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Genetic research and the collective good: participants as leaders to reconcile individual and public interests

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ABSTRACT

This paper problematises the notions of public or common good as weighed against individual sovereignty in the context of medical research by focusing on genetic research. We propose the notion of collective good as the good of the particular collective in which the research was conducted. We conducted documentary and interview-based research with participant representatives and research leaders concerned with participant involvement in leading genetic research projects and around two recent genetic data controversies: the case of the UK Wellcome Sanger Institute, accused of planning unauthorised commercialisation of African DNA samples, and the case of the company Genuity Science, which planned genetic research on brain tumour samples in Ireland with no explicit patient consent. We advocate for greater specificity in circumscribing the collective to which genetic research relates and for greater efforts in including representatives of this collective as research coleaders in order to enable a more inclusive framing of the good arising from such research. Such community-based participant cogovernance and coleadership in genetic research is vital especially when minorities or vulnerable groups are involved, and it centrally requires community capacity building to help collectives articulate their own notions of the collective good.

INTRODUCTION

Medical ethics has for a long time centred around the question of how to balance the public or common good with individual rights. One of the most famous cases in which this tension became visible is that of Henrietta Lacks. Henrietta Lacks' cells opened up one of the most fruitful chapters of contemporary medical research and care; they contributed to a better understanding of, and the development of treatments or vaccines for, a broad range of diseases (https://osp.od.nih.gov/scientific-sharing/hela-cells-timeline/). Simultaneously, they opened up one of the most controversial chapters of medical research: the person these essential cells came from, Henrietta Lacks, was an African American woman who died of cervical cancer in 1951, at the age of 31, leaving four children behind. Neither Henrietta Lacks, nor her family, knew that the cells were used for medical research.[1] After seventy years, the case of Henrietta Lacks is still one major cause of concern around participating in medical research among African American communities.[2 3] Research on Henrietta Lacks' cells is often seen as an exemplary infringement of the principle of respect for the person, one of the 'basic ethical principles',[4] and of Henrietta Lacks' and her family's sovereignty. Yet, given the invaluable contribution that the HeLa cells have made to medical research, shall we argue that Henrietta Lacks (or her family) had a moral duty to share her biospecimens? Shall we, along the same line, argue that everyone has a duty to share their biospecimens or their data for medical research, given the potential deriving good? And if there is some duty for data sharing or participation in medical research, then how can research programmes reconcile individual rights with the 'greater' good to which they may give rise?

In this paper, we argue that this debate cannot be resolved unless we move from abstract or broad notions of the public or common good towards answering the questions of 'whose' good and 'what' good is created in medical research. We put forward the notion of collective good and propose practical ways of framing this good in the case of genetic research. We thus strengthen prior calls for a focus on the collective rather than pitching the individual versus the public in biomedical and genetic research,[5] and we add to previous insights by specifying how genetic research initiatives may help collectives govern 'their' goods. Most importantly, we scrutinise the specific challenges and concerns for vulnerable, marginalised, or historically exploited communities related to such collective governance.

We develop our argument conceptually as well as through documentary and interview-based research around two illustrative recent controversies around genetic data (mis)use related to particular communities: the case of the UK institute Wellcome Sanger accused of planned unauthorised commercialisation of African DNA samples,[6] and the case of the private company Genuity Science planning genetic research on brain tumour samples from the Beaumont Hospital in Ireland with no explicit patient consent.[7–9]

The ethical conundrum: a duty to participate in medical research or a right not to?

Different approaches to ethics would prioritise different values in the context of medical research. Well-established moral principles provide solid arguments both for an obligation to benefit a patient community even at the expense of the protection for research participants, and for an obligation to protect the research participants even at the expense of the benefit for a patient community. A crucial contrast that, we argue, is not irreconcilable if research participants and potential beneficiaries are considered as part of the same collective and as such are centrally involved in any negotiation of its 'goods'.

Consequentialist ethics: contributing to the public good

From a consequentialist ethics perspective such as utilitarianism, which morally assesses choices or actions solely on the basis of the state of affairs

they bring about, the use of Henrietta Lacks' cells for medical research, with or without consent, would be acceptable. Acritical consequentialism is actually notorious for permitting harm in principle in the name of a greater good, which can lead to counterintuitive consequences such as accepting the death of an innocent healthy person in order to obtain their organs and save multiple lives through transplants[10]: an increment of the overall good that is ridden with ethical concerns. The use of Henrietta Lacks' cells has undoubtedly caused an overall good, and at a much lesser cost than this extreme 'transplant case', and as such it is expected to be even more acceptable in a consequentialist framework (we will dedicate the next subsection to discuss what harm may have been caused in this case).

A key point in the consequentialist ethical approaches around sharing data or materials for medical research is that it is not supposed to cause (physical) harm to those the data or biosamples belong to. As a matter of fact, while there is general agreement among moral philosophers that 'benefiting others' is good, positions diverge on when and whether it is also an 'obligation'.[11]

Importantly, one major distinction in the arguments around moral obligation to beneficence concerns the 'risk' the moral agent may run into. This risk is variously formulated but generally argued in these terms:

> a person P has an obligation of beneficence to help another whenever […]P's action does not present significant risks, costs, or burdens to P while the benefits that the rescued person can be expected to gain outweigh any burden that P is likely to incur (ibidem).

