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**CHAPTER 2**

# Preventing "Exit", Eliciting "Voice": Patient, Participant and Public Involvement as Invited Activism in Precision Medicine and Genomics Initiatives

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## Introduction

Over the decades, we have seen many and diverse expressions of healthcare activism, some of which are scrutinized in other chapters of this book: especially when their own or loved ones' health is at stake or jeopardized by contentious medical or regulatory practices, people often mobilize and/or publicly articulate their interest to ensure they are taken into account. While activism may not always be comfortable to public or private organizations, the contributions of this book demonstrate that it is a vital mechanism for these institutions to consider the overflows, oversights and invisible effects arising from their actions and decisions. This chapter considers how organizations may react if there is a *lack of* such voices and thus no opportunity to learn from those affected by an organization's decisions and practices. By grounding ourselves on Albert Hirschman's (1970) "exit, voice and loyalty" framework, we argue that the fervent activism we see around access to healthcare therapies and services, described in several other chapters of this book, is *not* as often directed at concerns around sharing data for medical research. We particularly focus on this absence in the case of genomics and more generally of precision medicine initiatives, which have exponentially grown in significance and in financial investment as a proportion of overall medical research. Participation by individuals in such initiatives by sharing their data is, we

argue, a peculiar case in the healthcare domain. Health and, derivatively, healthcare, as extensively elaborated by the political philosopher Norman Daniels (see for example Daniels 1981, 1985, 2008, 2017) are quite literally vital to an individual given the essential contribution they make to the opportunities people can exercise in their lives. Accordingly, much activism is aimed at widening access and participation options. On the other hand, the benefits deriving from sharing data with precision medicine and genomics initiatives are usually very long term and often directed at future populations rather than those who decide to share their data. If there are concerns about any aspects of sharing data, then people might find it easier to simply not participate in these initiatives than to articulate their concerns.

In this chapter, we thus explore the power of the voices described in the upcoming chapters of this book through a counterfactual: namely the mechanisms that organizations have to implement to learn from participants, patients and the wider public if voice is absent – mechanisms that we call "invited activism". Echoing the concept of "invited space" for participation (Cornwall 2002, Bucchi and Neresini 2007, Pratt 2018), we define invited activism as those voices that do not arise spontaneously among concerned actors, but that are initiated by organizations to make up for the lack of "spontaneous" activism and as opportunities for institutional learning. In particular, we scrutinize how this "invited activism" has developed around data-sharing programs for medical research in general and genomics initiatives more specifically, and how it became epitomized in these spaces as Public and Patient Involvement (PPI) practices.

The German economist Albert Otto Hirschman (1970) distinguishes two essential reaction mechanisms related to dissatisfaction: exit (that is, opting-out from an "objectionable state of affairs") and voice (that is, interest articulation to try to change that "state of affairs"). Hirschman's notion of voice is very closely related to the concept of *activism*, core object of the analyses in this volume, which might be understood as a particular instance of voice: the

current book volume offers an array of cases and examples where voice is mobilized and exercised in relation to healthcare issues and institutions, and many chapters also chart how said institutions learn from such exercise of voice.

According to Hirschman's framework, in many situations the relative ease of exit tends to "drive out" voice, while conversely voice is pushed to the surface when exit is unavailable. From this perspective, voluntary data sharing for medical research and access to medical care can arguably be situated at opposite ends of the spectrum in terms of reaction mechanisms. In a healthcare context , *exit is often not an option at all*. To the contrary, voice is typically directed at gaining or improving access to a service or a medical product in the first place – these are the 'health access movements' (Brown and Zavestosky 2004), one of which Moran and Mountford describe in their chapter. By contrast, it is arguably almost too easy to opt out from voluntary data sharing for future-oriented medical research, and this ease, according to Hirschman, *discourages* interest articulation.

By revisiting Hirschman's classic analysis on exit and voice, we argue that in principle, when the perceived or real "costs" related to sharing personal genetic information are not acceptable, the exit (or opt-out) option prevails over voice. On the other hand, we argue that involvement practices made available by precision medicine initiatives can be understood as institutional attempts to increase voice and therefore as "invited activism": facilitation to articulate interests in order to provide a possible alternative to opting out and a feedback mechanism around (potential) participants' concerns. We discuss the implications of PPI in data sharing initiatives as invited activism, and we conclude by discussing its instrumental value by critically distinguishing between *public* involvement, *participant* involvement, and *patient* involvement as subcategories of invited activism. We finally interrogate the limits of voice in this invited format in the context of genomics initiatives.

This chapter focuses on *participation* in genomics initiatives in many senses: from mere data sharing to active roles in research programs' governance. In order to avoid ambiguities, we follow Woolley and colleagues' (2016) terminological distinction between *participation*, *engagement*, and *involvement*. We thus refer to 'participation' as mere acting as "human subjects" or, more specifically in our case, sharing one's data. Consistently, by *participants* in genomics initiatives, we refer to individuals who share their data with those initiatives, without implying any further active role for them. To refer to more active forms of "participation", we use the term *engagement*, in the sense of communication with the public about the purpose or aims of the research, and the term *involvement* to describe situations in which "members of the public have an active role in in the planning and conduct of the research itself, even to the level of choosing the scientific questions to be addressed" (ibid., 18). It is in this latter sense that PPI is scrutinized in this chapter. The "participatory medicine" approach, as we explore it here, is the tendency to encompass these three levels of participation: to ultimately promote research participants from mere human subjects to proper research "partners", fully informed on, and fully informative for, an organization's research agenda.

