

# Shaping the Future of Health and Healthcare

## Leapfrogging with Precision Medicine

Addressing Ethical Tensions in Genomic Data Policy: Case Studies and Learnings

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# Introduction

The World Economic Forum's Leapfrogging with Precision Medicine project focuses on co-designing and piloting policy, governance and business frameworks that enable healthcare leaders in emerging economies to prepare for and integrate precision medicine approaches into their health ecosystems. Leapfrogging with Genomic Data is one workstream within this project.

Genomic data – the digitized record of a person's DNA – is an especially sensitive form of health data, and its collection and use support scientific research, improved diagnosis and disease treatments that underscore precision medicine. Precision medicine is a more precise and targeted way of screening, diagnosing, treating, or even curing a person of their disease based on an understanding of their own unique biologic and genetic makeup.

Since the completion of the Human Genome Project in 2003, genomic sequencing has become a more cost effective and available technique for gathering data needed to understand individual and population health. The value of genomic data is driving the acceleration of genomic data collection, including in low- and middle-income countries (LMICs) and emerging economies,<sup>1</sup> to fill critical gaps in the understanding of populations not traditionally included in genomics and precision medicine advances.

Governing the collection and use of genomic data – through policy, regulations, guidelines and other approaches – comes with ethical considerations and trade-offs. Policy-makers, business leaders, researchers and others must consider ethical issues before taking actions that affect or involve the collection and use of human genomic data for research and clinical use. This need is heightened further in the context of LMICs, where the history of exploitation and discrimination, existing global healthcare disparities and power dynamics overlay many health and healthcare research and treatment efforts.

This guidance document highlights six broad ethical tensions to be aware of when crafting sound, long-lasting genomic data policy. We do not imply that one ethical position is right or wrong, but that thorny ethical issues surround genomic data. As such, there is no overarching way to resolve the ethical tensions, nor are there concrete answers to questions that inevitably arise when crafting genomic data policy. Solutions will differ in different circumstances and cultural contexts. The document, therefore, seeks to provoke a thorough, diligent and nuanced exploration of critical ethical issues in the development of balanced policy, regulations, guidelines and practices.

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<sup>1</sup> While this document refers to LMICs, it is important to note that the project scope also includes high-income but emerging economy countries, such as some in the Middle East, whose populations have not traditionally been included in genomic research and who are advancing their health ecosystems to include precision and genomic medicine.

## How to Use this Guide

This guidance document offers a collection of case studies and set of questions to prompt deeper discussions about ethical tensions pertinent to the collection and use of genomic data. It is a companion to the *Genomic Data Policy Framework and Ethical Tensions White Paper*.<sup>2</sup> The document is intended for policy-makers, business leaders, researchers and others who seek to gain awareness of ethical tensions pertinent to genomic data and elucidate an ethical position that can be reflected through policy, regulations and guidelines regarding the collection and use of genomic data. While it is not entirely possible to predict how populations will react to future approaches to the collection and use of genomic data, it is both preventative of potential conflict and beneficial to societies to reflect their ethical values through mechanisms that govern these approaches.

This document addresses six universal ethical tensions – developed through research, workshops and stakeholder feedback<sup>3</sup> – that should be addressed in the development of genomic data policy. For each of these tensions, the document explores real-world examples that reflect different ethical situations, their outcomes and lessons that can be drawn from them. The examples are synthesized from publicly available sources and include situations that occurred in a diversity of geographies, organizational structures and cultural contexts. They are intended to be instructional and are paired with a corresponding list of suggested ethical questions to help guide a discussion of ethics and prompt awareness of gaps or barriers when developing a genomic data policy that balances ethical concerns.

The cases and questions in this document are presented as a starting point to develop or refine a set of guiding principles and ethical standards as genomic data policy, regulation and guidelines are developed or modified by your government or organization.

We suggest exploring cases and questions through multistakeholder working sessions. In addition to the case studies in this document, local examples or even hypothesized scenarios can be used to drive discussion. Including stakeholders who are affected differently by genomic data collection and use – research participants, patients, researchers, physicians, business leaders and others – will expose issues that may otherwise be overlooked and uneven power dynamics that often complicate ethical positions and corresponding actions. A multistakeholder approach will help cultivate a comprehensive understanding of ethical dynamics and sound path forward regarding genomic data. A companion mini-guide to running scenario-based workshops is available<sup>4</sup> as a reference. It will be beneficial to return to this document as applications of genomic data and society's comfort with those applications continue to evolve.



Note that this paper is written from a “future of healthcare” and patient-centric perspective with a focus on LMICs and emerging economies. This is not to imply that there should be a different standard among countries but to ensure consideration of the differing perspectives and needs informed by these countries diverse historical, societal and cultural contexts. Further, this work was developed with a focus on activity that takes place within the medical and scientific establishment and is specific to human genomic data and not other forms of human health data, though it may be possible to extrapolate the tensions to other areas.

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<sup>2</sup> This document is available on the World Economic Forum’s [Leapfrogging with Precision Medicine](#) project page.

<sup>3</sup> Desk research is collated in the Genomic Data Policy Resource Guide, available on the World Economic Forum’s [Leapfrogging with Precision Medicine](#) project page. Workshops included the Leapfrogging with Genomic Data workshop on 18 July 2019, a Roundtable on Ethical Tensions on 8 November 2019, and two co-led events: Genomic Data Policy Consultative Session with the Rwanda Ministry of Health, and Roundtable on Governance of Human Genome Sequencing with the Dubai Future Foundation. Throughout, we conducted numerous interviews with thought leaders in government, academia, research, medicine, civil society and industry living in and working across emerging economies.