The proponents of an obligation to participate in medical research claim that the use of medical data or samples falls under this case. The use of Henrietta Lacks' cells is a typical example of what the bioethicist Rhodes calls 'use of leftover biological samples', a research practice with which she associates no anticipated risks or burdens and for which, as a consequence, she argues, informed consent may be 'unnecessary'.[12] Rhodes argues that in cases like this, which involve 'no physical risk to the individual', individual liberty limitation is justifiable in the pursuit of 'the common good', and to participate in medical research is in fact a 'duty' (ibidem).

On a similar note, Chadwick and Berg,[13] referring to sharing genetic information in the context of rare diseases, argued that: 'It is questionable whether individuals should be free, from an ethical point of view, to refuse to help in an effort to relieve suffering for what could be regarded as trivial reasons'.[13] Harris[14] argued that a moral obligation to participate in medical research is 'straightforwardly derivable from either of two of the most basic moral obligations we have as persons'[14]: the obligation not to harm others (elsewhere referred to as the argument of beneficence[15]) implies a moral obligation to contribute to medical research if this likely leads to a lessening of disease burden. Likewise, the principle of fairness (the free-rider argument in Schaefer *et al*[15]) implies that, as everyone is likely to benefit from the advances of medical research, 'we have an obligation in justice to contribute to the social practice which produces them'.[14] For Ballantyne and Schaefer,[16] obligation to participate in medical research is all the more binding in relation to sharing health data, as 'bodily integrity is maintained and the harms of participation are much lower'.[16]

In the last decade, advances in precision and personalised medicine have further emphasised the role of participation in medical research for public good benefits. The central feature of precision and personalised medicine is the emphasis on the relevance of individual differences for health and disease onsets and for treatment responsiveness.[17] Precision and personalised medicine initiatives are typically cast across large-scale research cohorts where research participants' genetic, biometric, demographic and in some cases lifestyle data are analysed against their health conditions, with the aim to uncover or better understand how individual specificities play a role in health and to maximise good health outcomes. Within this framework, the argument around participation as a contribution to others' benefit is further reinforced: if certain categories or groups of people do not participate, the relevance of their specific health conditions will likely be under-represented, to the detriment of health equity. Against this background, Rhodes argues that the duty to participate in medical research is all the more imperative for those groups most affected by social injustices and health disparities:

> existing injustices can only be exacerbated by members of those groups refusing to participate in research. If your group is not studied, it is less likely that advances to benefit people with your disease or with your genetic susceptibilities will be developed. And if your group does not participate in studies that assess health disparities, no one will know that health disparities of the sort that negatively affect you exist, and corrective measures will not be taken.[18]

By following this reasoning, if people from minorities, marginalised or deprived groups do not participate in medical research, this would be to the direct detriment of those same minorities, marginalised and deprived groups, thus exacerbating medical inequity.

Deontological ethics: protecting individual sovereignty

Against voices arguing for a duty to participate in medical research, widespread advocacy calls for a right not to participate in medical research. This position is supported by deontological ethics that assesses the morality of actions or choices in relation to their conformity with moral norms, independent from the state of affairs that they bring about, and that prioritises the Right over the Good—in sharp contrast with consequentialist ethics. The Nuremberg Code's first article establishes that 'The voluntary consent of the human subject is absolutely essential'. The centrality of informed consent and respect for individual autonomy has been reiterated in all contemporary official guidelines for research with human subjects.[4 19 20]

Beyond protecting research participants from grievous bodily harm, the rationale behind informed consent and the right not to participate in medical research is explicated variously in terms of individual liberty, respect of autonomy, integrity, self-ownership or sovereignty.[21 22] Moreover, individual liberty is often justified in terms of self-ownership,[23] and in that respect unwanted or unconsented use of biological samples is a double infringement, as it would violate both individual liberty and the principle it is grounded on. It also violates autonomy, understood as acting 'freely in accordance with a self-chosen plan'.[19 24 25] But unlike any other coercion diverting someone from their 'self-chosen plans', in the case of biological samples (including cells or DNA samples), at stake are parts of the body, parts of the self. An unwanted or unconsented intrusion or a trespass on someone's body is cause of particular concern in the ethical debate: unlike any other object, this object is 'irreplaceable and inescapable'[26]—the individual *is* that object.[27] Henrietta Lacks did not incur any physical harm from the use of her cells for medical research, nor

did anyone in her family or beyond. But her (and her family's) liberty, autonomy and sovereignty were violated.[28]

It is important to note—and this is a key point in our subsequent analysis—that the principle of autonomy is not the only ethical principle deontological approaches recognise. Rather, they take full account of all moral norms, including the principle of beneficence—which is the background for the moral obligation to participate in medical research. But from a deontological ethics perspective, the moral ideal to benefit others cannot unseat the respect for individual sovereignty: if someone refuses to help others, a deontological approach may classify this as contemptible, but it will still legitimate the decision to refuse, especially if body parts and third parties such as family members are involved. Similarly, deontological ethicists may forefront a right not to participate in medical research even if they recognise that participation is a good thing to do. In each case, the consent of the individual gains primary importance, even at the expense of the greater good.