This is a conceptual chapter. Our initial argument – the general failure of concerned actors to voice *spontaneously* around voluntary data-sharing for future-oriented medical research – is *not* developed *inductively* after the observation of empirical data. As per the notorious "problem of induction" (Henderson 2018), empirical research is problematic around arguing that something is *not* (or is scarcely) there. This argument is mainly developed *deductively*, through the application of Hirschman theoretical framework to the medical research domain. On the other hand, this theoretical deduction is, if not validated, at least not confuted by observations. As a matter of fact, the applicability and the application of Hirschman's theoretical framework to medical research, as well as all the subsequent implications here

discussed – in particular our central argument of PPI as "invited activism" to compensate the lack of "spontaneous" voicing – are grounded on years of research, observations and fieldwork around precision medicine initiatives and their PPI practices. Galasso, in her four years of doctoral research, analyzed in depth the promises, the expectations and the concerns around the two precision medicine projects here referred to – Genomics England and the All of Us Research Program – through document and discourse analysis, qualitative interviews with key actors in the projects' governance and in the debates around them, and through direct experience of PPI gained by participating herself in consultation practices open to the general public (Galasso 2018). Together, Galasso and Geiger, as part of the ERC-funded project "MISFIRES and Market Innovation", have analyzed the PPI practices implemented in the context of genomics and precision medicine initiatives – in particular, again, Genomics England and All of Us – by also interviewing project staff engaged with participant representatives, and in some cases participant representatives themselves. Although this chapter is not aimed to present the results of this empirical research, those results, as well as the authors' experience around precision medicine research initiatives, offer indirect background for our conceptual claims.

This chapter aims to contribute to this volume in two ways: 1. We aim to provide further cause of reflection around the key role of activism in healthcare by scrutinizing the "participatory turn" as an institutional endeavor to expand voice; 2. We aim to provide insights into the diversity of voice articulation in the health domain and on its diverse roles, by focusing on the implications of the invited nature of PPI as opposed to other forms of voice analyzed in this volume. We hope that contrasting our arguments with the other cases in this book will contribute to the critical analysis of the transformative role of activism in general, and of the potential and limits of invited activism and of participatory medicine in particular.

In the next section, we describe contemporary medicine, embodied by precision medicine, as essentially data-fed, and reflect on the potential benefits and the costs related to sharing one's data, and in particular genetic data, as intrinsic part of precision medicine – bringing together two of the core dynamics described in Geiger's introductory chapter: personalization and datafication. In section 2 we discuss the individual choice of opting out from these initiatives or of articulating discontent, as framed by Albert Hirschman in terms of "exit" versus "voice". In section 3 we critically discuss the rise of participatory medicine and of PPI practices as "invited activism" in genomics initiatives.

## 1. Sharing (genetic data) in contemporary medicine: "benefits" and "costs"

### *1.1 Contemporary medicine: inclusive, precise, data-fed*

If medical knowledge and practice have always been grounded on comparative observations of similarities and differences in health and disease states – this is actually the principle of epidemiology itself - contemporary medical research facilitates and relies on these comparisons at an unprecedented scale. Cheaper, more powerful and more widespread technologies for data collection and processing allow scaling up from molecular, to individual, to population levels and all the way down again to understand and possibly intervene in the development of health and disease conditions with unprecedented precision: this is exactly the precision boasted by the emerging medical approach called "precision medicine".

Precision medicine, a concept that does not equate to, but substantially overlaps with the notion of "personalized medicine" (several scholars engaged with the relationship between these terms, see for instance Juengst et al. 2016 and Chan and Erikainen 2018), is generally

defined as “prevention and treatment strategies that take individual variability into account” (Collins and Varmus 2015, 793). In precision medicine, this is typically done by following an essentially *data-driven* approach (Hogle 2016): individual data are analyzed against those of the general population. Consequently, in this framework, it is vital that truly population-wide data are available: the more massive and the more diverse the dataset, the better. Accordingly, the cutting-edge frontiers of precision in medicine are pursued by implementing huge national and international research cohort programs: Genomics England in the UK, the All of Us Research Program in the US, GenomeAsia 100K, and the forthcoming 1 + Million Genomes initiative in the European Union are some leading examples.

Participating in precision medicine research initiatives may involve sharing several different kinds of data: genetic data by providing specimen, lifestyle or demographic data by filling in surveys, biometric data by undergoing physical measurements, physiological and lifestyle data by providing access to wearable devices, medical history data by sharing electronic health records… . In fact it is the combination of these different kinds of data that is supposed to foster “precision”. Although the argument developed in this chapter around opting-out prevailing over voicing in case of dissatisfaction is in principle applicable to all these types of data – actually, it is applicable to any sort of data one can voluntary share without expecting direct benefits – the main focus in this chapter are *genetic* data. Precision medicine research initiatives are very diverse, and different kinds of data are differently emphasized to the extent that to provide a univocal definition of ‘precision medicine’ may be challenging (Galasso 2018). Nonetheless for most initiatives identified as precision medicine, genetic data play a preeminent role: genetic predispositions and the genetic components of diseases, although at interplay with other factors ranging from lifestyle to social and environmental determinants, are assumed to play a key role in the pursuit of precision in medicine. Accordingly, performing massive whole genome sequencing is considered as the

most promising frontier for the understanding, the prevention and the treatment of a broad range of adverse health conditions.

### *1.2 Sharing genetic data: individual and social benefits*

In principle, by sharing their (genetic) data with genomics initiatives, individuals could benefit both themselves and others (Tutton and Prainsack 2011). Participants could gain benefits themselves because, by receiving their own genetic information back – as offered by most precision medicine research initiatives - they learn about their specific conditions and predispositions. They could benefit others by contributing to the advancement of medical research itself, as their genetic data provide the basis of comparison for understanding the key factors for specific disease onset and treatment.

