July 2023.

[4] E.g., https://www.ancestry.com/corporate/community-impact & https://blog.23andme.com/articles/empower-the-people. Both accessed Nov. 2023.

[5] 'All of Us' also solicits information about lifestyle, diet, family history, etc. 'All of Us' is a PM institution, but not *only* a PM institution. The points here about empowerment and participation still stand.

of patient participation in PM is 'contributory,' not collaborative. In contributory participation, non-professionals produce or contribute data for professionals to use; no collaboration or sharing of goals necessarily occurs. I contend this fits cases of people signing up for 'All of Us' or buying a DTC testing kit. For researchers, the overarching goal of having the public involved is epistemic, i.e., increasing the amount of PM data. The goals of patients that contribute are heterogeneous, however, PM institutions explicitly appeal to empowerment as a goal for patients, therefore, it warrants examination. Section 3 thus aims to answer the empowerment question, i.e., question (2). By looking to definitions of empowerment given by the World Health Organization (WHO), we see that there are two broad senses of empowerment in medicine: empowerment as *knowing* and empowerment as *acting* or having the ability to act.[6] I argue that achieving either of these faces challenges due to genetic literacy, the practical use or actionability of genetic data, the astronomical cost of precision drugs, and the form of participation. Moreover, by looking at empowerment through the lens of bioethical principles like 'autonomy' and 'informed consent,' I argue there is an additional lack of empowerment when it comes to control over one's contributed genetic data. Section 4 then draws analogies to other participatory practices in medicine to show that PM is no pioneer of patient partnerships. Finally, I conclude in section 5 by highlighting implications of the analysis for patients, clinicians, and policymakers. These include what expectations we ought to have when engaging in PM and how to better include empowered stakeholders in PM research.

2. Participation in Science & Medicine

2.1. The Participatory Turn

In recent decades, the sciences have experienced – and to some degree have encouraged – a 'participatory turn' (Wynne 2007). While public involvement in the 'modern' scientific process has roots going back over a century, the recent rise coincides with social movements, advocacy, and lay scrutiny of science (Kimura & Kinchy 2016; Evans & Potochnik 2023). Historically, public or lay involvement has been common in environmental, ecological, and astronomy contexts.[7] In medicine this participatory turn coincides with the recognition of and aversion to paternalism, as well as the adoption of shared decision making and informed consent practices. Active participation in medicine

[6] This strategy is one that follows recent work on empowerment in medicine, e.g., Kapeller & Loosman (2023).

[7] These fields have active amateur communities, e.g., 'amateur astronomers' or 'herpers' – the amphibian/reptile equivalent of 'birdwatchers'. This involvement in science has been recently addressed e.g., Quinn (2021).

and medical research has also been spurred on by dissatisfaction with institutional medical practice. For example, in the 1990s, thalidomide was difficult to access for patients due to its nefarious history of teratogenic side effects. However, at the time there was some evidence that thalidomide could treat HIV-related 'wasting' syndrome. So, a group of activists acquired and monitored thalidomide use in the San Francisco Bay Area to some success (Sharpe et al. 1997).

Participation in medicine is also on the rise due to the 'datafication' of the individual through mobile-health tracking technology. 'Biohacking' that takes the form of individuals improving their 'datafied' metrics is common (Kuch et al. 2020). Medical institutions also encourage participation, and health journals and funding bodies often encourage public involvement (Harrison et al. 2019). Bodies like the Canadian Institute for Health Research (CIHR) have initiated programs on 'citizen engagement' described as the 'meaningful involvement of individual citizens in policy or program development.'[8] The 'All of Us' program at the NIH uses similar language,[9] and the NIH in general encourages individuals to seek out clinical trials to participate in.[10] Additionally, this rise in participation has not gone unnoticed by scholars.

2.2. Taxonomies of Participation

Scholarly address of this participatory turn varies. Different umbrella terms are common in describing research where the public is engaged, e.g., 'citizen science' (Kimura & Kinchy 2016), 'participatory research' (Dunlap et al. 2021), 'community science' (Kovaka 2021), and 'patient/public involvement or engagement' (Frith 2023) among others. Different disciplines and methodologies have different historical and conceptual relationships to these practices, so clean-cut terminological distinctions are elusive (Peters et al. 2021). For the sake of consistency and simplicity, moving forward I will just adopt 'participatory research' as any context where non-professionals play some role in the research process.

Because participatory research denotes a heterogeneous group of practices, taxonomies have been developed to help understand and guide these projects. One way to delineate different kinds of

[8] https://cihr-irsc.gc.ca/e/41592.html. Accessed July 2023.

[9] https://allofus.nih.gov/protecting-data-and-privacy/precision-medicine-initiative-privacy-and-trust-principles. Accessed July 2023.