Solving the conundrum through a focus on the collective good?

Scholars debating the merits or drawbacks deriving from participation in medical research, as briefly sketched above, often refer to the notion of common good or public good. In their narrow economic definitions, public goods are described as goods that are 'non-rivalrous and non-excludable'[29 30]; a person cannot feasibly be prevented from access to the good. The public good, then, truly is the property of all; it is the most collective of all goods. Samuelson himself emphasised that 'true' public goods are in fact very rare, and similarly the benefits deriving from medical research are rarely public in this strict sense: healthcare provision is typically based on limited resources, and for various reasons some individuals or groups might be excluded from the benefits of medical research. Common goods, meanwhile, are those that are rivalrous but non-excludable. They are 'goods' in the sense that they constitute private property but this property is collectively owned or controlled. Common grazing lands are exemplars of common goods, but they are more difficult to find in healthcare (though see Prainsack[31] on the potential of health data as a common good in this narrow sense). If used in a non-economic sense and particularly in a healthcare context, the notions of public or common good typically refer to a non-specified and often future benefit arising to a public at large—such as the benefits that arise to future generations from basic medical research conducted in the present.[32] Particularly in this more abstract sense, the use of public or common good obscures vital questions that are at the centre of the current paper: that of 'whose good' it is referred to, which 'good' exactly this is, and how its creation and (future) distribution may be governed. We argue that it is crucial to confront these questions if one is to make judgements on the 'good' that medical research may deliver and that is potentially pitched against individual sovereignty, as argued above. Against this background, we propose the notion of collective good.

The collective good, in our definition, corresponds to the good for a given and identifiable collective, and it is defined by the collective itself: it is articulated through practices and discourses and negotiated by the collective of concerned actors themselves as an overall specified benefit arising for a given and clearly circumscribed community.[33]

We argue that this notion is particularly helpful in ethics debates around the obligation to participate in medical research (as well as the obligation to beneficence more generally): rather than juxtaposing the protection of individual data or biosample donors on one side against the potential benefits arising for a non-specified public on the other, it considers the good for the donors and for the potential beneficiaries simultaneously, as part of the same collective. The notion of collective good, applied in the context of medical research, escapes the conundrum of whether to prioritise the protection of the research participant or a greater good: in our definition, these are both interests of the same collective. The collective in our definition is formed by all stakeholders in a given issue, including data/biosample donors (and their family and community, if relevant) and those who expect to benefit from the research. Within a collective good framework, the balance between the duty to participate and the right not to participate in medical research would ideally be negotiated among all the concerned actors of this collective. Within it, research participants and beneficiaries may sometimes overlap, for example, genetic disease patients participating in disease-specific research, or people exposed to particular environmental or social conditions participating in research on that exposure, may benefit directly from that research. In these cases, the voices of the people affected by that disease or exposure, or belonging to that population, can be made to count directly in the negotiation, pursuit and governance of the collective good.

While in such cases the collective will be relatively easy to identify, many public health and precision medicine studies recruit people not related to any specific condition, with the aim to uncover new correlations that are not necessarily to the benefit of the research participants: as medical research is generally future-oriented, the group of potential beneficiaries in such cases is much broader and less clearly defined than the group of research participants. In those cases, circumscribing the collective at stake and the potential benefits arising to unspecified or future beneficiaries could be a more difficult undertaking, making the determination of 'whose good' and 'what good' is concerned much harder. Yet, we would argue that the voices of the research participants and of the potential research beneficiaries are always vital to explicate or at least explicitly consider when defining and pursuing the collective good. For instance, if research benefits are likely to arise to future patients of a given conditions only, then current patients and particularly current research participants could stand in as spokespersons for those future beneficiaries. In cases where benefits are less clear and may arise to a more general population, a citizen oversight board could take the role of the collective negotiating that collective good. The crucial aspect of the collective good understood as the good of a given collective as defined by the collective itself is that, by definition, if relevant voices are not included, the collective good cannot be identified. Meaningful consultation, involvement and engagement of the concerned actors are therefore essential requisites for the identification and pursuit of our understanding of the collective good in medical research.

To test and refine this notion of collective good as a way to reconcile the interests of different parties in medical research, we now consider two illustrative controversies in medical research before moving on to our empirical investigation, which engaged with concerned actors to identify the challenges and the requirement for defining the collective good through meaningful and inclusive negotiation.