<sup>4</sup> This document is available on the World Economic Forum’s [Leapfrogging with Precision Medicine](#) project page.



# Exploring Case Studies of Ethical Tensions Underpinning Genomic Data Policies

This section will unpack the six ethical tensions and summarize a selection of publicly available cases that illustrate the complexities surrounding genomic data. Within each tension, two case studies are presented that illustrate elements of the ethical issue at play, along with reflections on what lessons can be learned from the events described.

## Ethical Tension I: Balancing Individual Privacy and Societal Benefits

Conflicts between individual privacy and societal benefits affect almost every aspect of the tensions that follow. In the realm of genomic data, disregard for the people providing the data can have lasting, irreversible ramifications for them, their relatives and the communities to which they belong. Without robust privacy laws and protections, societies run the risk of harming those who choose to participate in research or their relatives, whose data may be divulged by proxy. Yet absolute privacy ultimately hurts everyone – it is the aggregation of large genomic data sets that help us to understand how genes affect our health and wellness.

Policy-makers must carefully consider where the ethical balance sits between individual privacy and societal benefits. The two case studies below illustrate different ways of approaching this problem and remind us that there are always opportunity costs at any point along the ethical spectrum.

### **GenomeAsia 100K project**

[GenomeAsia 100K](#) is a non-profit consortium with a goal of sequencing 100,000 Asian genomes to accelerate the understanding of global genomic variance and to advance precision medicine. Presently, the dearth of genomic studies outside of Caucasian populations has made many of the discoveries in fields such as pharmacogenomics (how genes affect drug interactions) useful for only a small slice of the globe. Developing more diverse reference genomes, representative examples assembled from analysing the DNA of numerous donors, for underrepresented populations will be necessary to close the gap and ensure all can share in the benefits of precision medicine.

To close the gap between Caucasian datasets and the rest of the world, the project is committed to what they call “an unprecedented commitment to open information”. This includes approaches to gathering data and obtaining consent that are not considered orthodox by many in the research community.



### *Action taken*

As an initial pilot, the consortium has now sequenced individuals from 219 populations groups in 64 countries across Asia. To make the most of this data, both during the pilot phase and future steps, GenomeAsia has decided that the project is committed to continuing to make data publicly available and accessible. As data are contributed to the consortium, they will be made immediately available in individual form wherever possible and not limited by the bounds of informed consent, national privacy laws and regulations or other external restrictions that may apply.

### *Citations*

- [The GenomeAsia 100K project enables genetic discoveries across Asia](#)
- [GenomeAsia 100k website](#)

## **United States Common Rule**

In the United States, genomic privacy is governed by several overlapping entities and regulations. One of the most important is the Federal Policy for the Protection of Human Subjects, or [Common Rule](#), a set of rules and regulations surrounding research conducted on human subjects, including genomic research.

A particularly contentious issue in Common Rule debates centres on how consent should be enacted. If a researcher acquires DNA, should they be able to reuse that sample for future studies? Must the researcher recontact everyone who donated their samples each time? Those who believe consent should cover secondary uses of genomic data want consent to be “broad” while those who think that each consent must be obtained each time a person’s data are used wish consent to be “informed.” It should be noted that the debate between broad and informed consent is nuanced, and this is a high-level description.

Prior to 2015, the Common Rule allowed “non-identifiable” specimens to be re-used in research without the consent of the donors. However, advances in science have brought concerns about the possibility of re-identifying the donor to the fore, with many researchers arguing that there is no such thing as a non-identifiable [sample](#).

### *Action taken*

In 2015, the US federal government proposed revisions to the Common Rule that would require researchers to obtain consent for all research on all new biospecimens, regardless of whether they were de-identified. These proposed changes angered many researchers who believe that such a system would dramatically decrease access to biospecimens and genetic data and create an enormous administrative burden.

Before such rule changes are implemented, there is a period during which the public can comment on the proposed changes. In this case, over 2,000 comments were received, some from researchers and physicians concerned about the pace of research and others from donors worried about their privacy. A participant with a rare mutation [wrote about](#) how she willingly consented to be a research subject, but was unsettled when she discovered her information publicly available for other studies, while a physician spoke about the medical breakthroughs that might never have happened with more stringent privacy rules, [saying](#) that “every patient with a form of cancer...deserves the right for more research on any tissue available... if not for testing on past tissue...malignant melanoma [would still be] a death sentence. Today the death rate is decreasing due to tissue testing.”

#### *Citations*

- [Notice of Proposed Rulemaking](#)
- [Comments on Proposed Common Rule Change](#)
- [Your Cells. Their Research. Your Permission?](#)

#### **Takeaways and lessons**

GenomeAsia 100K has set itself apart from most programmes presently underway, which consider consent to be an indispensable part of any research endeavor. Yet, as the leaders of GenomeAsia point out, the amount of data available for a continent that is home to nearly 4.5 billion people is paltry relative to the information available to scientists in Europe and the United States. They are prioritizing the societal benefit of correcting this inequity and supporting research. Should perceived urgency influence one’s position on the ethical spectrum and, if so, is this adjustable in the future?