[10] https://www.nih.gov/health-information/nih-clinical-research-trials-you. Accessed December 2023.

participatory projects is by the actual function or role the public plays in that project. Spearheaded by ecologists at the Cornell Ornithology Lab, Jennifer Shirk et al. (2012) provides a taxonomy that divides participatory research into five categories: contractual, contributory, collaborative, co-created, and collegial. *Contractual* research is when members of the public ask professional scientists to carry out a specific task. We might imagine a case of this in the medical context where a group of patients with a similar, unknown sickness reach out to researchers with a task or tasks in mind, e.g., diagnosis and treatment. Any specific research or data acquisition is designed by the professional researchers, but under the obligation of fulfilling the specific task or tasks requested by the patients. *Contributory* participatory research occurs when the public just contributes or volunteers data to a project initiated and executed by professional researchers. In the medical context, practices like soliciting patient-reported outcome measures (PROs/PROMs) after surgery to gauge the effectiveness of different procedures fit this mold. *Collaborative* participation occurs when the public actively defines or revises a project initiated by researchers or plays a role in the analysis and dissemination of results; something like community-based participatory research (CBPR) in urban and environmental health justice research fits here with the health context in mind. *Co-created* participatory research occurs when members of the public initiate or jointly initiate a specific project and are involved in most of the research process. The case above of the thalidomide and HIV-related wasting trial would be such a project in the medical context. Finally, *collegial* participation is when a project is ran solely by members of the public with varying degrees of recognition from professionals and professional institutions. Things like 'n-of-1' trials or self-ran 'biohacking' which may or may not be used by clinicians in decision-making fit here. We might imagine a case where a depressed patient reports to their physician that they are taking St. John's Wort – not regulated as a drug by the FDA – for their depression with middling success and minor side effects.[11] The clinician may or may not use that information in further decisions about the patient's treatment.

[11] One might ask if this is too loose of a conception of 'research.' I see no reason to preclude such language here or to say that these are not proper experiments. Firstly, this maps onto our colloquial language, e.g., "I'm doing my own research" or "I'm experimenting with St. John's Wort to see if it works for me." Secondly, it also coheres with philosophical assumptions of experimentation, i.e., that one of the functions of experimentation is to explore causal relationships between phenomena (Franklin 2005; Colaço 2017). Of course, since there are no 'proper controls' in such anecdotal experiments, that might mean that according to hierarchies of evidence used in 'evidence-based' medicine this would be 'low quality' research that cannot determine cause-effect relationships, though, this is contentious (Aronson & Hauben 2006; Howick 2011).

Appealing to the functions or roles of the public in participatory research is not the only way to taxonomize. Sociologists Aya Kimura and Abby Kinchy (2016) highlight that participatory research can be further delineated along the virtues or goals it instantiates: increasing data for scientists, expanding scientific literacy, building social capital, facilitating community leadership, levelling inequalities between experts and laypeople, challenging authority, supporting social justice, driving policy change, and catching polluters in the ecological context. For example, CBPR in urban and environmental health justice is traditionally aimed at building community capacities, knowledge, and policy change (D'Alonzo 2010; Alang et al. 2021). Increasing data is an inevitable part of the scientific process, but that is not the reason *why* this kind of research is done. There are usually more concrete goals in mind while engaging in CBPR, e.g., decreasing diabetes in church-going Black women in South Dallas (Kitzman et al. 2017) or strengthening pollution protection for Latino communities around San Diego (Minkler et al. 2010). On the other hand, volunteers monitoring flora and fauna in their backyards might help ecologists model environments and learn more about their local ecology, but this does not necessitate anything about social justice or levelling inequality; that is not to say it is not important participatory work, just that for such projects there are different goals in mind.[12] So, in short, from both Shirk et al. (2012) and Kimura and Kinchy (2016) we have two ways to analyze participatory research insofar as functions of the public and motivating goals or virtues.

Philosophers have added to the fineness of grain of this taxonomy. Lucas Dunlap et al. (2021) highlight that the goals mentioned by Kimura and Kinchy (2016) can be divided along epistemic, practical, communal, societal, and political lines. The goal of increasing data is an epistemic goal. One's enjoyment in learning about their local ecology is a case of what Dunlap et al. (2021) call a 'practical' goal. Communal goals might be those that increase a community's autonomy or capacities. Societal goals are those directed at social justice, and political goals address disputed arenas like regulation. Moreover, these goals are perspectival, i.e., the goal for the participant in some project might be different than the goal of the researcher in that project. If I am interested in modeling the migration of a species of bird, my goal as a researcher in a participatory project hinges on increasing data or epistemic goals. As a lay participant, my goals in participating could range from personal enjoyment to being a part of a community to learning and general altruism for science. In short, what we gain from considering the works of Shirk et al. (2012), Kimura and Kinchy (2016), and Dunlap et al. (2021)

[12] One might think it odd that the epistemic goal of increasing data might be secondary to practical or social goals, but this is not unprecedented – or even improper – in scientific practice (Elliot & McKaughan 2014).

is a relatively detailed taxonomy or analytic framework of functions/roles and virtues/goals with which to examine cases of participatory research.

2.3. PM on the Taxonomy

Returning now to the context of patients participating in PM, we can revisit the first question this paper aims to answer: (1) what is the nature of participation in PM? Let us first look at the role or functions of patients. This is not contractual participatory research. By giving genetic data to a PM database there is no obligation whatsoever for researchers to study or use that information, even if you are ill. In the NIH's frequently-asked-questions for 'All of Us,' a question posed is: "Will you be studying my disease or condition?" To which the response given is: "Researchers will use the data collected by the All of Us Research Program to study many different diseases and conditions. It is up to the researcher to decide what they study."[13] There is no 'contractual' exchange where an investigation about treatments must be made with volunteered data. One might say there is still something contractual here since I volunteer my data or pay for my own genetic information in return. However, this only shows that the process of genetic testing might be contractual. This is different than saying PM as a form of medicine – i.e., a process of diagnosis, prognosis, and treatment that uses genetic testing – is contractual. I am not obligated any diagnostic, prognostic, or treatment related information by participating.[14]

If not contractual, what about collaborative? Are patients in this context active collaborators as proponents of PM claim, i.e., are participants playing a role in setting research agendas, defining problems, analysis, and the dissemination of information? For the most part I think not. As of mid-2023, 'All of Us' did have a board of 43 'participant partners' who "…help support the program's design, implementation, and governance…provide input on specific aspects of the program, such as research priorities, participant retention, privacy and security, and the meaningful return of

[13] https://www.joinallofus.org/faq. Accessed July 2023.