The collective good in practice: genetic data controversies

While the identification of a specific collective and its mobilisation to frame and govern the creation of a good may be a solution to the aforementioned tensions between individual sovereignty and public good, countless examples exist where such a focus on the collective good was foregone by researchers or never entered

their decision-making frame. Focusing on cases where participation does not involve a physical risk to participants, we centre our exploration of the collective good on controversies involving genetic research, as they could bring considerable benefits and also cause serious sovereignty violations.

While genetic research promises previously unthinkable life-saving or life-changing medical advancements for particular disease groups or demographics, genetic information is particularly sensitive and may cause severe discrimination at different levels: from social stigma, to racism, to exclusion from some insurance plans or even from the job market.[34–36] Moreover, unlike other kinds of individual data, genetic information also directly affects family members and even whole communities with common ancestry.

Controversies around research on genetic material often arise when the concerned communities perceive the research to be carried out or planned without or beyond the consent of the research participants. Such concerns arise, for example, when a genetic research company is incorporated by, or sold to, another company: an example is the case of SharDna spa, a research society instituted in 2000 that collected genetic data from 13 000 people in Ogliastra, Sardinia (Italy) to study the factors influencing the above average longevity of that area. In 2016 SharDna filed for bankruptcy and was acquired by the UK company Tiziana Life Sciences to research cancer treatments: as Tiziana was a foreign and for-profit company, some research participants took legal action against this transaction and requested their samples back.[37 38] Another cause for concern is related to the use of genetic data for additional research purposes beyond those agreed with research participants. An example is the case of the Havasupai Native American Tribe: some Tribe members shared their DNA material with the University of Arizona to allow them to study the above-average diabetes rate in their community. In 2010, they discovered that the University was using their DNA samples for a variety of research studies, including schizophrenia, which they had not consented to: the Havasupai took legal action and obtained a US$700 000 award in damages and the right to have their samples returned.[39]

This paper is focused on two particularly illustrative contemporary controversies that the authors had the opportunity to follow in real-time: the case of the UK institute Wellcome Sanger accused of planning unauthorised commercialisation of African DNA samples,[6] and the case of the company Genuity Science planning genetic research on brain tumour samples in Ireland with no explicit patient consent.[7–9]

The Wellcome Sanger Institute controversy

The Wellcome Sanger Institute is a major UK-based genomics centre, which has been partnering or collaborating with several African-based universities and research institutes to sequence genomes from different areas of Africa, with the goal to develop microarrays—or gene chips—specifically suitable for the African continent. These chips would make genetic research on African people cheaper and easier. Sanger has conducted genome sequencing, and the company Thermo Fisher has developed gene chips from it. Four Sanger researchers complained, first privately and then publicly, that in 2017 Sanger and Thermo Fisher were planning the commercial launch of the developed gene chips without consulting nor organising permission from their African partners, even though some of the material transfer agreements Sanger had signed with African universities did not allow for commercialisation.[6] As a result of this controversy, Stellenbosch University in South Africa requested for the samples to be returned. Researchers involved in the Human Heredity and Health in Africa (H3Africa) consortium, an organisation aiming to facilitate research into diseases on the African continent led by African scientists (https://h3africa.org),voiced major concern that this controversy could compromise the trust of African institutions and people around genomics research,[6] and foster fears of exploitation in research collaborations and commercialisation.[40] On their part, the Wellcome Sanger Institute appointed an independent barrister to investigate the case, who concluded that no commercialisation or wrongdoing had taken place (https://www.sanger.ac.uk/news_item/sanger-institute-refutes-allegations-misuse-african-dna-data-partner-institutions/).

The Sanger case is an illustrative example of concerns around the use of data and materials beyond consent, but importantly it also illustrates the disruption caused among the concerned actors when a non-agreed profit component emerges in a context of beneficence. Moreover, this case is particularly important as it concerns a historically exploited population: even if the company claimed that the accusation was unfounded, it was still perceived as a case of European misconduct over African populations, and as such mirroring colonisation. While no misconduct was legally established, the accusation caused major and long-lasting concern in terms of ethical challenges for genetic research on the African continent, as it raised the risk of exploitation and of replicating colonialist practices. Significantly, this case was recalled as a must-avoid scenario by the renowned medical geneticist Wonkam who 2 years later proposed a major African genetic study.[40]

It is beyond our aim, scope and expertise to take a position on the investigation or on the validity of this allegation. The relevance of this controversy for this paper is related to the concerned communities' reactions to, and expected consequences of, the juxtaposition of the potential good deriving from facilitating medical research on African populations on one side, and commercial interests and perceived illegitimate passing over the concerned populations on the other.