The situation in the United States offers a counterpoint to the GenomeAsia project, exploring the possibility of making privacy and consent requirements *more* stringent, potentially impeding research and delaying medical breakthroughs.

These case studies exemplify the tension between individual privacy and societal benefit and, in both scenarios, illustrate inevitable trade-offs. It is easiest to see what the harm could be to individuals, as the damage done here is “positive” or causal – many people participate in genetic research for specific reasons and might have qualms with their information being used elsewhere, or they could be concerned about who will have access to their information. On the other end of the spectrum are the “negative” harms done – the discoveries not made, the genetic information not gathered. These negative consequences are much more difficult to quantify, but must always be considered when deciding what sorts of tradeoffs should be made.

## Questions to guide ethical policy development

Questions to discuss that will help develop an approach to this ethical tension are:

- Does society lean towards autonomy or societal good or balance both? How might this manifest regarding genomic data?
- In what context should individuals who supply their genomic data be decision-makers on that data versus having researchers or healthcare providers be the decision-makers?

Once an ethical approach is developed, more specific questions that will help guide implementation through policy, regulations, guidelines or other means are:

- Should consented data be identifiable, anonymous, or de-identified? How will that be ensured? Under what circumstances is identifiability appropriate?
- Will genomic data be linked to other pieces of health data? How might this increase the risk of re-identification?
- Should consent be broad, tiered or specific as pertaining to genomic data use in research and medical testing?
- How will data governance be addressed:
  - Who owns the data?
  - Who has access to the data?
  - Who benefits from the data and how?
  - Who is responsible for safeguarding the data?
  - Who is accountable for upholding requirements?
  - Do these roles and responsibilities shift at certain points throughout the lifecycle of the data?
- Should consent be static or dynamic? Should scientists be required to re-obtain consent each time a donor's genetic data is used in a study?
- Are appropriate types of consent and privacy different depending on the risk of re-identification?
- Does the potential gain from a study change the calculus about respect for privacy?
- If broad consent is used, what are the limits? Can only researchers access the data? What about corporations, insurers, or law enforcement?

## Ethical Tension II: Balancing Open and Restricted Data Access

In the past decade, examples of data, especially health data, falling into the wrong hands have become more frequent, driving debates over how, and by whom, sensitive data should be accessed. Deciding who will have access to genomic data sets and under what circumstances is essential to ethical policy creation and sound regulation.

Allowing open access to genomic data will increase the speed at which precision medicine can advance, while leaving data in silos may stymie important research efforts, blocking urgently needed breakthroughs. This tension reflects the responsibility of genomic data holders to both the individuals who provide the data

and those who can benefit from the insights drawn from those data. Though open access may be a laudable goal, it is important to also consider what could go wrong if regulations do not put enough stipulations on entities holding and using genomic information. Who might misuse data that can flow too freely? What are the consequences of allowing entities to freely access genetic data?

Adding to the conflict embedded in this tension is the belief that population-level genomic data are valuable, considered by some to be equivalent to a natural resource. Restricting access may be a way for a business, organization or jurisdiction to increase or singularly benefit from the value inherent in a certain genomic dataset, or it could leave them behind as collaborators shift elsewhere. More open data access could lead to insights that carry more value than one dataset alone, yet those insights may confer uneven benefits to those who are already technologically advanced.

When considering ethics around genetic data, balancing open access and restrictions on data flows is essential. Below are two illustrations of how the ethics of data access has played out under different policy structures, both of which offer valuable lessons.

### **Project Nightingale**

In November of 2019, a story broke about a Google initiative, [Project Nightingale](#), which aimed to aggregate and analyse detailed personal health records, including genetic data, of 50 million Americans to create new, AI-backed software that could suggest individual treatments to patients depending on their health history and environmental factors. According to *The Wall Street Journal*, Google began Project Nightingale in secret with St. Louis-based Ascension, a Catholic chain of 2,600 hospitals, doctors' offices and other facilities, with the data sharing accelerating since summer 2019. The data involved in the initiative encompasses lab results, doctor diagnoses and hospitalization records, among other categories, and amounts to a complete health history, including patient names and dates of birth. Though the project involved nearly one in six Americans and spanned 21 states, it was not disclosed to patients until the newspaper broke the story.

Most privacy experts do not believe any laws were broken. The Health Insurance Portability and Accountability Act (HIPAA) allows for business associates of medical providers to use patient data in many ways that are not explicitly defined. A Google spokeswoman agreed, saying: "We believe Google's work with Ascension adheres to industry-wide regulations (including HIPAA) regarding patient data, and comes with strict guidance on data privacy, security and usage."

### *Action taken*

The story generated anger and backlash, including a [federal inquiry](#) into the project that had yet to begin at the time of this document's publication. Additionally, several IT executives and prominent politicians have called for an [overhaul of HIPAA](#) in the wake of the WSJ publication. As the [chief information officer of Boston Children's Hospital](#) put it: "HIPAA was crafted many decades ago now and it's probably time for it to be updated for the current world...The safeguards provided for in HIPAA probably lack specific granularity and detail for the instances like the one we just saw unfold before us." Following the story, Google has halted the project.