[14] It is true that as of writing, '23andMe' offers 'genetics informed clinical care' in their $1100+ USD per year 'total health' package (e.g., https://www.23andme.com/compare-dna-tests/). This may indeed by contractually obligated diagnostic, prognostic, or treatment related information one gains by participating. However, patients that engage in this way are clearly (1) exceptions from the general rule of the general public that would engage in PM and (2) are still not likely achieving 'empowerment' from this participation due to the reasons provided in section 3 below.

information to participants."[15] However, these 43 individuals are far outnumbered by the millions of PM participants that are not. Moreover, we can ask if these are 'non-experts.' Ambiguity aside of what 'expertise' here constitutes, nearly half of these individuals hold graduate degrees, some in medicine and medicine adjacent fields.[16] This is not surprising since the complexity of PM and genetic information might entail that meaningful communication must be through experts. Also, it is an empirical question to what degree this board has influence over policy and procedures. No such information is available on publicly accessible NIH resources. Either way, most PM participants are not acting as collaborators.

It might be said that by participating in PM patients are collaborating not with an organization like 'All of Us', but with their physicians. But this also does not seem right. Firstly, one can sign up for 'All of Us' without their physician's knowledge. Secondly, bringing genetic information to a clinician does not necessitate collaboration. As I will discuss in the proceeding section, the clinical utility of most information from genetic testing is low (Caulfield 2011; Felzmann 2015; Hey & Barsanti-Innes 2016). Even if this does spur on collaboration of some sort, this is no different than non-PM forms of medicine, e.g., someone independently tracking their blood pressure over a few weeks and bringing that information to their doctor. Regarding collegial and co-created participation, patients themselves are not running genetic tests and the research has been initiated by professionals, so neither of those forms of participation fit here.

That leaves us with contributory participation, which I argue best describes the PM participatory process for most patients. PM research has been initiated and continues by professional researchers in the public or private sphere. The role of the public is, overwhelmingly, as contributors or volunteers of data. From the vantage point of function or role in the process, the person sending their genetic data to 'All of Us' has more in common with someone reporting flora and fauna in their backyards than someone engaged with CBPR or the thalidomide trial above. However, looking at role or function is just one of the components of our taxonomy of participatory research. Thinking about what goals or virtues are explicit and instantiated here allows for further analysis and understanding. From the perspective of the professional researchers in PM, the main driving goal of including participants is an

[15] allofus.nih.gov/about/who-we-are/all-us-participant-partners. Accessed June 2023.

[16] According to biographies available at the link in footnote 15.

epistemic goal – more contributors means increasing data for PM research. Expanding scientific literacy is also sometimes appealed to, but genetic literacy in the lay public remains tenuous (Vayena 2015). If a patient is told they have a mutation in *HLA-DQA1* they may know the propositional fact "I have a mutation in *HLA-DQA1*." However, what that fact *means* is, still for most of the lay public, ambiguous. It is not clear how patients might build social capital via participating, but researchers might build social capital in terms of publications and research grants using that data. The goals of community leadership or challenging authority are not necessarily instantiated here either. Neither are leveling inequalities or mitigating social injustice – things scholars have criticized PM as possibly intensifying (Kraft et al. 2018; Fleck 2022; Green et al. 2023). For private companies goals are largely financial, where epistemic aims are means to monetary ends.

In other words, the goals or virtues of the PM participatory project are mostly epistemic, i.e., increasing data for researchers. This is not uncommon for contributory projects. Reporting flora and fauna in backyards functions as data generation as well. However, just like in the flora and fauna context, we can ask what the goals from the perspective of contributors are. What motivates a volunteer or contributor to contribute? We might imagine a heterogeneous set of reasons why people might participate in PM from the recreational to the medical. However, since it is the case that patient empowerment is a goal made explicit by PM institutions and used as an incentive, this is worth examining. If it is *not* the case that participating in PM is as empowering as PM proponents claim, that could have concrete implications about how these institutions incentivize contribution. How or even if that goal is achieved or achievable leads us to the second question of this paper: is participating in PM really that empowering for patients?

Before moving forward, a summary of this section may be useful. The first question this paper aims to answer is about the nature of the patient participation in PM. Through looking at a taxonomy of participatory research stressing the roles/functions of participants and the virtues/goals instantiated in such projects, we located PM participation as overwhelmingly contributory. For professional researchers, this participation allows for epistemic goals like the creation of new PM data. Goals for the public are likely heterogeneous, but since PM institutions make *empowerment* explicit as a goal that patients can achieve and is used as an incentive, seeing if this is the case is warranted and now follows.

3. Empowerment in PM

3.1. Defining Empowerment in the Medical Context

Before determining to what degree contributory participation in PM is empowering, we should first consider what 'empowerment' means in the health or medical context. By looking to the WHO, we see that in 2009 they defined empowerment as "…the process that allows an individual or community to gain the knowledge, skills, and attitude needed to make choices about their care…" (2009, p. 190). However, this 2009 document also references another, slightly different definition from 1998: "…a process through which people gain greater control over decisions and actions affecting their health…" (2009, p. 190). Moreover, literacy is taken to be a fundamental aspect of empowerment (2009, p. 191). As of 2021, WHO documents maintained that empowerment is "…a process through which people gain greater control over decisions and actions affecting their health" (2021, p. 14), mirroring the 1998 definition. As Alexandra Kapeller and Iris Loosman (2023) point out in an analogous analysis on empowerment in mobile health technologies or 'mHealth', we glean two 'types' of empowerment from these definitions. The 2009 definition stresses *knowledge* to inform actions and the 1998/2021 definition stresses *control* over actions or the ability to act. The 2009 definition does highlight that knowledge is needed to make choices, but we can distinguish between gaining knowledge to make choices and gaining control over the ability to choose.