The Genuity Science controversy

Genuity Science (https://genuitysci.com/), formerly known as Genomics Medicine Ireland, is a private genomics company that received multimillion euro Irish government funding through the Ireland Strategic Investment Fund. The funds were allocated to the firm to sequence the genomes of 400 000 Irish people, corresponding to 10% of the population of the Republic of Ireland and yielding deep insights into a genetically relatively homogeneous population.[41] Researchers and medical staff at public universities were enrolled to collect the samples. In August 2021 Genuity Science was acquired by theUS-based company HiberCell.[42] The tension between public funding and private commercial interests in the context of Genuity has brought patient advocates to publicly criticise the company as well as the government support of a private company and the former's inaction around its sale. We focus here on one particular episode of major concern to patient advocates: in 2020 Genuity Science, in partnership with Beaumont Hospital (an academic teaching hospital in Dublin), was planning a research study including whole genome sequencing of brain tumour samples from patients who had been treated at the hospital, to establish a 'Brain Tumour Information System' to improve diagnosis and treatments for brain tumour patients (http://btis.ie/).They planned to conduct this study on the genomes of over 9000 brain tumour patients who were treated at Beaumont Hospital between 1978 and 2018. The patients whose samples were to be used in the study were never asked for consent, nor were their outliving relatives; they were only given the opportunity to opt out. Genuity and Beaumont

gave notice of the study and of the opt-out process through three national newspaper ads in March and April 2020, in the most critical first phase of the Coronavirus pandemic in Ireland—at a time when it was unlikely that people went out to buy newspapers and when public attention was captured by the news around the pandemic.[8] Some patient advocates and relatives of Beaumont patients ferociously protested and raised public awareness on Twitter and on LiveLine, a very popular radio broadcast in Ireland. As a result, the Minister of Health extended the opt-out deadline.[9] In this case too, the potential good of facilitating diagnosis and treatment for brain tumour patients was juxtaposed with ignoring patients and their rights, which was seen as a breach of trust.[7] This is a very important illustrative case of the damage caused by the bypassing of consent even when the expected benefits are high, and it is all the more noteworthy as it directly involved a very vulnerable community: brain tumour patients and their families.

METHODS

Based on these two contemporary controversies, we analyse the concept of collective good in a recursive way: we took the controversies described above as illustrative cases to speak to representatives of the collectives about the challenges to frame and govern the collective good in genetic research. Our full research design was approved by our institutional research board.

We examined the public debates and all available public documents around the case of the Sanger Institute with African DNA and the Genuity Science case. We followed the media reports and the discussions on social networks (Twitter); we participated in public events discussing these controversies (in particular, two events on genomics organised by the Irish Health Research Forum in November 2020 and May 2021); and we conducted 21 in-depth interviews. We interviewed participants from different contexts, recruited through purposive and snowball sampling. In particular, we interviewed five Ireland-based concerned actors around the Genuity Science controversy—including patient advocates, politicians and journalists—and three experts in the ethics of community engagement in genetic research on the African continent specifically concerned with the controversy. Additionally, to gain a more complete picture of possible framings of the collective good in genetic research and derive best practices, we interviewed participant representatives or research leaders concerned with genetic research participant protection and involvement more broadly. They were affiliated with two leading genetics research projects: the All of Us Research project in the US and Genomics England in the UK. We interviewed four engagement coordinators from All of Us (including two members of the Tribal Collaboration Working Group, the All of Us working group dealing with the inclusion of American Indian and Alaska Native populations in the programme), and six people from Genomics England (a project leader and five participant representatives). Finally, we interviewed three research leaders from FinnGen, the Finland-based genetics project that was indicated as a model of good practice during the events that we followed in Ireland.

The interviews were semistructured: a similar structure was followed with all participants, however, questions were adapted to their role, expertise, and particular concerns and were sensitive to the issues raised by the participants themselves. All interviews were conducted remotely (via telephone, Skype or Zoom, per participant preference) between November 2019 and September 2021, and they lasted on average between 30 and 60 min. They were audiorecorded, transcribed by a professional transcriber, and inductively analysed in NVivo together with documentary evidence on each case.

FINDINGS

The tension between the potential collective good and the potential 'bads' associated with research involving genetic data resonated throughout our interviews, in relation to the controversies in question as well as in broader terms. Our interview participants took different perspectives, but overall they were aligned in their conclusions. They helped to delineate the specific challenges around this tension and to critically frame different ways of negotiating the good arising, in full consideration of the expected healthcare benefits but also of the historical and social vulnerabilities of the concerned populations. Three key points emerged, summarised here and presented in detail in the three sections below: (1) in order to engage with the tension between sovereignty and benefits, involved actors first of all need to ensure that the potential good is actually made transparent for the collective and equitably shared—an aspect often taken for granted erroneously; (2) as a way to cope with the tension, many saw the solution in appropriate (truly informed) informed consent. In alignment with our notion of the collective good as a result of collective framing efforts, they claimed that informed consent needs to go beyond the formal approval of individual research subjects and be case-specific and dynamic to provide participants as well as beneficiaries with a full understanding of the research, including the related benefits and risks. Importantly, consent needs to move beyond a passive acknowledgement towards an ex ante participation in key research decisions ('engagement' and 'involvement', as defined by Woolley *et al*[43]). (3) Finally, beyond consent, respondents directly concerned with minorities or vulnerable groups went further by arguing that the safest way to ensure that a good for the collective actually arises is that representatives of those groups are part of the leadership and governance of the research, codetermining what good can and should be derived from the research.