### *Citations*

- [Google Is Slurping Up Health Data – and It Looks Totally Legal](#)
- [IT execs call for HIPAA overhaul in 'Project Nightingale' wake](#)
- [The tricky ethics of Google's Project Nightingale, an effort to learn from millions of health records](#)
- [Google's 'Project Nightingale' Gathers Personal Health Data on Millions of Americans](#)
- [Google's 'Project Nightingale' Triggers Federal Inquiry](#)

## **Genomics England**

Genomics England, an undertaking mainly funded by the British government and the Wellcome Trust, sequenced 100,000 whole genomes from National Health Service (NHS) patients with rare diseases and their families in addition to patients with common cancers. The initiative was launched in 2012 and reached its goal in 2019, passing 100,000 whole genomes in July of that year. From the beginning, the project aimed to share the genetic information, along with other health data, broadly among researchers in the public and private sectors. As with any project hoping to aggregate so much data, privacy was immediately identified as a concern – who would have access to the data and under what circumstances?

### *Action taken*

To address questions about the data access and better understand what citizens were comfortable with, Genomics England undertook several actions to engage the public, including a public dialogue on genomic medicine so members of Genomics England could understand where ethical red lines are and what constitutes acceptable usage to participants. The three themes that emerged from this dialogue were reciprocity, altruism and solidarity. Red lines included using the data to enhance human capabilities via genetic modification, stratification of citizens using predictive analysis of genomes, and monitoring participants for surveillance or marketing purposes. Additionally, the programme has been cognizant of how important openness about data access and use is to participants; private companies are allowed access to de-identified samples only if they are specifically approved, and participants can always see which companies are involved.

### *Citation*

- [Genomics England website](#)

### **Takeaways and lessons**

Google's Project Nightingale and Genomics England share much in common. In both cases, the underlying goal was to aggregate huge amounts of sensitive health data, including genetic information, to improve the care of individuals. Yet, one project has now ended under public scrutiny, prompting US lawmakers to talk about revamped data access legislation, while the other has largely been successful and is powering the NHS's push toward genomic medicine across the UK healthcare system. Deciding to share data broadly or narrowly is not necessarily an ethical decision, but the manner in which laws are created and information is disseminated does often carry ethical valence. To navigate between the potential excesses of open data access and possible damages to research that could come of restrictive data sharing laws, policy-makers, researchers, business leaders and others should ask themselves several questions.

### **Questions to guide ethical policy development**

Questions to discuss that will help develop an approach to this ethical tension are:

- What does open access mean in this context?
- Should patients or research participants have access to their own data?  
Is there a moral obligation to return this data if requested? Should data be removed from access if requested?
- Should participants receive regular updates about where their data is being used?

Once an ethical approach is developed, more specific questions that will help guide implementation through policy, regulations, guidelines or other means are:

- Are data sharing protocols different for entities in your country versus internationally? Should data collected always remain in country? How might this benefit or hinder advancements in genomic based healthcare?
- Who gets to decide who has access? Are there mechanisms in place to ensure consistency?
- Who is the gatekeeper of this data? What is the gate?
- Is there a transparent way for people to see who is using their data?
- Is there a protocol in place for participants to withdraw their data?
- Which types of organizations or professions should have access to human genomic data and how should that access differ? For example, will the data only be shared with researchers, or will entities like corporations, insurance companies or law enforcement be granted access in some circumstances?

### Ethical Tension III: Balancing Benefits and Altruistic Donations

Deciding whether and how to compensate those who participate in research or whose genomic data is included in a dataset that is monetized or leads to monetizable insights and applications is a nuanced question. The distribution of value derived from research is known as benefit sharing. Most international ethics guidelines support providing some form of benefit for research participation, but the nature of that benefit will vary by situation, and the provision of additional benefits stemming from the use of someone's data is often a controversial issue. Genomic data represents an especially difficult benefit sharing use case as these data may lead to a discovery that benefits human health, and this discovery may be monetizable or it may not. In either case, questions will arise regarding what constitutes a benefit, when it is appropriate to provide a benefit, what form that benefit should take and on whom it should be conferred.

Some experts believe people should be directly compensated in a monetary or non-monetary way for their participation research and also for value derived from their data (e.g. commercial application based on the research). Others believe participation should be viewed as an altruistic act. Health discoveries often require large numbers of research participants and have the intent of benefitting society, though sometimes the discoveries come from a few patients who want to help doctors find a solution to a disease. Putting a price on genomic data may infringe upon a social norm of altruism and lead to negative consequences such as less research participation, slower scientific advancement, or valuing people differently based on their genetic uniqueness, prevailing research priorities and prevalence of certain diseases.

In regard to receiving benefits, some believe benefits should be devolved not to the individual, but to the communal level. However, there is no consensus on how far one should “zoom out” when defining a “community”. Regardless of how this difficult term is defined, it is essential to remain aware of the impact of power differentials between those conducting the research, and those participating in the research. Consideration of this tension is an indispensable part of the ethics of genomic data policy. The two examples below illustrate what the pros and cons might be of relying on altruism, or compensating those who donate their genomic data.

#### **RD-Connect**

Rare disease patients often spend years going through a “diagnostic odyssey” as they seek answers about their malady. The main barrier to diagnosis is the paucity of similar patients in most data sets. If a particular disease is literally “one in a million,” the odds that a clinician or the data set they query has another patient with the same condition can be very small.



### *Action taken*

The [RD-Connect Community](#) is a non-profit international organization of people and organizations sharing the vision of building an open community that works to improve rare disease research. It was established in 2012 “to promote, facilitate and accelerate rare disease research by maximizing the availability and (re)use of rare disease data and biosamples through provision of infrastructure, tools and services to share, analyse and link datasets and biosamples in a secure and regulated way.”