Is one of these definitions better than the other? I do think they are both intuitive, though I think one is a 'stronger' sense of empowerment than the other. Namely, empowerment-as-control or as-action is a stronger sense than empowerment-as-knowledge. For example, imagine a case where a person has knowledge and skills relevant to their health status but no control over decisions that affect it. Say someone knows that they live in a 'food desert' without access to fresh, unprocessed food and produce. This person may know the negative health outcomes that food deserts are associated with. However, say they have no control over decisions and actions that would better affect their health, e.g., moving or accessible transportation to areas outside the 'desert.' Is this person *equally* empowered to someone in a similar circumstance that *can* leave the food desert? I think clearly, no.

Moreover, the 'guise' of empowerment when there is none or it is lacking can be harmful (Kreitmair 2023) since empowerment colloquially confers a kind of self-responsibility. If empowerment hinges only on knowledge, then the person suffering the effects of living in a food desert without means of escape or outside access might be deemed responsible or at blame for those effects. That does not

seem right. I think in such a case we would want to say something else broader about social determinants of health, failures of public health infrastructure, etc., as playing a causal role in this person's negative health outcomes. If one *knows* but can *do* nothing about it, the blame or responsibility seems to fall on the factors that hinder the knowing individual. If we work with the empowerment-as-control definition we avoid this altogether. In that case we would recognize this individual and their neighbors have been *disempowered* by not having means to mitigate being in a food desert. Empowering such individuals and communities is tantamount to changing those factors that hindered the knowing individual's ability to act. With that in mind, moving forward I will refer to empowerment-as-control as the 'strong' sense of empowerment, and empowerment-as-knowledge as the 'weak' sense of empowerment.

3.2. PM v. 'Weak' Empowerment

PM institutions seem to be working mostly with the 'weak' sense of empowerment in mind. For example, 'All of Us' conceives of empowerment as guided by three principles: (a) PM should enable participants' access to their medical information they contribute in consumer-friendly ways, (b) educational resources should be made available to participants to assist them in understanding their health information and empower them to make choices about their health, and (c) Consumer-friendly and innovative ways of sharing aggregate data, findings, and information should be developed.[17] Principles (a) and (c) stress information and the sharing of that information, and (b) stresses educational resources to understand that information. Principle (b) also stresses the ability to make choices, which we will examine in the next section on 'strong' empowerment. For now, let us just focus on how or if participation in PM achieves 'weak' empowerment, i.e., empowerment-as-knowing.

Importantly, achieving 'weak' empowerment by participating in PM is hindered by low – but slowly improving – genetic literacy in the lay public (Little et al. 2022). Many genes and genetic variations are not determinate about disease and disease risk (Caulfield 2011). Genetic information gleaned from participation is usually given in terms of probabilities, which are themselves opaque to a lay public (Felzmann 2011; Vayena 2015). For example, in testing for predisposition to Celiac Disease, 23andMe

[17] allofus.nih.gov/protecting-data-and-privacy/precision-medicine-intitiative-privacy-and-trust-principles. Accessed Jan. 2024.

looks at variations in the *HLA-DQA1* and *HLA-DQB1* genes to determine if one is at risk.[18] These are common genetic variants in Celiac but testing positive for these variants does not entail one will develop the disease, it is just a high probability (Megiorni & Pizzuti 2012). If one tests positive and is not experiencing symptoms of Celiac, e.g., abdominal pain after eating gluten, it is hard to determine the value of this knowledge. To know I have some variation in some gene or genes is not necessarily to have knowledge about my future health status. For someone who learns this after the 'diagnostic window' of Celiac, say someone in their 70s, they may also wonder about the value of this knowledge. And as above, without knowing the correlation between these variations and Celiac Disease, the value of the knowledge of just the proposition "I have a genetic variation in *HLA-DQA1*" is ambiguous.

However, in considering the 'weak' conception of empowerment, one might say that asking the 'value' of this knowledge is unfair, i.e., going beyond what the 'weak' conception entails. Just having knowledge of the proposition may suffice. Knowledge is of course valuable in itself, even if there is nothing I can do with that knowledge. Notice though that this 'weak' empowerment is abundant and easily achieved. I am empowered when I know how many steps I took today, or what my heart rate was at 3 p.m. last Thursday. These are facts about my body and health, and it is probably better to know these things than to not know these things. Thinking back to the person living in the food desert, one who knows but cannot escape is probably *more* empowered than the one who also cannot escape and also does not know. In short, barring the issue of genetic literacy, having the information about my own genes and genetic variations does seem to suffice a 'weak' sense of empowerment – it is hard to imagine any such information-generating process that would *not* suffice the 'weak' sense.