The promise of individual benefits is particularly significant for genetic disease patients (including cancer and many rare disease patients): participation may sometimes lead to a long awaited diagnosis and/or point to appropriate treatment; in other cases a mutation can be identified that can help decisions about the most effective therapy, as in the famous case of Trastuzumab (better known under its brand name Herceptin), a monoclonal antibody specifically effective for treating HER2 positive breast cancer (www.drugs.com). Beyond such special cases, genomics initiatives mainly provide research inputs about associations between genetic traits, external factors, and different disease onsets and responses to treatments, which will help prevent or better understand *future* cases rather than diagnosing or treating those patients who provided the data. Moreover, most genomics initiatives request data not only from genetic disease patients, but from the general population in order to better understand associations and efficient interventions (among those mentioned in the section above, Genomics England is the only exception). In those cases, discourses mostly focus around the notion of *empowerment* (for a critical analysis of empowerment in precision

medicine see Prainsack 2017): individuals are promised insights into their overall predispositions and genetic risks, which may aid them in managing their own health and regulate their lifestyle accordingly. However, the concrete advantages are in most cases limited, as structural means or social support are also needed for the individual to actually put informed choices into practice (Egger and Swinburn1997, Juengst et al. 2012, Chiapperino and Testa 2016, Prainsack 2017), and as information related to risk and predisposition are questioned as not always reliable, significant or actionable (Buchanan et al. 2006, Millikan 2006, Prainsack et al. 2008, Rose 2013, Remuzzi 2014, Tutton 2014, Hogle 2016, Prainsack 2017).

To sum up, it is unlikely that individuals will derive direct benefits from sharing genetic data, with the exception of some particular cases among genetic disease patients. The benefits from genetic data sharing, as for most kinds of medical research and epidemiological studies, are generally only materialized in the long term and not necessarily to the direct advantage of those who shared.

### *1.3 The costs of sharing genetic data*

Despite the potential individual, communal and societal advantages deriving from participating in genomics initiatives, sharing one's genetic data is not costless. These costs may not be financial – while the consumer costs for sequencing charged by private consumers genomics companies start from less than 100 €, participation in national cohorts is generally free, and some even offer nominal compensation to cover travel expenses (in the case of All of Us, US$25). The costs of participating in genetics initiatives – whether potential, perceived or real - are related to the many remaining uncertainties, most evidently among them loss of privacy and control over own genetic data.

Given the exceptional sensitivity of the data involved, concerns over data protection are often central in decisions to participate in genomic research initiatives (Middleton et al. 2019). Among other things, genetic data contain information that is unknown to the data-sharing individuals themselves. Moreover, this information relates not only to the sharer, but also to their relatives. Who has access to these data, and how these data are used now and in the future, are major concerns around genomics initiatives. Apart from concerns over political surveillance, other potential considerations of data use and misuse range from commercialization by private entities to new forms of discrimination. The most serious of these concerns have been advanced in terms of "genetic discrimination" in case genetic information became accessible to insurance companies or to employers (Billings et al. 1992, Kitcher 1996, Clayton 2003, Wolf 2005, Epstein 2007; van Hoyweghen 2007).

It is important to note that many people might not be aware of the risks mentioned above, for instance that such a thing as "genetic discrimination" exists. Or, even if this is specified in consent forms, they might not realize that there is a risk for example that third parties access their genetic data, or that their data sharing might have consequences for their family members as well. By contrast, some people might be concerned about less realistic risk, such as being cloned, or having their DNA copied and planted on the scene of a crime (Middleton et al. 2019).

### *1.4 Called upon for sharing data: weighing up costs and benefits*

In the case of large-scale genomics initiatives, whatever the perceived costs and benefits, virtually every individual is invited to share their genetic data. Weighing up the costs and benefits of this data volunteering leaves individuals with a stark choice: if they do not share their genetic data for sequencing, individuals will miss out on information about themselves, which will remain invisible. If individuals want their genetic information to be visible to

themselves, they have to share it with others. The same holds if they are moved by solidaristic or altruistic motivations about 'donating' their genomic information to benefit their community or the broad society by contributing to medical research: they can do so only by incurring the risks related to genetic information disclosure. For patients suffering from genetic diseases, this equation might be a simple one: bearing the "cost" of the disease they hope to treat might well exceed the risk of losing privacy and control over their data, or even the more remote risks of future surveillance or discrimination. For the general public, however, the risk-benefit balance might not be always so straightforward.

In this chapter, we analyze the dynamics developing around the *refusal* of incurring the costs and risks of data sharing. We acknowledge that if some people decide not to participate in genomics initiative, this is not always necessarily because of the perceived "costs", however broadly framed. Many people may never be reached by an invitation to participate, may not care, may for a variety of reasons deliberately not want to know the information embedded in their genomes, may not wish to contribute to medical research, or may not believe their contribution would bring significant benefits to their community or to society. However, in our analysis, we focus on what we call the 'opt-outs' - those people who, in principle, would be interested in participating in genomics initiatives, but are held back or hesitant because of the above-mentioned "costs".

## 2. Exit, opt-out and voice in genomics initiatives

### *2.1 Hirschman's framework*

As we scrutinize the dynamics around opting out of participation in genomics initiatives, we ground our argument on Albert Otto Hirschman's classic book "Exit, Voice and Loyalty"

(1970). Hirschman argues that there are essentially two *reaction mechanisms* pursued by discontented customers or members of an organization: *exit* and *voice*, with possible combinations of these two. In general terms, through exit, costumers leave or opt-out of the organization that dissatisfies them; on the opposite, through voice, as in the activist movements analyzed in this volume, they "attempt to change" what dissatisfies them by expressing their discontent to the organization itself and hope that it will learn.