Expanding access to data sets and gathering new data from patients is essential to shortening the diagnostic odyssey and finding cures. The urgency of the problem has made the rare disease community particularly altruistic: EURORDIS found that 97% of rare disease patients are willing to share their data not because they expect direct compensation, but because they understand how important each contribution is to the community as a whole.

### *Citations*

- [RD-Connect](#)
- [EURORDIS study](#)

### **Nebula Genomics**

The explosion of direct-to-consumer (DTC) genetic testing companies over the past decade has resulted in several different business models for contributing genomic data. Nebula Genomics, started by geneticist and Harvard professor George Church in 2016, is creating a model in which customers could potentially receive direct compensation for their genetic information.

Most DTC companies hope to stay profitable not by selling sequencing kits but by relying on customers to consent to having their de-identified data used by the company in various ways, including development of new therapies. 23andMe, a US DTC company, reports that over 80% of customers consent to having their data used in research, a number that highlights the altruistic spirit many people have toward donating their information even when they might not directly benefit. As explained in the Risks and Benefits of Participation section on 23andMe’s website, “If 23andMe publishes study results in peer-reviewed journals, there may be an indirect benefit to you as scientific knowledge increases and/or new drugs or tests are developed.”

### *Action taken*

Taking a different strategy, Nebula states that customers will retain data ownership and can choose to whom their genomes will be available for sequencing and the compensation desired. The company hopes to develop a marketplace where researchers can query Nebula’s datasets for specific traits and then be connected, via blockchain, with a customer whose profile matches those traits. Nebula’s hope is that customers may be compensated by research companies that are willing to pay to access their anonymized genetic data.

In 2019, Nebula announced their first pharma partnership with EMD Serono. As part of the deal, EMD Serono will be able to use Nebula's network of anonymized genomic data. This new pilot is reportedly focusing on lung cancer patients and in exchange Nebula is offering participants fitting the criteria germline and tumor whole genome sequencing at free or reduced cost.

#### *Citations*

- [Nebula Genomics website](#)
- [23andMe consent document](#)

#### **Takeaways and lessons**

While the RD-Connect Community and Nebula Genomics are not directly comparable, they present two paths forward vis-à-vis benefit sharing in genomic data. While many considered the possibility of directly compensating individuals for their data unrealistic, Nebula Genomics is in the early stages of building a model of benefit sharing for access to genomic data that may very well prove that technologies such as blockchain can enable individual negotiations between citizens and companies wishing to use their data.

However, many argue that the idea of compensation, beyond being logistically difficult, is inherently an unethical way to think about research. RD-Connect stands in contrast to Nebula by relying on a spirit of altruism and a belief that advancing genetics should not be a market-driven venture. Both arguments have their merits, and policy-makers should carefully consider their unique scenario when deciding what constitutes an ethical path forward for their circumstances.

The cases above present two options, but are not the only paths. Benefits may include non-monetary or monetary exchanges of value, and distribution of benefits can occur at different points along the value chain and for different purposes. Sharing benefits can be a transactional exchange or a mechanism for training, knowledge sharing and development of research labs in low-resource settings. Receiving benefits is a highly complex, nuanced topic on its own, and balancing it against altruistic donation will require careful consideration.

#### **Questions to guide ethical policy development**

Questions to discuss that will help develop an approach to this ethical tension are:

- Who decides how benefits will be shared? Is the process democratic? Representational?
- Should data contributors be consulted about what sorts of benefits they wish to see? How will this take place?
- Does benefit sharing differ depending on the type of research? Is altruistic donation more acceptable if the research has no commercial value?

Once an ethical approach is developed, more specific questions that will help guide implementation through policy, regulations, guidelines or other means are:

- At what points before, during and/or after research should benefits be discussed and determined? Should there be options to reassess based on research outcomes or commercial potential?
- To what level should the benefits trickle down and how broadly should benefits be distributed?
- If benefits are returned to communities, who decides what constitutes a community?
- What is the timeframe for returning benefits?

#### Ethical Tension IV: Balancing Researcher and Community Oversight

As medical research became standardized in the 20th century, it became clear that ethical oversight of research endeavours was essential, leading to now standard institutional bodies such as national ethics boards, institutional review boards and research ethics committees. Genomic research raises new ethical issues, including issues related to the handling of incidental findings, findings with implications for family and the community, or the risk of conflict with cultural or religious beliefs. Determining how to adjust practices or procedures to ensure appropriate oversight, with checks and balances, and participant or community engagement, is a timely issue and will vary in different contexts.

Awareness of and attentiveness to this tension will help keep those with power from imposing their own cultural contexts on communities with different conceptions of the body, inheritance and communal belonging. It may not even be apparent to some that they are perceived as having power, which could influence the behaviour of the researchers or the participants with whom they engage.

Deep considerations must be given as to how to best assess and uphold what is ethical across contexts. When decisions are made about what counts as “ethical” research without input from the communities participating, cultural needs and nuances may be passed over. When decisions are made without input from participants on study design, the number of people willing to participate may drop or meaningful insights may be overlooked. Yet, it is also true that the complex nature of genetic research demands multidisciplinary input from the scientists and researchers who understand the implications of their project. A balance must be struck so that research may proceed in a manner that respects the deep knowledge communities have of their needs and aspirations and that researchers have about the scientific aspects of their work.