Making 'goods' and 'bads' transparent and sharing the benefits

> I just don't see where the public good is being benefited here (concerned actor around the Genuity Science controversy).

Our research participants acknowledged both potential data sensitivity-related concerns and potential health-related benefits around genetic research. However, especially participants concerned with the controversies under analysis and/or with historically exploited communities such as Native American or African communities, worried that commercial interests could prevail over the good of the community providing genetic data:

> while you are contributing to genomic research there is an aspiration that products are going to be coming out that are beneficial, but who is gaining out of that research, how has the benefit of sharing been considered? (expert in the ethics of genetic research on the African continent).

In particular, in the context of the Irish controversy, interview respondents complained that patients were treated as commercial 'assets' rather than beneficiaries, inverting a potential collective good into a private one:

> The patients are your assets here. They are the commercial gold within this. They are the assets of this and they are the people that this affects. It is their data. It is also their health. Maybe they will be the beneficiaries as well, but they are not being treated as

> if they have any involvement in this other than they are an asset (concerned actor in the Genuity Science controversy).

In the context of African-based genetic research, interviewees expressed concern that research could be (perceived as) exploitative, to the benefit of commercial profit of other parts of the world, rather than of African populations:

> Research is still seen very much as likely to be exploitative rather than contributing to the overall good and that is a challenge that researchers will continue facing for a long time (expert in the ethics of genetics research on the African continent).

Native American representatives in the context of All of Us strongly stressed the importance of making explicit the benefit expected specifically for their community:

> one of the things that we think about is how does it impact our community…And is there a benefit back to the tribal community (Native American representative in All of Us)

In general, interview respondents engaged with genetics research in all the contexts covered in our study advocated for full transparency about the expected benefits, which should be clearly articulated to research participants:

> I think a very important role that the patients have is to create by asking these questions by saying well that's fine, I kind of understand what you are doing here, but tell me, which patients are going to benefit, and when do you think this will happen. (Genomics England board member)

Thus, a first step in framing the collective good is full transparency over the likely benefits arising from the research for a particular community, which may include commercial benefits to third parties, but which need to be laid open for the collective to decide on its own just share of those benefits.

Consent and beyond: collective engagement

> She [Henrietta Lacks] might not have given her approval, but look at all the people that she saved. It might be just nice to ask her (concerned actor in the Genuity Science controversy).

Somewhat unsurprisingly, a major concern about most genetic controversies was related to the lack of full consent of the concerned actors. More importantly, rather than situating the issue of consent purely at an individual level, interview respondents concerned with the Genuity Science controversy implicitly took as unit of reference a collective in which the interests of the research participants and the interests of the beneficiaries are equally important, as they acknowledged the importance of research, but did not accept consent bypassing:

> I am pro research but patients and their informed consent must always be prioritised. (concerned actor in the Genuity Science controversy)

Similarly, interview respondents argued that a major issue around the Sanger controversy was that consent was not respected:

> there are several things that could have been done and an obvious one was obviously communicating to people, just abiding by what people agreed to (expert in the ethics of genetics research in the African continent).

Crucially, while interview respondents across different contexts highlighted informed consent as essential, they were also very critical of its limits, and they proposed formats that give the collective an opportunity to negotiate consent terms. For example, they criticised the way and circumstances consent is taken, which may not give research participants the opportunity and the tools to understand what they really consent to:

> patients weren't being consented properly, samples would be taken when they were under anaesthetics without their consent, so that is abuse. That is assault, technically that is assault. Sometimes they were consented on the way in, but they would be asked maybe for four vials of blood and they took seven, for example. And patients were being consented when they were under pre-med, patients didn't understand when the consenting nurse said 'I don't think you should consent them', they are not capable (concerned actor in the Genuity Science controversy).

Others—particularly Native American representatives in the context of All of Us—were deeply concerned around the concept of 'broad consent' and advocated for more explicit descriptions of the concrete risks, and for participants to be recontacted about the specific use of their data:

> Alaska Native Tribes decided not to participate in the All Of Us initiative because of the broad consent. I know that they are getting ready I think in the future to kind of go back to participants. American Indian and Alaskan Native participants and I think to really go back over the consent and kind of make it a little more explicit the potential harms in what people consented to (Native American representative in All of Us).

Interview respondents across contexts advocated for proper participant engagement as part of, and beyond, the consent process, to let research participants understand in full and participate in the decisions around their data. They claimed that if research participants are properly informed and consulted about the specific uses of their data, they generally accept uses that otherwise they would not consent for:

> I think the broad consent was quite a tricky concept. 'If I give now the consent and samples and data can be used for many, many years and years after this, how can I cancel the consent? Can I cancel?' […] of course that was said very carefully in the information letter, those results that have been already produced cannot be withdrawn anymore. So the withdrawal of consent is starting from the date that you withdraw the consent. People understood. (Researcher with FinnGen)

While it is unlikely that consent is negotiated individually, community representatives may play a vital role in engaging early and continuously in genetic research projects over consent issues. In this regard, respondents involved with Genomics England described the inclusion of research participant representatives in the project's 'Access Review Committee' (the committee dedicated to examining and responding to data access requests):

> These are very interesting discussions about when you give access to a commercial organisation, it is important to understand what they could do, how they could contribute to patients. […] If it is properly expressed and understood then mostly the patient representatives, clinical representatives are supportive of these commercial applications (researcher with Genomics England).