Hirschman's examples range from consumer firms to parties and nation states and do not explicitly refer to the domain of health, healthcare or health data sharing. However, Hirschman's framework is very broadly applicable, relevant to any instance of participation as voluntary activity (Kelty et al. 2015): it is virtually applicable to any situation in which there is a choice about being part of, or subscribe to, or accessing, any sort of transaction, service, organization, group, institution or initiative, provided it is possible to opt out and to articulate discontent. Concerning the medical domain, Hirschman's analysis has been applied to patients' reactions to discontent toward healthcare providers (Annas 1997, Brüggeman 2017) or health systems (Ippolito et al. 2013). In relation to genetic testing specifically, Hirschman's work has been used to advocate for the development of proper consultation instead of a binary opt in/opt out choice (Benschop et al. 2003), and for public consultation around genomic testing regulations (De Vries and Horstman 2008).

In line with these works, we think through people's reaction mechanisms when there is discontent about the conditions for sharing genetic data for medical research. In particular we focus on the importance of voice in a field that, as discussed in the sections above, is characterized by doubts and uncertainties (Benschop et al. 2003). We interrogate how genomics and precision medicine initiatives deal with the problem that in the context of genetic testing, "informative voice" tends to be drowned out by "silent and uninformative participation or silent and uninformative exit" (ibid., 147), or in other words, that "the

potential of voice to improve practices is clearly under-used" (De Vries and Horstman 2008, 185). Much has changed in the years since these two studies applying Hirschman's framework in the domain of genetic testing have been written: on the one hand genomics initiatives have reached unprecedented spread and preeminence, making a renewed scrutiny of the reaction mechanisms of "exit" and "voice" in the genomics context necessary. On the other hand, over the past decade medical research has experienced a 'participatory turn', giving "voice" a central role, actualized most prominently in the implementation of Public and Patient Involvement (PPI) practices. This participatory turn is particularly evident around genomics initiatives where "the advantages of voice as a feedback mechanism" (ibid., 182) have gained a renewed institutional recognition.

The centrality of voice in current genomics initiatives' practices is the object of section 3. In this section, we apply the framework developed by Hirschman to contemporary genomics initiatives.

### *2.2 Exit: withdrawing vs. opting out*

With regard to the first of Hirschman's two options, namely exit, we pursue a broad interpretation of the notion of exit, one that extends the notion from former customers or participants to what we call opt-outs, that is people who are *invited* to be participants in precision medicine initiatives but who have not participated before. Exit in the narrow sense of withdrawal of former participants may be questioned as somehow incomplete in the context of genetic data sharing: although withdrawal generally guarantees destruction of the provided specimens and prohibition for any further use of those data, this does generally not apply to data already used, and in any case nothing can be done about information that has already circulated. As a consequence, some costs and benefits cannot be reversed through exit: the benefit of becoming aware of one's own genomic information is received as soon as

information is delivered first and cannot be withdrawn, while the costs are not (entirely) canceled out either as disclosed information that had previously been circulated can never be really destroyed.

Given the peculiarity of the exit-as-withdrawal option in the genomics domain, in our analysis we compare voice with opt-out or non-participation, as *the only way to really exit from a genomics initiative is not entering at all*. We argue that Hirschman's analysis remains applicable to our argument if we shift the reaction mechanisms to an earlier stage, namely, when the patient or consumer still has to decide whether becoming a genomics consumer or data donor at all: it is (only) at this stage, through opt-out, that in the case of genomics initiatives invited participants can truly "escape from an objectionable state of affairs" (Hirschman 1970, 30).

In the case of genomics initiatives, the opt-out option generates a no-win situation: individuals opting out lose the opportunity to access (and possibly be empowered by) their own genomic information; the genomics initiative loses future profits and possibly breadth of research applicability; society and specific communities lose benefits possibly deriving from future healthcare design and services. As a matter of fact, precision medicine and data-fed research in general is a prototypical case in which "exit [opt-out] of a member leads to further deterioration in the quality of the organization's output" (ibidem 101) as far as this research grounds its "precision" and applicability on massive and diverse data. An extreme case of mass opt-outs (refusal to participate) could signal the potential collapse of data-driven initiatives. The exit option, then, is *a multi-edged failure* in the context of genomics initiatives. Nonetheless, in line with Hirschman's analysis, the opt-out option is likely the prevalent reaction mechanism in the context of dissatisfaction or suspicion around genomics initiatives. Opt-out is a straightforward action for potential participants: it only requires to ignore advertisements or invitations to share data, and it even avoids the mundane "costs" of

participation, related for example to getting in touch with the initiative, going through the informed consent process, undergoing potential physical tests and giving samples. Thus, consistent with Hirschman's intuition that "easy exit" drives out voice, people who are invited to participate in precision medicine initiatives and are unhappy with the conditions provided can simply ignore the invitation and are very unlikely to articulate their discontent or negotiate different conditions.

Importantly, this reflections does not imply that all potential participants will choose to exit: some will share their genetic data because of a variety of reasons that can range from expected empowerment to mere curiosity (Geiger and Gross 2019); some will still share their data out of loyalty and solidarity (despite some concerns we are going to discuss), in view of the benefits they expect genomics initiatives might provide to society; others, because they have not considered the costs or risks of participation. Many individuals, despite the possible concerns discussed in the sections above, are happy enough with the conditions, as demonstrated by the fact that millions of individuals globally have accepted to share their genomic data both with private companies and with national programs. Nonetheless, if our analysis is correct, dissatisfied individuals are likely to simply opt out, without ever articulating why they chose to do so, depriving the organizations in question of a vital learning mechanism.