## San peoples

The San peoples of Southern Africa have intrigued researchers for decades; their DNA suggests that they have been isolated from other human populations for over 100,000 years, yielding a unique window into human ancestry. However, the methods and goals of the studies conducted on the San were decided upon with little or no input from the San. The one-sided nature of the research was highlighted in a 2010 *Nature* study examining genetic markers in the San. The study included use of insulting language such as the term “bushmen,” using jargon when communicating with the San, failing to consult study communities about findings before publication and approaching individuals before asking community leaders for permission.

### *Actions taken*

In response, the San peoples published their own [Code of Ethics](#) to help researchers understand how consent can be acquired and research can be done in the context of San cultural traditions. The code describes key tenets researchers should follow, going into detail about how to act with respect, honesty, care, justice and fairness and due process within the context of San culture. Though it is not legally binding, it is the first code of its kind to come from an indigenous group in Africa. As Hennie Swart, director of the South African San Institute, said: “We’ve been bombarded by researchers over the years. It’s not a question of not doing the research. It’s a question of doing it right.”

### *Citations*

- [San people of Africa draft code of ethics for researchers](#)
- [Complete Khoisan and Bantu genomes from southern Africa](#)
- [San Code of Research Ethics](#)

## Community-based participatory research in Pacific Islander populations

Community-based participatory research (CBPR) is a model of ethical oversight that seeks to equitably represent stakeholders from all facets of the research endeavour. In practice, this means being more cognizant of community representation when designing studies, a process that has often been left to researchers. The method is still nascent, but has been quite successful in several circumstances.

One specific [case study](#) involved Pacific Islander communities in Arkansas. According to the study published by the National Center for Biotechnology Information, Pacific Islanders face many health disparities, including higher rates of cardiovascular disease, cancer, obesity and diabetes compared to other racial and ethnic groups. Specifically, the Marshallese population suffers disproportionately from type 2 diabetes, with rates 400% higher than the general US population.

Traditionally, barriers to research recruitment among Pacific Islanders include fear, mistrust and concern over misrepresentation. These concerns stem in part from nuclear weapons testing carried out near islands occupied by Pacific Islanders following World War II. Communities living on nearby islands became research subjects without informed consent or appropriate language translation.

### *Actions taken*

To right historical wrongs and engender more trust among Pacific Islanders, researchers partnered with members of the Marshallese community in north-west Arkansas to understand how they could work collaboratively and what sorts of research would be most useful for the community. Through a multi-year engagement process, the Marshallese worked with researchers to identify diabetes as their primary health concern. To help abate these health disparities, researchers requested DNA samples to understand what could be done. The trust engendered by the CBPR process paid off; the study yielded a 96% recruitment rate, 97% of participants agreed to be contacted for future studies, and 97% gave permission for researchers to link information from the study to others in which they participated.

### *Citations*

- [Leveraging community-based participatory research capacity to recruit Pacific Islanders into a genetics study](#)
- [Using CBPR to address health disparities with the Marshallese community in Arkansas](#)
- [Community-based Participatory Research – An Approach to Intervention Research with a Native American Community](#)

### **Takeaways and lessons**

When deciding who should oversee genomic research, traditional models have made researchers the primary decision-makers about what types of research will be carried out. Studies are vetted by institutional review boards, but these approaches often exclude the participant voice in everything from study design to culturally and socially appropriate engagement. This study speaks to the nuance and caution that should be deployed when carrying out research on communities that do not necessarily share cultural foundations. Scientists from outside the community assumed they knew what was best, and damage was done.

The tension between including communities in ways that cause harm and leaving them out of research entirely presents a difficult ethical issue. Few would argue that underrepresented communities should not be brought into research more often than they have been historically, but questions remain about how this can be done in a way that is beneficial for all.

The San Code of Ethics and the methods used in the Marshallese study can help provide a road map for policy-makers and researchers to understand how research participants can become an integral part of crafting research studies and speaks to what an ethical balance between scientist and participant could look like. Regulators, researchers and others should consider both examples above when thinking through how approaches to ethical research should be crafted.

## Questions to guide ethical policy development

Questions to discuss that will help develop an approach to this ethical tension are:

- Who should be included on an ethics review board? How much say is given to community members versus researchers?
- Do community authorities or leaders have a place? What is the relevant local authority?
- Does your system include multiple ethics bodies? Does this lead to increased oversight, or redundancy and diffusion of responsibility?

Once an ethical approach is developed, more specific questions that will help guide implementation through policy, regulations, guidelines or other means are:

- What does an ethics board look like? If one exists, should its structure or purview evolve to address new issues pertinent to genomic data collection and use? How should it evolve?
- Does anyone have veto power? Who? Is it someone on a local ethics board, or a national one?
- Who is the governing body for ethical violators?

## Ethical Tension V: Balancing Inclusion and Exclusion

Most genomic and genetic research has been performed on people of Caucasian descent. However, minor genetic variations between populations often means that information about how genes interact with drugs and how genes affect risks of diseases such as cancer cannot be extrapolated to other populations. To gain a more holistic understanding of how genes affect everyone's lives, research must become far more inclusive and reach out to indigenous, historically excluded or less studied populations. Not considering diverse populations in research and clinical testing leads to data gaps that can result in the incorrect interpretation of genomic information and cause harm.