A similar model of ongoing research participant consultation about data access and use was advocated in the context of All of Us by Native American representatives:

> I think that's really important to have native researchers on the Research Access Board. And then once you decide that there are

> findings that could be published, do you go back to the tribal community? Do they get to have final sign-off on that publication or at least provide some interpretation around that research that perhaps researchers might not understand without having the tribe have one more last look at that publication (Native American representative in All of Us).

Thus, while past research has considered the practical challenges of dynamic consent, a collective good perspective may help think through pragmatic ways in which to involve the community in question on a continuous basis, ideally from the early stages of the research process as long as the genetic data collected is likely to yield benefits and that new uses may have to be negotiated.

Beyond engagement: cogovernance by 'people like us'

> We spend quite a lot of time telling the world that one of the reasons that we trust what Genomics England are doing with our data is because there are people like us overseeing what happens to it (participant representative in Genomics England)

Across the cases we analysed, beyond the consultative role discussed above, interview participants advocated for community representatives to be the leaders, or the coleaders, of the research itself, in order to make sure that the benefits of that community are at the heart of and pursued throughout the entire project. While there may of course be misalignments within the collective as to the goods arising from genetic research, respondents identified that the surest way to ensure that negotiations around the collective good are facilitated in the first place is to involve community representatives in the governance and leadership of the research. Respondents across case studies advocated for research participants or concerned community representatives to actively and meaningfully oversee genetic research. The African controversy was particularly illustrative from this perspective and was heavily referred to in this context. Respondents concerned with genetic research on the African continent insisted on the vital importance for the research to be conducted with local leadership, not just (token) involvement:

> It is not about coming to get the samples, fly over to Europe or wherever and do your analysis, get whatever and that's it. It's not. It's about really investing in the lives of people here. It is research conducted here for the people here undertaken in Africa, I think that is the conversation completely. So if you have got a general investment in research in Africa then the investment should generally be in Africa and not be taken out (expert in the ethics of genetic research on the African continent).

While they explicitly welcomed partnerships with institutes and organisations based in different parts of the world, they also worried about the risk of exploitation, and they envisioned African leadership as the way to overcome it:

> There is often something about commercialisation, whether true or perceived, in conjunction with African data and the perceptions of very limited control by Africans and very limited interest really in the interests of African participants or African researchers. That then very quickly gives rise to accusations of coloniality or exploitation or any of these other kinds of concepts that have been used. […] I think those concerns are real and they need to be taken seriously, which is why there is another reason why African leadership is so important, in design and conduct of genome research. It is because at least partially it is a way of ensuring that the perception of exploitation is addressed (expert in ethics of genetic research in the African continent).

In parallel—and arguably for parallel fears of replicating historical exploitation and colonisation—the need for inclusion in the research leadership and governance was strongly highlighted by Native American representatives. For these respondents, it is vital that tribal representatives are part of the research governance in order to ensure that no harm arises to them and that their interests are pursued at all times:

> It's really important that Native people are overseeing specimens from themselves and from their community members and so they can make sure harm isn't done (Native American representative in All of US).

They advocated for a model in which native tribes themselves can lead research *on* themselves, at a local level, rather than outsiders researching on them in a 'hit and run' format:

> one of the benefits that Tribal leadership would like to see is really that there be capacity built within the community to hopefully lead research themselves over time and be involved and be in the research studies. So it is not outsiders coming in and doing the research and then leaving, you are building this capacity in the communities and in the local settings to do the research (Native American representative in All of US).

Although articulated in different terms, a similar argument around the need for research to be conducted by those whose interests and good are at stake was also presented in the context of the Genuity Science controversy: interview respondents claimed that a private company naturally acted in their *private* interest, and called for a public Irish genome project that would act in the public interest:

> This current mess could be avoided if the Government invested in a public genomic project, in tandem with large-scale public engagement. A state-led project could lead to huge breakthroughs in cancer and rare disease care without the privacy violations associated with a more privatized model (concerned actor in the Genuity Science controversy).

Moving beyond issues of consent and involvement, and in parallel with research in natural common pool resources, our respondents thus confirmed that the collective good can only be a truly collective one if it is the community themselves who governs it. To be effective, this involvement needs to move beyond consultation and superficial patient–public involvement measures toward proper cogovernance and coleadership.[44] We are fully conscious that this may create concrete practical issues in terms of length and depth of community involvement, and we will discuss below several basic considerations that need to be engaged with for such collective governance to be realised.