### *2.3 Voice: political and costly*

In Hirschman's analysis, voice is "political action par excellence" (ibid., 16). Similar to activism, which might be understood as a particular instance of it, voice "can be graduated, all the way from faint grumbling to violent protest" (ibid.), but it always implies clear "interest articulation": in contrast to exit, voice is defined "as any attempt at all to change,

rather than to escape from, an objectionable state of affairs, whether through individual or collective petition to the management directly in charge, through appeal to a higher authority with the intention of forcing a change in management, or through various types of actions and protests, including those that are meant to mobilize public opinion" (ibid., 30).

A crucial point emphasized by Hirschman is that, in general, when the exit (or opt-out) option is available and easy to use, it "drives out" voice. The argument proceeds by remarking that "in comparison to the exit option, voice is costly" to the individual (ibid., 40). As a matter of fact, "buyers of a product or members of an organization spend time and money in the attempt to achieve changes in the policies and practices of the firm from which they buy or of the organization to which they belong." Moreover, "voice will depend also on the willingness to take the chances of the voice option as against the certainty of the exit option" (ibid.).

The consequence of people simply opting out without making themselves heard, engenders, in line with Hirschman's argument, institutional entropy: there is no way for the organization to know whether individuals are not sharing their data because of lack of interest or information or because they have any specific concern about the procedures or the conditions, what these concerns are, and how they could be addressed (van Hoyweghen 2007, Middleton et al. 2018).

With this argument, we claim that discontented potential participants generally fail to articulate their dissatisfaction, but with this we do *not* want to give the misleading idea that no concerns and no requests at all are ever articulated around the way genetic data are managed by genomics initiatives. On the contrary, regulators, ethicists, and some non-governmental organizations are very active on that front – counter-institutional voice, so to speak, does exist, but it is usually the voice of the expert and not of the users themselves. Also, in line with our characterization of having shared genetic data as creating a "no-exit

situation" to the extent that full withdrawal cannot be guaranteed, individual or public voice is most likely to take place after "the damage is done", for instance when conditions change after data have already been shared, such as when the genomics initiative is acquired by or start partnering with another company, or when data are used beyond participants' consent. Famous historical and contemporary examples include the use and publication of Henrietta Lack's genome (Skloot 2010), the accusation to the Wellcome Trust Sanger Institute of commercialization plans for African DNA (Grens 2019), the use of Havasupai Indian's genomes for broader research than initially understood (Harmon 2010), and the acquisition of the Ogliastra people's genomes by an English company (Manis 2018). In these cases, although often "partial exit" is pursued by withdrawing, as discussed, total exit is not possible. Consequently, voice generally finds some space in these contexts, contrary to cases of discontent when opt-out is still available.

### *2.4 Loyalty: participating for the sake of public good?*

In Hirschman's analysis, the binary distinction between exit and voice is elaborated in connection with a third concept, which may also be relevant in the context of genomics initiatives: *loyalty*. Hirschman defines loyalty as "a generalized concept of penalty for exit" (ibid., 98), which occurs when for some reasons consumers/members do not want to quit a service that they are dissatisfied with. Whatever these reasons are, they are very important in Hirschman's analysis insofar as the derived loyalty "helps to redress the balance by raising the cost of exit".

According to Hirschman, "loyalist behavior" typically arises, among other scenarios, in the context of "public goods". He defines public goods as "goods which are consumed by all those who are members of a given community, country, or geographical area in such a manner that consumption or use by one member does not detract from consumption or use by

another" (ibidem, 101). Public health features among the standard examples of public goods provided by Hirschman himself. Thus, as far as they are contributing to the general advancement of healthcare, medical research projects in general and genomics initiatives in particular might be considered as "organizations producing public goods". As a consequence, participating (or not) in these initiatives means participating (or not) in the production of a public good. Awareness of this point is deeply connected to the altruistic motivations for sharing data for medical/genomic research discussed above and could in principle encourage data-sharing even when there is (some) dissatisfaction around the initiative's terms and conditions.

On the other hand, and potentially thwarting the 'public good' argument (as well as those voices calling for an obligation to participate in medical research, among others: Petersen and Lupton 1996, Chadwick and Berg 2001, Schaefer et al. 2009, Faden 2013, Rhodes 2005, 2008 and 2017) there is widespread concern that medical innovation might exacerbate existing healthcare inequalities by predominantly benefitting people who are already advantaged in the healthcare system, and this concern is especially emphasized in the context of precision medicine (Galasso 2018). The debate about the effects of precision medicine on healthcare costs and accessibility is an open one, and not one we are likely to solve in this short chapter. In any case, those individuals who cannot access even basic healthcare will no doubt be similarly unable to access precision medicine treatments, both under private as well as public healthcare systems (Mody 2017). Thus, as long as they are not accessible by a (large) part of society, precision medicine benefits cannot be defined as "public" goods. Conversely, in some cases they risk being very exclusive and exclusionary goods. In such cases, as argued by Dickenson (2013), the premise of altruism and solidarity collapses in favour of a highly individualistic and entrepreneurial framework.

To summarize our argument thus far, health research and care generally are one of the few contexts in which exit is generally costlier than voice: given the essential relevance of health in terms of opportunities people can exercise (Daniels 1981, 1985, 2008, 2017), while exit may theoretically be possible - in the sense that it is *possible* not to access therapies, or to accept that your disease is not recognized or addressed by research - it tends to be so costly to the individual that it cannot practically be considered as an option at all. Thus we argue that access to healthcare and inclusion in medical research, especially when there are direct individual health interests at stake, can be considered as no-exit situations. Consistent with Hirschman's thinking around no-exit situations, and as demonstrated across this book's pages, this makes voice the predominant reaction mechanism (although not availing of therapies for economic reasons is a widespread problem, Osservatorio Donazione Farmaci, 2018).