However, careful consideration must be given as to how these populations will be included and under what circumstances – examples exist where populations participated in genomic research that resulted in stigmatization and, in some cases, even persecution of their communities, leading them to feel they were taken advantage of by those in power, and to mistrust future research requests. Inclusion of communities in a way that is ethical and allows for mutual benefit is an essential undertaking requiring careful consideration by all engaged.

## **Havasupai**

In 1989, a Native American tribe in the Southwest United States, the Havasupai, approached a researcher with whom they had a preexisting and trusting relationship with the goal of understanding why rates of diabetes were so high in their community. If a gene could be identified that correlated with development of diabetes, perhaps a cure would be forthcoming. Approximately 100 members of the Havasupai tribe donated their blood and signed a consent document to study the causes of behavioural/mental disorders. The donors believed that their samples would be used solely for diabetes research. However, other researchers at Arizona State University (ASU) went far beyond diabetes research, publishing papers describing the tribe's "inbreeding coefficient", a potential for increased schizophrenia risk and alcoholism, and an analysis of the Havasupai's migration patterns over the Bering Strait. These claims humiliated the Havasupai and undermined deeply held cultural beliefs.

### *Action taken*

Following this incident, the Havasupai issued a "banishment order" to ASU employees and filed a lawsuit against the Arizona Board of Regents. The geneticist responsible for the work that went beyond diabetes, Therese Markow, defended her actions, saying that those judging otherwise "failed to understand the fundamental nature of genetic research, where progress often occurs from studies that do not appear to bear directly on a particular disease." Today, the Havasupai and other tribes in the Southwest refuse to work with researchers from ASU due to mistrust.

### *Citations*

- [Genetic Research among the Havasupai: A Cautionary Tale](#)
- [Indian Tribe Wins Fight to Limit Research of Its DNA](#)

## **Botswana GWAS testing for HIV acquisition**

Many regions of Southern Africa still contain populations where more than 20% of the population is HIV positive. In such places, precision medicine has helped help alleviate some of the disease burden, and designing treatments tailored to the specific genetic makeup of these populations could be a further help.

To date, most HIV research has focused on Caucasian men living with HIV. In 2017, a genome-wide association study (GWAS) was conducted on 556 Botswanans living with HIV who had not previously received treatment. The study found two genetic regions that are significantly associated with HIV-1C acquisition or progression in these populations, regions which are not correlated with Caucasian HIV susceptibility.



### *Actions taken*

Designing and carrying out a study such as this one, in which the goals of the researchers were aligned with needs of the participants, helped to instil trust and led to results that were both interesting for the scientific community and helpful for those who participated. These results suggest “new potential targets” for preventing and treating HIV and indicate the potential for using genetic markers as HIV disease progression indicators in sub-Saharan populations.

### *Citation*

- [Genome-Wide Analyses Reveal Gene Influence on HIV Disease Progression and HIV-1C Acquisition in Southern Africa](#)

### **Takeaways and lessons**

The need for greater inclusivity and more information about genetic variation can often clash with cultural sensitivities and create the potential for stigmatization. The process of understanding the needs and norms of different communities takes time and resources that some believe would be better devoted to more direct research that could result in actionable findings.

In the case of the Havasupai, policies and regulations around how researchers should engage communities were not explicitly defined, leading to a situation where the scientific community received a short-term benefit at the cost of harming the tribe and future engagement. On the other hand, aligning the goals of researchers and participants in Botswana led to an outcome where both sides were able to gain.

### **Questions to guide ethical policy development**

Questions to discuss that will help develop an approach to this ethical tension are:

- How many resources should be allocated to programmes such as CBPR in lieu of direct research funds?
- What is in place to ensure historically excluded and less studied populations are included in research?
- How can researchers and participants work together to craft a plan that is mutually beneficial?

Once an ethical approach is developed, more specific questions that will help guide implementation through policy, regulations, guidelines or other means are:

- How are you identifying individuals/representatives for engagement and engaging them? How can you ensure they are representative and knowledgeable of the participant community?
- What power does the community have in the process?
- What are the incentives for the community to be engaged?
- What is in place to protect these groups from exploitation?
- Are they consulted about expectations from the use of their genomic information?

### Ethical Tension VI: Balancing Confidentiality and Duty to Inform

Genetic and genomic test results can reveal serious, life-altering information contained within a person's DNA. When these maladies are heritable, this information may have life-altering consequences for relatives or partners of those with the genetic mutation. Healthcare practitioners typically adhere to consent forms and do not return results or incidental findings to family members; however, this increasingly places them in a difficult position regarding delivery of care and prevention of harm.

While many researchers and clinicians feel strongly about their duty to inform individuals, questions about the possibility and desirability of returning individual results to genomic research participants or patients still requires resolution. Policy-makers should consider how to handle cases in which the duty to inform runs up against situational constraints and participant or patient well-being. They should also consider when the duty to inform conflicts with the duty of confidentiality to not inform family members of findings that could affect their health and well-being.

A quintessential example of this is the test for [Huntington's disease](#), a fatal genetic disorder that progressively breaks down nerve cells in the brain. The disease generally begins to manifest symptoms, including personality changes, mood swings, unsteady gait and involuntary movements, between the ages of 30 and 50.

Genetic tests for Huntington's are readily available. Every child of a parent with Huntington's has a 50% chance of inheriting the currently incurable disorder, evoking questions about who has a right to know about these test results and who has a duty to inform the relatives of those with the disorder. Two court cases in Britain and Germany, respectively, illustrate the difficulty of balancing confidentiality with a duty to inform.