3.3. PM v. 'Strong' Empowerment

Looking back at principle (b) in the 'All of Us' conception of empowerment we see an emphasis on empowering patients to make choices about their health. Where (a) and (c) lined up more closely with the 'weak' sense that, as above, is plausibly fulfilled barring genetic literacy, (b) aligns more with the 'strong' conception of empowerment-as-control or choice. The biggest hinderance here has been mentioned above, i.e., the clinical utility of most genetic information is low (Vayena 2015; Caulfield 2011; Felzmann 2015; Hey & Barsanti-Innes 2016). Outside of the success cases of imatinib, trastuzumab and others mostly in oncology, genetic factors that are linked to some diseases have no

[18] https://permalinks.23andme.com/pdf/samplereport_geneticheath.pdf. Accessed Jan. 2024.

interventions associated with them (Lohse 2022). And for those that do, the average gain in life expectancy from precision drugs is only about 2 months (Darrow 2023). In other words, even if I gain some knowledge from participating in PM I might not be able to *do* anything about it, or do anything terribly significant about it. One might find themselves in the position of the person who knows they are in a food desert who cannot escape; they might *know* something but be unable to *act* on it. In that sense, the 'strong' form of empowerment would be unmet for the majority of individuals who would participate in PM.

That such interventions do not exist is not necessarily a fault of PM institutions or PM researchers. The advancement of scientific and medical knowledge can move slowly. That not even a decade after the Precision Medicine Initiative was announced we would be rid of diseases because genetic science would be a naïve expectation. To say that participating in PM is *as of now* not empowering in the 'strong' sense is not to say it could not be. At the same time, it is not unreasonable to speculate that the roots of illness are not squarely genetic: we acknowledge that most diseases have multiple etiologies and causes from the environmental to the molecular. My point here is just to highlight that as per current practice and affairs, the kind of empowerment overwhelmingly achieved in participating in PM is likely not of the 'strong' sort.

However, even if a drug is available to an individual based off information gleaned in PM participation, the 'strong' sense of empowerment can still be hindered because of the cost of precision drugs. The average precision drug in the US is about $50,000 a month and not always covered by insurance (Fleck 2022; Tabery 2023). Thinking back to the example of the person knowingly living in the food desert, that could be mitigated if they simply bought a car or moved to a more affluent neighborhood. That there *are* options does not mean one is able to *choose* one. There are social determinants that have a concrete impact on health outcomes and health choices. Similarly, someone not able to afford precision drugs is likely not in a 'strongly' empowered position. Knowing that I have genetic variation *z* that correlates to a cancer treatable with precision drug *y* is not the same as being able to get *y*.

Other than cost, 'strong' empowerment is also hindered in PM participation via the mode or form of participation. As we saw in section 2, contributory participation requires little to no input other than the patient's biological data. Contributory participation is the most 'passive' of the roles on the taxonomy, as participants have no say in the research done or what research questions are to be asked.

Even if I am sick and want some sort of research done on my own sickness, I have no control over this. My data might just 'sit' in a database until some interested researcher comes along. Or, what is more likely, is that one would seek out researchers to do specific work, i.e., contractual research outside what PM institutions consider in their prerogative.

There is an additional hinderance to 'strong' empowerment in PM participation when we look to bioethical principles. Namely, no participant in 'All of Us' has full autonomy or control over their donated data. If we consider that autonomy extends to the control of one's data, there is a clear violation of control and choices. The NIH states in their frequently-asked-questions: "…you can decide to withdraw at any time. If researchers already have your data or samples for their studies, we at *All of Us* cannot get it back. Also, we will let researchers check the results of past studies. If they need your old data to do this work, we will give it to them."[19] Even barring the question of why the NIH cannot re-acquire your samples, they still will maintain your data for replication purposes or meta-analyses. This runs contrary to the idea that a core component of consent is that it can be rescinded (O'Neil 2003). This seems analogous to problematic cases in the history of medicine, e.g., the violation of consent for the Havasupai in the 1990s. Genetic data was given for the purpose of studying diabetes, but then the data was used – unknown to the participants from the Havasupai Tribe – for studies *not* consented to by the participants (Beauchamp 2011). This case is a common exemplar of problematic informed consent in health research. If we think that this is a violation of autonomy and choice, and that the ability to choose what is done with one's data is part of being empowered, we see this is a further possible limitation in PM's being 'strongly' empowering.

Something might be said about the recreational motivations for PM participation and the subjective 'feeling' of empowerment one may feel in virtue of participating. People may feel empowered insofar as they are taking active steps in their healthcare management. It is hard to imagine how that is not a good thing. I will just say that given the definitions of empowerment above, empowerment goes beyond being a subjective phenomenon. I may feel empowered but not be. Likewise, I may not feel empowered but still be so. Having a positive attitude about my healthcare management might make me seek out to be more collaborative with my doctor, but that is not something caused specifically in virtue of participating in PM. That is not to say there are not harms in recreational genetic testing

[19] https://www.joinallofus.org/faq. Accessed July 2023.

(Haddad 2023), nor is it to say there are not positive outcomes of participating like learning one's heritage and connecting with distant relatives. My point is just that when 'empowerment' is a goal used as an incentive for contributions, we ought to be precise about just what that means, or more importantly, what it does *not* mean.

Finally, one might consider conceptions of 'empowerment' outside of the 'strong' and 'weak' sense discussed here. Might it be empowering for an underrepresented group to be active and become more represented in the dataset PM utilizes? Perhaps so, and perhaps we could partly cash this out in terms of 'weak' empowerment of gaining genetic information. But there does seem to be something additional here, something about amending representation or being better represented because of one's or a community's actions. This does not seem to fall squarely in the 'weak' or 'strong' sense. But, if one grants that something like this is empowering, we can still notice that 'strong' empowerment is elusive. Moreover, this would presuppose a different relationship of trust in institutions than what scholars point out is currently the case (Kraft et al. 2018).