The situation is very different in the case of sharing genetic data. Given: 1) Hirschman's argument on the prominence of exit over voice whenever exit is easily available, 2) the observed extreme ease of opt-out from genomics initiatives, and 3) the discussed potential inability of these initiatives to produce public goods and to foster loyalist behaviours to counterbalance exit; we conclude that exit (opt-out) is expected to be the prevalent reaction to dissatisfaction in the context of data-sharing for future-oriented medical research, at the expenses of interest articulation through voice.

## 3. Participatory medicine

### *3.1 Switching from exit to voice*

In the first section, we discussed how large-scale and diverse participation in genomics initiatives (and more generally in medical research) is essential to guarantee the advancement and broad applicability of medical innovation. As long as opt-out appears the obvious option for dissatisfied potential participants, the applicability, inclusivity and equitability of genomics research might be jeopardized. In parallel, massive opt-out also jeopardizes the goals and even the existence of the genomics initiatives themselves, as they ground their success on the results they can extrapolate and use from participants' data.

Against this scenario, it would be in the interest of all stakeholders to "redress the balance" and encourage voice over exit. According to Hirschman's analysis, the most straightforward way to do so is to eliminate the exit option, by creating a no-exit situation in which voice becomes the only option. This scenario – provided that is desirable – is not possible in the case of genomics initiatives and of medical research, unless by repudiating all the ethical principles that have been established in the last century and fostering a society in which everyone is *forced* to share their genetic information. Another option, as discussed in the previous section, involves "raising the costs of exit" through loyalty by improving and expanding accessibility to forthcoming healthcare benefits as "public goods". However, as mentioned, as long as there is potential exclusivity of the goods produced by precision medicine initiatives, loyalty has limited applicability in this context.

If increasing loyalty or the cost of exit is not possible or is dismissed as an option, the only other way to "redress the balance" between exit/voice is, quite obviously, decreasing the cost of voice. Or, in other words, providing infrastructures and facilities to encourage interest articulation. In the words of Hirschman:

> The creation of effective new channels through which consumers can communicate their dissatisfaction holds one important lesson. While structural constraints (availability of close substitutes, number of buyers, durability and standardization of the article, and so forth) are of undoubted importance in determining the balance of exit and voice for individual commodities, the propensity to resort to the voice option depends also on the general readiness of a population to complain and on the *invention* of such institutions and mechanisms as can communicate complaints cheaply and effectively. (Hirschman 1970, 43, emphasis in the original text)

In contemporary medical research, the creation of "channels through which consumers can communicate their dissatisfaction", might be envisioned by the emerging framework of "participatory medicine". This model promotes a more extensive implementation of participation in medical research, also embracing what Woolley and colleagues (2016) refer to as *engagement* and *involvement*. Within this framework, citizens are invited to participate at many levels: not just to take part as human subjects, but also to be *engaged* in the research, in the sense of understanding the background, the purposes and the utility of the research itself and their own roles in it, and even to be *involved* in decision-making and priority-setting (ibid.).

Although not all genomics and precision medicine research studies - and certainly not all at the same level and in the same way - embrace a 'participatory turn', perhaps unsurprisingly given our analysis thus far, this rhetoric has been heavily embraced in the context of precision medicine and genomics initiatives that entirely rely on massive and diverse voluntary participation in data-sharing: "without patients contributing data, time, effort and self-care, current vision of personalized medicine cannot be realized…it is not a coincidence that we see a renewed emphasis on patient participation at a time when medicine is particularly hungry for data and other contributions from us all" (Prainsack 2017, 11).

### *3.2 "Participants as partners"*

With the recurring motto of involving "participants as partners" (allofus.nih.gov), some of the main national precision medicine cohort studies have opened up several kinds of channels through which (potential) participants are facilitated to express their concerns and articulate their interests. All of Us in the US and Genomics England in the UK, are especially active on that front: they have circulated surveys and "requests for information" to the general public, organized public dialogue, focus groups, panel discussions and public events, made available (online and offline) forms for nominating diseases to be included in the research, and they have leaned on digital platforms allowing people to share their "ideas" about research priorities. Moreover, both All of Us and Genomics England have involved lay participants in their governance: both initiatives have "participant panels", which are composed of participant representatives and are to act as advisory bodies and be engaged with decision-making across the initiatives.

In this framework, given the variety of "channels" provided to meet the preferences of everyone, voice becomes less "costly" and in fact is also supposed to be *easy*. Channels for voice are broadly advertised and made to be easily accessible. Voice still remains not completely costless, as certain skills, time and energy are required to formulate interests or concerns. But these costs are no longer so disproportionate to the 'free' exit option. The "invention of these channels" might, at least in principle, succeed in "redress[ing] the exit/voice balance" and "to have the members of the organization switch from exit to voice" (Hirschman 1970, 123).

### *3.3 "Voice from within and voice from without": patient, participant and public involvement*

The specific "channels of voice" offered by precision medicine and genomics initiatives in alignment with the paradigm of "participatory medicine" might take on very different forms. Here we focus on one of the most relevant distinctions to our analysis on exit and voice: the channels for "voice from within", and the channels for "voice from without" (Hirschman 1970). In other words, we propose to analyze the significance and implications of offering and facilitating the opportunity for voice for those who *opted out* (have not participated in) vis-à-vis for those who have *opted into* genomics initiatives.