DISCUSSION: 'PARTICIPANTS AS LEADERS' TO DETERMINE AND DIRECT THE COLLECTIVE GOOD

The analysis of historical and current genetic data controversies, and the interviews we conducted with concerned actors, gave us important material to think through the concept of the collective good in the context of genetic research, and whether the collective good argument could be used to unpack genetic data controversies when individual or community sovereignty is at stake. It also allowed us to consider how a concerned community could be supported in framing, identifying and governing the collective good. If collectives themselves are able to articulate what the good is that they may gain from a particular genetic research

initiative and what harms may arise, then more informed debates can be had on whether any sovereignty violation could be potentially offset by the benefits the initiative brings to all members of the collective.

With our study, we have engaged in a reflection on the definition of the collective good itself and on how to determine 'what is good' within a collective. The proposed notion of collective good, in which the collective itself contributes to negotiating and framing what is good, is in principle expected to meet the needs of all stakeholders, as long as they (or their representatives) are involved in the negotiation. Particularly important in terms of equity is the role of the vulnerable individuals and communities who are part of the collective as concerned stakeholders: within this framework of negotiated collective good they are expected to benefit of the collective good like anybody else—unless they are excluded from the negotiation.[45] Indeed, the appropriate format of framing and pursuing the collective good emerged as a major matter of concern in our analysis. As stressed in the context of the controversies that we analysed, informed consent is an important and well-established means to negotiate the collective good, which both minimises sovereignty violations and ensures that individuals are informed of the good they produce. However, sole reliance on (individual) informed consent can be insufficient or even detrimental to the collective good, particularly if it is too broad and/or too unspecific about what good may arise from the research. The concerns expressed in this regard are aligned with a notion of the collective good that is the outcome of a bilateral and ongoing negotiation process, rather than of the passive acceptance of a unilateral proposal or ex ante consultation. In alignment with a framework of scientific democracy,[46 47] we argue that more directly engaging democratic practices can overcome both these limits of informed consent. A strong theme emerging from our interviews was the meaningful involvement of the concerned communities, to be actively and dynamically consulted about the use of their data: consent through meaningful case-by-case consultation makes explicit what and for whom the expected good may arise, while sovereignty remains intact. The time and resources required for continuous consultation of the concerned participants and communities, in cases analogous to those we analysed, would be compensated by the reciprocal trust built and by the higher rate of consent gained when participant representatives are meaningfully involved and engaged.[43] The advantages are demonstrated for instance by the success of Genomics England's Participant Panel and participants' full inclusion in the Access Review Committee, highly appreciated by the participant representatives we spoke to.

A critical further step, pursued by organisations such as H3Africa, especially when minorities or historically exploited communities are concerned, brings concerned communities directly to the decision-making table. In these cases, to use an analogy from the political domain, concerned communities are not only voters, they are also governors. Rather than seeing 'participants as partners', to rephrase a popular slogan from All of Us, a collective good approach would thus advocate a 'participants as leaders' approach.

This 'participants as leaders' approach emerged as a central means to frame and govern the collective good, to prevent replication and exacerbation of exploitation and injustice, particularly in cases in which this is a real concern due to historical, socioeconomic or geopolitical reasons, such as around genetic research in the African continent and with Native American communities. In contexts where such particular collective vulnerabilities are not at stake, meaningful consultation rather than cogovernance may be accepted by stakeholders as sufficient for the pursuit of the collective good, as reported by the patient representatives involved in the Genomics England Participant Panel for instance. On the other hand, as noted in the context of the Irish controversy, research participants and potential beneficiaries always need 'allies' situated at the core of a project: someone whose interests are aligned with theirs and not solely aimed at profit-making at their expense. This is indeed the prerequisite to ensure that the good of the collective is at stake at all, preeminent to any negotiation or coleadership to frame it.

CONCLUSION: OFFERING 'A SEAT AT THE TABLE' IS NOT ENOUGH

The 'participants as leaders' approach that we propose is expected to maximise health benefits and minimise sovereignty violations for the collective in question. On the other hand, it makes the problem of inclusivity all the more pressing and challenging. While anyone can be fruitfully consulted, as everyone can in principle be considered an expert on their own conditions and needs, very specific competencies and capacities are required for coleading or cogoverning genetic research. As expressed by Creary[48]: 'programmes, technologies and policies, which aim to bring vulnerable individuals to the proverbial table to have a better stake at their own health status, do not often take into consideration that the table is unwelcoming, and is not equipped to deal with, understand, or hear the individual's total lived experiences that brought them to the table to begin with' (ibidem). Minorities, low-income countries, marginalised or socioeconomically disadvantaged communities are those who most need but also generally most struggle to be fully included in the definition and creation of the collective good. These communities are also likely to have limited access to the competencies and capacities for genetics research coleadership, or indeed the resources to request and engage in such cogovernance. More than investments in the research itself, the pursuit of the collective good in genetic research inclusive of disadvantaged and historically exploited communities therefore requires investments in capacity and competency building for cogovernance within the concerned communities. Such investment is vital, we would argue, to balance an inclusive definition and distribution of the collective good with sovereignty concerns through genetics research conducted *by* collectives rather than *on* them.

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