In sum, the 'weak' sense of empowerment is more operative in PM institutions than the 'strong' sense. By looking at the conception of empowerment provided by 'All of Us', we see that barring issues with genetic literacy, the 'weak' sense of empowerment seems to be met. The 'strong' sense is hindered by the clinical utility of that information, the cost of precision drugs even when they are available, the methods of participating in PM, and issues with data autonomy.

4. Analogies to Phase I & Pharmacovigilance: A Scale of Empowerment & Participation

Answering the question of how empowering PM participation is can be aided by looking at other instances of contributory participation in medicine like first-in-human 'phase I' trials and post-market drug surveillance or 'pharmacovigilance.' Both of these instantiate contributory participation, and both practices pre-date PM by decades; the mode of patient participation that PM practices is far from novel. Phase I trials are typically small, paid trials of around 20-80 healthy individuals. Participants are administered a novel or experimental drug to establish dosage and acute side effects. If the experimental drug is deemed safe enough, it moves on to phase II trials, phase III trials, and then regulatory approval if the trials are successful and deemed 'pivotal' by the FDA. Phase I trials are short, lasting usually no longer than a few days. There is little to no follow up with participants. These kinds of trials are not contractual, nor are they collaborative, co-created, or collegial. Participants

'contribute' their body and their body's data like blood samples having taken the experimental drug on controlled diets in controlled environments, hence the colloquial industry description of phase I trials as "feed 'em and bleed 'em" trials (Fisher 2020). Is there empowerment here? I think there is *less* empowerment in this sort of participation than in PM participation. Thinking about 'weak' empowerment, in phase I trials no information is gained for the trial participant other than things they likely already knew, i.e., height, weight, blood pressure, etc. 'Strong' empowerment is elusive here too. Participants in phase I trials are often financially compensated, sometimes in the thousands of dollars, but this has created a culture of dependency on being experimental subjects for some participants, who are usually from disadvantaged socio-economic classes. Movements to attain more rights for phase I participants have been prevented by private industry (Fisher 2020). However, some phase I oncology trials done explicitly on sick patients with no other options might be both strongly and weakly empowering.

Post-market drug surveillance or 'pharmacovigilance' utilizes contributory participation as well, especially in the US. Individual patients can report their suspected side effects to the FDA directly through the MedWatch database. Similar patient-accessible databases exist in other countries, and for those that do not, non-profit organizations like RxISK.org compile suspected side effect reports. From these databases of suspected side effect reports, researchers are motivated to analyze causal mechanisms of these adverse effects or do post-hoc statistical analyses to determine genuine from suspected side effects. Are patients that engage in such reporting achieving 'weak' or 'strong' empowerment? To report a suspected side effect, the patient of course knows that they have experienced a side effect. To have reported a side effect in the US also means that the patient knows how to report to the FDA – something few patients in the US know they can do. There seems to be control and knowledge present here both in reporting the suspected side effect and through things like the patient being able to cease or change medications in light of this. It can also have a concrete impact on the patient's treatment plans.

Where does participation in PM fall in relation to these practices? I think it seems right to say that it is somewhere in the middle. Where most 'phase I' trials are not even 'weakly' empowering, participating in PM is so, barring issues of public genetic literacy. Where reporting side effect information is 'strongly' empowering insofar as it constitutes action and can cause choices, this is limited in PM because of the factors discussed in section 3.3. Answering the question of empowerment

in PM is more complex than just a 'yes' or 'no,' and understanding the nuances of empowerment is illuminated by looking at other cases of contributory participation in medicine. Moreover, these examples show that a great deal of patient engagement in medicine is merely contributory, contrary to 'hype' one often finds in discussions of 'cutting edge' approaches to medicine.

5. Conclusion

In summary, PM institutions incentivize the donation of genetic data appealing to creating collaborative partnerships and empowerment. Here I argued that the partnerships in PM participation are overwhelmingly contributory, not collaborative. The average PM participant is not making decisions about what research questions are being asked, doing analysis, or playing a role in information dissemination. The overarching goals of such projects are epistemic, i.e., increasing data with which scientists can do research. The goals of the individuals contributing are likely various, however, since empowerment is a goal used as an incentive to acquire donations, it is worth analyzing. I argued that participating may be 'weakly' empowering insofar as genetic knowledge is gained by the participant, barring issues of genetic literacy. However, participating in PM is far from 'strongly' empowering, due to the low actionability of genetic data, the cost of precision drugs, the mode of participation, and bioethical issues of autonomy over one's data. Comparing with other contributory practices like 'phase I' trials and pharmacovigilance, we see that PM participation is more empowering than some practices and less than others.