As seen, the practices made available in participatory medicine to extend the scope of participation are often addressed as Patient and Public Involvement or "PPI". However, scholars have urged to "split apart the familiar acronym, drawing a distinction between patient and public involvement, rather than treating PPI as a single practice", as "justification for involving the public differs in ethically significant ways from the justification for involving patients" (McCoy et al. 2019, 709). In this section we follow McCoy and colleagues' suggestion. In our case, as people who opt into precision medicine initiatives are not necessarily "patients" in the strict sense of the term, rather than only distinguishing between *public* and *patient* involvement, we suggest to add another term of distinction that, coincidentally, also starts with the letter P: *participant* involvement (we might talk of PPPI!). In our analysis, participants are all those individuals who opted into a precision medicine initiative with which they shared their data, irrespective of their clinical conditions. Consistently, participant involvement is defined as all those practices to articulate interests or concerns available to individuals who have shared their (genetic) data with the initiative at issue, or, in some specific cases, to their guardians or carers. In other words, the concept of participant involvement is applied to all those participatory practices that *exclude* those who opt out. Conversely, we define the public as all individuals belonging to a population, irrespective of whether they shared their (genetic) data or not. Consistently, we define public

involvement as all those practices to articulate interests or concerns that are available to any individual in the population, *including* those who opt out. As for the definition of "patient", it is especially problematic in the context of genetic testing: virtually anyone can be included in this category, especially if *risk* of disease is included. To avoid ambiguities, in our analysis, we refer as "patients" to all those people who are addressed *because of* their clinical conditions (or, in some cases, their carers). In some cases, patient and participant involvement might coincide: this is the case of research initiatives only recruiting specific patients, as Genomics England does. However, most genomics initiatives invite the general population to share data, independent of their clinical conditions, and if there are no individuals specifically participating *as* patients, then there is no space for a proper patient involvement outside of participant involvement – unless specific events or forums are set up by specifically focusing on a given health condition. Other initiatives, such as Genomics Medicine Ireland, run studies on the general population *and* on specific patients in parallel. In these cases, patients are a subcategory of participants, and as a consequence, patient involvement might be seen as a subcategory of participant involvement (when implemented).

The two precision medicine initiatives that we already mentioned as outstanding in terms of embracing the framework of 'participatory medicine' – All of Us and Genomics England - involve the general public, participants and patients in different ways (Galasso and Testa 2017, Galasso 2018). Genomics England is mostly, if not entirely, focused on patient/participant involvement (coinciding in this case, as all participants participate *in virtue of* their condition as patients): some *participant* representatives are included in the governance of the project, while the general public is generally addressed in terms of *engagement*, in the sense that diverse public events and dialogues are implemented to provide wide and deep understanding of the project, without including a proper involvement of the public for decision making. On the other hand, All of Us – which likewise involves some

participant representative in the project governance - has also made available several practices for *public* involvement, such as digital platforms and online forms where virtually anyone in the world could provide comments and proposals on specified aspects of the project. All of Us, in comparison to Genomics England, provides space for a plurality of voices, but on the other hand they offer poor transparency around the impact of those voices. This may undermine what, according to the analysis by Kelty and colleagues (2015), is one of fundamental dimensions of 'proper participation' as opposed to tokenism.

Where our analysis casts the facilitation of voice as a counterbalance to exit and as a feedback mechanism to avoid institutional entropy, public, patient and participant involvement each have a deeply different meaning. *Public* involvement offers individuals an alternative to opt-out. *Participant* involvement is, by definition, solely addressed to people who accepted to participate and aimed to either prevent their satisfaction from deteriorating or to improve it to build further barriers to exit. Providing participants with continuous opportunities to articulate their interests and concerns gives them the chance to express their dissatisfaction as soon as it emerges. Apart from that, participants, given their *insider* experience of the initiative and of the participatory process, become "experts" of sorts around data sharing issues. As a consequence, participant involvement also embeds an important *instrumental* value to the organization (Sen 1999, McCoy et al 2019): participants can provide valuable insights and suggestions to improve the organization and consequently the satisfaction of current or future participants. Beyond this insider's perspective, *patients*, be they participants or not, can provide a unique expertise: they are proper experts, more than anyone else, on the conditions related to their own diseases. This unique expertise is explicitly valued for example in the context of Genomics England Participant Panel. As discussed in the first section of this chapter, patients, in some cases, are those who can expect to benefit directly from participating in genomics initiatives, and thus they may balance risks

and benefits in a different way to less directly concerned individuals. If patients decide not to participate in a genomics initiative, that decision is likely made on other grounds than simply opting for the ease of exit over voice. As a consequence, we can assume that patient involvement does not make a significant difference in terms of broadening participation. On the other hand, it is especially significant in terms of the *informativity* of voice (Benschop et al. 2003). Participant and patient involvement, especially if extended to the level of governance, would hence benefit both the quality and the democratic capacities of genomics initiatives and minimize opt-out.

In comparison with patient and participant involvement, in public involvement individuals may lack the direct internal expertise of the data sharing initiative, but bring the perspective of those who are in principle interested in participating. By articulating their concerns, they can contribute to changing any conditions that would prevent them from doing so. Thus, public involvement has the advantage that it *directly* increases the likelihood of participation.

In summary, public, participant and patient involvement may all contribute, in different and complementary ways, to more participant-friendly genomics initiatives, thence to broader and more diverse participation, thence to more equitable healthcare benefits, and vice versa, in a sort of a virtuous circle. However, as it will be briefly discussed in the next section, it is essential that inclusivity and consistent power distribution are pursued in order to avoid a totally uninformative and even deceiving "presence without voice and voice without power" (Pratt 2018, 2).

## 4. Invited activism

The picture that emerges by observing the forms of voice around voluntary data sharing for precision medicine, in line with Hirschman's analysis, is an almost exclusive pre-eminence of

"invited spaced" over "created spaces" (Cornwell 2002, Pratt 2018) or, from another perspective, of "sponsored participation" over "spontaneous participation" (Bucchi and Neresini 2008). Two important implications emerge from this observation in the context of this book volume on activism in healthcare: first, that organizations have realized the unique importance of individual and collective voice for institutional learning and innovation, to the extent that the contemporary paradigm of participatory medicine can, at least in part, be understood as compensating for the lack of activism in certain areas. And second, that despite these efforts, given this exclusively 'invited' nature, quintessential differences exist between voice in the form of PPI / PPPI in data-sharing medical initiatives and healthcare activism in other contexts.