While reading these cases, which feature two western European countries, keep in mind that the ethical issues can be more tenuous in an LMIC or emerging economy context, where the absence of population-specific data makes it difficult to determine whether one's genes could increase the risk of developing a disease or cause a disease. A genetic mutation linked to a significant risk of developing disease in one population may not carry the same risk, if any, in another population. How should this be communicated, and who would provide the information and guidance given the lack of clinical geneticists and genetic counsellors? Additional ethical questions remain about providing findings if a patient is unable to access treatment, and how to disclose findings that can affect one's standing in society.

## **Britain**

In Britain, a woman is suing three NHS trusts, including a London hospital, for not sharing her father's diagnosis of Huntington's with her. She was pregnant at the time of his diagnosis and she argues that had she been aware of the diagnosis, she would have terminated the pregnancy. The woman's father was tested for Huntington's in 2009, at which time doctors at St George's Hospital requested he tell his daughter about the condition, but he refused. She later tested positive for the disorder. This is the first case in England to deal with a familial claim over issues of genetic information and raises questions around genetic responsibility.

### *Action taken*

Initially, the case was struck down due to concerns it would undermine doctor-patient confidentiality. In Britain, doctors have a duty under common law to protect a patient's confidentiality and are released from that duty only with the patient's consent. However, an appellate court overturned the decision, concluding that a duty of disclosure may sometimes override the doctor-patient relationship. Professional organizations such as the General Medical Council recognize that breaching patient confidentiality may sometimes be necessary in circumstances where not doing so would probably result in death or serious harm. The case is being heard by the High Court in London at the time of this publication.

### *Citations*

- [Woman who inherited fatal illness to sue doctors in groundbreaking case](#)
- [Duty of care versus patient confidentiality: High Court hears test case on Huntington's disease](#)
- [In genetic disease, who has the right to know – or not know – what?](#)

## **Germany**

Juxtaposed with the British case is a lawsuit in Germany, where patients have a right not to know genetic information. Nevertheless, in 2011 a doctor informed a woman living in Koblenz that her divorced husband – the doctor's patient – had tested positive for Huntington's disease. Prior to their divorce, the couple had two children together, both of whom have a 50% chance of inheriting the disorder. The ex-husband gave his consent to allow the doctor to inform the mother of the children. As minors, neither child could legally be tested for the disease, which, as the woman's lawyers pointed out, is currently incurable. They argued that she was therefore helpless to act on the information, and as a result suffered a reactive depression that prevented her from working.

### *Action taken*

The woman's case was initially rejected by a district court, successfully appealed, and then once again rejected by the German Federal Court of Justice in 2014.

### **Takeaways and lessons**

The relationship between patient and doctor has long been considered sacrosanct, and for good reason: without the reassurance of strict confidentiality, many people would be (reasonably) reticent to share such intimate details about their health and habits, leading to less effective care. This confidentiality is usually not controversial if the only people affected are the patient and the doctor, which is generally the case.

However, the growing prevalence of genetic testing may soon alter this calculus, making it more difficult to decide when confidentiality must bend to other duties. Though Huntington's disease is a particularly salient example, it is likely that advances in genetics, precision medicine and understanding of heritability will soon make clashes between confidentiality and duty to inform more common. Policy-makers must carefully consider which of the duties trumps the other.

Though such questions are now percolating into the medical field in a new way, they are not without precedent. Policy-makers can look to other areas of medicine and fields where confidentiality and duty to inform have clashed in the past, such as in infectious diseases and in the legal and psychiatric professions. In both cases, serious thought has been given to what circumstances constitute serious enough risk to break confidentiality.

### *Citations*

- [In genetic disease, who has the right to know—or not know—what?](#)
- [To Know or Not to Know? The Gene Testing Question](#)

### **Questions to guide ethical policy development**

Questions to discuss that will help develop an approach to this ethical tension are:

- Is the duty of confidentiality always absolute?
- Are there circumstances under which relatives will be informed of a result? What are those circumstances?
- If a participant explicitly refuses to share their results, must their wishes be respected in all circumstances?

Once an ethical approach is developed, more specific questions that will help guide implementation through policy, regulations, guidelines or other means are:

- Who is responsible for informing others of findings? Researchers? Participants? Physicians? What lengths should the person responsible go to locate relatives?
- Which relatives should be informed?
- Are there legal protections/punishments in place for those who share this information without permission, or do not share this information?
- How can results be delivered in a way that respects cultural norms and avoids stigma?
- Does the duty to inform change when results are not medically actionable?

## Conclusion

Testing the applicability of this guidance document through real-world applications with geographically diverse government partners will enable its revision and refinement as it continues to scale to a variety of stakeholders. Learning from local customization to refine the ideas herein, as well as expanding the set of real-world use cases, will improve the usability and usefulness of this document.

As the field of genomics continues to evolve, so too will humanity's knowledge and perspective on how to ethically govern it. Considering ethical tensions before and during policy-making processes helps policy-makers, business leaders, researchers and others think ahead to balance the possibilities of genomic data with the real-world response to and acceptance of such initiatives. It is the hope of the authors and those engaged in this community that such tools support the goal that genomic data from LMICs and emerging economies will be collected and used in a just, understanding, respectful and responsible way.

For more information, or if your government or organization has related work underway they wish to share, please contact the World Economic Forum's [Precision Medicine team](#).

## Contributors

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