What does the above analysis offer for patients, clinicians, and policymakers? Firstly, for policymakers, steps to make the process more 'strongly' empowering ought to be taken. As mentioned above, it might just be a misfortune of time that genetic information is not yet more widely clinically utilizable. However, that does not mean steps cannot be taken *now* by policymakers to have PM participation be more 'strongly' empowering. Reducing drug costs, allowing for better control over one's data once donated, and creating institutions that give patients more of an active say in what research gets done – i.e., calls for more active collaboration or the creation of a more 'contractual' research system – are things that could be done at present even given the promissory nature of PM. For patients and clinicians, care should be taken regarding expectations. Clarity around what is intended by PM institutions appealing to 'empowerment' is required in order to ensure patients are not expecting something they may not achieve. Participants ought to know where there are possible risks or violations to their autonomy that can arise via participating. Finally, one might ask if it is wrong or

somehow unethical that PM institutions appeal to empowerment as an incentive but only of the 'weak' sort. One might pessimistically claim this is manipulative or just using 'buzzwords.' Or, one might think there is nothing untruthful here once the 'weak' sense of empowerment is separated from its 'strong' counterpart. To have the 'strong' sense as the goal would place a great amount of agency on patients; agency that, as of now, is afforded only to scientific and private institutions. Either way I do not think there is any harm in being precise about incentives for patient donation, i.e., that the average patient donates for knowledge now and ideally, someday in the future, possible treatments. Whether or not shifting the language around incentives from empowerment to something more appropriate like 'altruism' would have an impact on rates of donation may be a question worth pursuing.[20]

References

Alang, S., H. Batts & A. Letcher. 2021. "Interrogating Academic Hegemony in Community-Based Participatory Research to Address Health Inequalities." *Journal of Health Services Research & Policy* 26.3, 215-20, DOI: 10.1177/1355819620963501.

Aronson, J.K. & M. Hauben. 2006. "Anecdotes that Provide Definite Evidence." *BMJ* 333, 1267-1269.

Beauchamp, T. 2011. "Informed Consent: Its History, Meaning, and Present Challenges." *Cambridge Quarterly of Healthcare Ethics* 20.3, 515-523.

Caulfield, T. 2011. "Direct-to-Consumer Testing: If Consumers are not Anxious, Why are Policymakers?" *Human Genetics* 130, 23-5.

Cesario, A., F.M. Lohmeyer, M. D'Oria, A. Manto, & G. Scambia. 2021. "The Personalized Medicine Discourse: Archaeology and Genealogy." *Medicine, Health Care and Philosophy* 24, 247-253. DOI: 10.1007/s11019-020-09997-6.

Colaço, D. 2018. "Rethinking the Role of Theory in Exploratory Experimentation." *Biology & Philosophy* 33.38. DOI: 10.1007/s10539-018-9648-9.

Collins, F.S. & H. Varmus. 2016. "A New Initiative on Precision Medicine." *New England Journal of Medicine* 372, 793-5. DOI: 10.1056/NEJMp1500523.

D'Alonzo, K.T. 2010. "Getting Starting in CBPR: Lessons in Building Community Partnerships for New Researchers." *Nursing Inquiry* 17.4, 282-288.

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Darrow, J.J. 2023. Two Views of Cancer Medicines: Imagery versus Evidence. *Health Marketing Quarterly* 40.2, 141-152.

Dunlap, L., A. Corris, M. Jacquart, Z. Biener, & A. Potochnik. 2021. "Divergence of Values and Goals in Participatory Research." *Studies in History and Philosophy of Science* 88, 284-291.

El-Alti, L., L. Sandman, & C. Munthe. 2019. "Person Centered Care and Personalized Medicine: Irreconcilable Opposites or Potential Companions?" *Health Care Analysis* 27, 45-59. DOI: 10.1007/s10728-017-0347-5.

Elliot, K.C. & D.J. McKaughan. 2014. "Nonepistemic Values and the Multiple Goals of Science." *Philosophy of Science* 81.1, 1-21.

Evans, A. & A. Potochnik. 2023. "Theorizing Participatory Research." In *Ethical Issues in Stakeholder-Engaged Health Research*, ed. E. Anderson. Springer.

Felzmann, H. 2015. "'Just a bit of Fun': How Recreational is Direct-to-Consumer Genetic Testing?" *The New Bioethics* 21.1, 20-32.

Fisher, J.A. 2020. *Adverse Events: Race, Inequality, and the Testing of New Pharmaceuticals*. New York University Press.

Fleck, L.M. 2022. "Precision Medicine and the Fragmentation of Solidarity (and Justice)." *Medicine, Health Care and Philosophy* 25, 191-206.

Franklin, L.R. 2005. "Exploratory Experiments." *Philosophy of Science* 72, 888-899.

Frith, L. 2023. "Democratic Justifications for Patient Public Involvement and Engagement in Health Research: An Exploration of the Theoretical Debate and Practical Challenges." *Journal of Medicine and Philosophy* 48, 400-412.

Green, S., B. Prainsack, & M. Sabatello. 2023. Precision Medicine and the Problem of Structural Injustice. *Medicine, Health Care and Philosophy* 26, 4330450.

Haddad, Y. 2023. "The Epistemic Harms of Direct-to-Consumer Genetic Tests." *Medicine, Health Care and Philosophy* 26, 559-571.

Harrison, J.D., A.D. Auerbach, W. Anderson, M. Fagan, M. Carnie, C. Hanson, J. Banta, G. Symczak, E. Robinson, J. Schnipper, C. Wong, & R. Weiss. 2018. "Patient Stakeholder Engagement in Research: A Narrative Review to Describe Foundational Principles and Best Practice Activities." *Health Expectations* 22, 307-316.

Hayes, D.F., J. Allen, C. Compton, G. Gustavsen, D.G.B. Leonard, R. McCormack, L. Newcomer, K. Pothier, D. Ransohoff, R.L. Schilsky, E. Sigal, S.E. Taube & S.R. Tunis. 2013. "Breaking a Vicious Cycle." *Science Translational Medicine* 5.196. DOI: 10.11226/scitranslmed.3005950.