As the introduction to this volume highlighted, definitions of activism are generally very broad, consistent with the variety of its forms and expressions. However, the distinctive feature of activism as commonly accepted is that "it assumes some intervention in the public domain *that goes beyond institutionally sanctioned…activities*" (Woodhouse et al. 2016, 313, emphasis added). As a consequence, 'invited activism' is in fact an oxymoron, and we are quick to admit this fact. Participatory medicine, as promoted by the initiatives themselves, is institutionalized, and, as such, cannot, by definition, provide a valid substitute for activism. Participatory medicine is different from proper activism as it is "invited", "sponsored", initiated, mediated and regulated by the institution itself towards which activism is supposed to be addressed. Thus, invited activism in the form of PPI/PPPI or other participatory mechanisms will always be incomplete.

The distinctively "invited" nature of involvement in participatory medicine may cause some concerns. Even more so than 'spontaneous' activism, invited activism, as initiated and mediated by the very same initiative toward which it is directed, might privilege certain voices over others (in terms of 'who' will take up the invitation and who will be heard),

might highlight selective messages over those that are particularly unwelcome by the organization in question (in terms of how the voicing will be understood and taken up), and might shape what can and cannot be articulated (in terms of the forums and channels provided).

More in detail, a first concern is related to exclusiveness: in addition to the barriers related to the skills and the means required for utilizing even the most accessible voice channels, the fact that these practices are 'upon invitation' and that invitations might be explicitly or implicitly targeted or even intentionally exclusive, exacerbates the risk that patterns of exclusion might emerge around involvement practices (Galasso 2018, Pratt 2018, Prainsack 2019). This may prevent some groups from switching from exit to voice, as well as erase their interests and needs from the initiative's agenda setting, thus exacerbating existing disparities.

A second concern is related to effectiveness - whether these voice channels lead to improvements that take account of the interests and needs expressed through voice. As a matter of fact, voice, *per se*, does *not* guarantee change. Voice is defined as the *attempt* to change (Hirschman 1970, 130), but it could be "mere "blowing off steam"" (ibid., 124), and similarly the space provided for voice could be just an instrument that "allows the powerholders to claim that all sides were considered, but makes it possible for only some of those sides to benefit" (Arnstein 1969, 216). In the case of participatory medicine, and of invited activism in general, effectiveness is all the more problematic as interest articulations are structured and channelled by "the powerholders" themselves (the initiative), through the channels and to the aims that themselves established. Even this 'tokenistic' scenario may lead to positive consequences for the organization: voice could still, in principle, decrease the opt-out rate through the *illusion* to have the possibility to change the state of affairs, and thus foster the "shift from exit to voice". This would still enhance participation and data sharing in

precision medicine initiatives and, as a consequence, enhance the robustness and applicability of research findings. However, tokenistic involvement would provide little or no benefit to the research setting and it would potentially further stifle the likelihood of spontaneous or uninvited activism. In other words, tokenistic involvement would be to the short-term advantage of the genomics initiatives but likely lead to institutional entropy in the long run.

Analyses of participatory medicine need to take the distinctiveness of its invited nature into full account: unlike other manifestation of activism discussed in this book, in participatory medicine it is the "object of debate" itself that initiates voice, that establishes its purpose, that establishes who participate and how (Pratt 2018). Research on PPI/PPPI needs to interrogate the extent to which this inherent conflict of interest influences the instrumental value of participation, and the extent to which it risks, voluntarily or involuntarily, to create bias and barriers for other types of activism, for a more inclusive redistribution of power, and for proper democratic innovation.

## Conclusion

In this chapter, we discussed the essential role of activism, as demonstrated by the strategies implemented by institutions to compensate for a lack of activism and to trigger voice when it is not initiated spontaneously. In particular, we have analyzed involvement practices embraced by precision medicine cohort programs as a remedy to the silent opt-out or non-participation of individuals from those medical research initiatives that are reliant on public participation. We have argued that participatory medicine can facilitate inclusive and diverse participation in these initiatives by (1) providing valid and easy voice alternatives to those who otherwise would just opt out (in the case of public involvement); and (2) ameliorating the participatory conditions by including the perspectives of those who experience the

participatory process from the inside (patient and participant involvement). In other words, the promotion of voice is expected to bring twofold advantages: broadening participation (voice instead of exit) and improving the organization of participation and of the research (voice as feedback mechanism). In principle, by granting concerned actors the opportunity to express their concerns and interests, activism promises a more inclusive framework of medical innovation, aimed at the pursuit of the public good by taking account the needs and interests of the public. However, we discussed some concerns jeopardizing such a positive outcome, which, as seen, are all the more relevant in the context of participatory medicine as a form of invited activism: as such, we argued it needs to be analysed taking this distinctiveness into full account.

Contrasting our arguments with the other cases in this book provides scope for further analysis of the transformative role of activism in general, and on the potential and limits of invited activism and of participatory medicine in particular, in contrast with 'spontaneous' activism. In line with our argument, activism, even when perceived as a nuisance, obstacle or a momentary slowdown from the perspective of the institutions towards which it is addressed, provides a unique opportunity for feedback and for triggering and regulating innovation. Ultimately, this is to the advantage of a multiplicity of stakeholders, as demonstrated by the fact that when activism is missing some surrogates are implemented by the institutions and initiatives themselves.

As for the essentiality of the role of activism for innovation, further research may helpfully compare our setting with other cases where activism for whatever reason does not generally arise spontaneously, to observe how institutions respond to missing activism in other contexts. Likewise, research around other instantiations of invited spaces for participation would help provide further insights for the understanding of the role of activism itself.

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