Hey, S.P. & B. Barsanti-Innes. 2016. "Epistemology, Ethics, and Progress in Precision Medicine." *Perspectives in Biology and Medicine* 59.3, 293-310. DOI: 10.1353/pbm.2016.0026.

Howick, J. 2011. "Exposing the Vanities – and a Qualified Defense – of Mechanistic Reasoning in Health Care Decision Making." *Philosophy of Science* 78.5, 926-940.

Kapeller, A. & I. Loosman. 2023. "Empowerment Through Health Self-Testing Apps? Revisiting Empowerment as a Process." *Medicine, Health Care and Philosophy* 26, 143-52. DOI: 10.1007/s11019-022-10132-w.

Kimura, A.H. & A. Kinchy. 2016. "Citizen Science: Probing the Virtues and Contexts of Participatory Research." *Engaging Science, Technology, and Society* 2, 331-361.

Kitzman, H., L. Dodgen, A. Mamun, J.L. Slater, G. King, D. Slater, A. King, S. Mandapati, & M. DeHaven. 2017. "Community-Based Participatory Research to Design a Faith-Based Diabetes Prevention Program: The Better Within Me Randomized Trial." *Contemporary Clinical Trials* 62, 77-90.

Kovaka, K. 2021. "Evaluating Community Science." *Studies in History and Philosophy of Science* 88, 102-9. DOI: 10.1016/j.shpsa.2021.05.004.

Kraft, S., M. Cho, K. Gillespie, M. Halley, N. Varsava, K. Ormond, H. Luft, B. Wilfond, & S. Lee. 2018. "Beyond Consent: Building Trusting Relationships with Diverse Populations in Precision Medicine Research." *American Journal of Bioethics* 18.4, 3-20. DOI: 10.1080/15265161.2018.1431322.

Kreitmair, K.V. 2023. "Mobile Health Technology and Empowerment." *Bioethics* DOI: 10.111/bioe.13157.

Kuch, D., N. Kearnes & K. Gulson. 2020. "The Promise of Precision: Datafication in Medicine, Agriculture, and Education." *Policy Studies* 41.5, 527-46.

Little, I.D., L.M. Koehly, & C. Gunter. 2022. "Understanding Changes in Genetic Literacy Over time and in Genetic Research Participants." *Am J Hum Genet* 109.12, 2141-2151.

Lohse, S. 2022. "Mapping Uncertainty in Precision Medicine: A Systematic Scoping Review." *Journal of Evaluation in Clinical Practice* 29, 554-64.

Megiorni, F. & A. Pizzuti. 2012. "HLA-DQA1 and HLA-DQB1 in Celiac Disease Predisposition: Practical Implications of the HLA Molecular Typing." *Journal of Biomedical Science* 19.88. DOI: 10.1186/1423-0127-19-88.

Minkler, M., A.P. Garcia, J. Williams, T. LoPresti, & J. Lilly. 2010. "Sí Se Puede: Using Participatory Research to Promote Environmental Justice in a Latino Community in San Diego, California." *Journal of Urban Health* 87.5, 796-812.

O'Neil, O. 2003. "Some Limits of Informed Consent." *Journal of Medical Ethics* 29.1, 4-7.

Peters, L., I. Kelman, G. Shannon, & D. Tan. 2021. "Synthesising the Shifting Terminology of Community Health: A Critiquing Review of Agent-Based Approaches." *Global Public Health*. DOI: 10.1080/17441692.2021.1938169.

Quinn, A. 2021. "Transparency and Secrecy in Citizen Science: Lessons from Herping." *Studies in History and Philosophy of Science* 85.C, 208-217.

Sharpe, M., J. Getty & J. Klausner. 1997. "Thalidomide Use Is Associated with Weight Gain in HIV1-Positive Clients." *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology* 15.5, 392.

Shirk, J.L., H.L. Ballard, C.C. Wilderman, T. Phillips, A. Wiggins, R. Jordan, E. McCallie, M. Minarchek, B.V. Lewenstein, M.E. Krasny & R. Bonney. 2012. "Public Participation in Scientific Research: A Framework for Deliberate Design." *Ecology & Society* 17.2. DOI: 10.5751/ES-04705-170229.

Tabery, James. 2023. *Tyranny of the Gene: Personalized Medicine and its Threat to Public Health*. Penguin Random House. New York, NY, USA.

Valent, P., A. Orfao, S. Kubicek et al. 2021. "Precision Medicine in Hematology 2021: Definitions, Tools, Perspectives, and Open Questions." *HemaSphere* 5.3(e536).

Van Dijck, J. & T. Poell. 2016. "Understanding the Promises and Premises of Online Health Platforms." *Big Data & Society*. DOI: 10.1177/2053951716654173.

Vayena, E. 2015. "Direct-to-Consumer Genomics on the Scales of Autonomy." *Journal of Medical Ethics* 41, 310-14. DOI: 10.1136/medethics-2014-102026.

Vegter, M.W. 2018. "Towards Precision Medicine; A New Biomedical Cosmology." *Medicine, Health Care and Philosophy* 31, 443-456. DOI: 10.1007/s11019-018-9828-z.

World Health Organization. 2009. *WHO Guidelines on Hand Hygiene in Health Care: First Global Patient Safety Challenge Clean Care is Safe Care*. Geneva.

World Health Organization. 2021. *Health Promotion Glossary of Terms 2021*. Geneva.

Wynne, B. 2007. "Public Participation in Science and Technology: Performing and Obscuring a Political-Conceptual Category Mistake." *East Asian Science, Technology and Society* 1, 99-110. DOI: 10.1007/s12280-007-9004-7.