

# Precision Medicine Vision Statement

A Product of the World Economic Forum Global Precision Medicine Council

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# Executive summary

The benefits of precision medicine in terms of superior health and healthcare outcomes are increasingly clear, but there are challenges to the equitable and widespread dissemination of precision medicine tools, technologies and solutions. The World Economic Forum convened more than 40 leaders from the public and private sectors, civil society and academia in a Global Precision Medicine Council (the Council) in 2019 to help shape the governance of precision medicine in the public interest. This document is the Council's synthesis of the key policy and governance gaps, and its vision for the solutions to overcome them. It should serve as a reference for the greater healthcare community with an interest in helping deliver these benefits on a global basis.

These five governance gaps are: 1) *data sharing and interoperability*; 2) *ethical use of technology*; 3) *patient and public engagement and trust*; 4) *access, delivery, value, pricing and reimbursement*; 5) *responsive regulatory systems*.

Using illustrative examples of solutions or analytical frameworks to overcome these five gaps, the Council provides areas of opportunity to accelerate precision medicine approaches globally. The main considerations and recommendations include:

- Increasing awareness of the benefits of data standardization and interoperability and fostering trusted mechanisms of collaboration involving patients to unlock the vast amounts of data needed
- Learning lessons from research efforts that were discriminatory or hurtful and focusing new efforts on inclusivity and representativeness to support ethical technology development
- Building public and patient trust and engagement by encouraging deliberation and mechanisms on if/how genetic and other sensitive health data are accessed or used by commercial companies and law enforcement
- Innovating intellectual property protection regimes for biomarkers and algorithms as part of the process of incentivizing investment in foundational new diagnostics
- Funding and publicly reporting post-market clinical trials and studies for fast-track therapeutics that allow healthcare providers to clearly understand the value of precision medicine treatments and receive payments based on performance
- Designing and implementing consistent and appropriate regulatory frameworks that protect the health information generated from direct-to-consumer genetic services in a way that support the values of patients and participants

Unfortunately, more than half of the world's population still has no access to precision medicine and is unable to reap the benefits. We must be ever vigilant about increasing the capabilities of many countries and populations to join this global movement towards more personalized and targeted ways of screening, preventing, diagnosing, treating and curing patients with disease. The importance of worldwide access and of addressing these inequities is urgent. With this in mind, the Council aims to contribute positively to the global debate and activity by framing solutions that may be scalable and useful in many settings, as well as by identifying ongoing challenges that remain resistant to solutions in order to focus new creativity on finding appropriate paths forward.

# Introduction to the charge of the World Economic Forum Global Precision Medicine Council

Precision medicine is a term widely used to denote the application of scientific processes, technology and evidence to improve the care of patients by optimizing the therapeutic benefit of interventions to treat, manage, cure and ideally prevent human diseases. Often, this involves matching a sophisticated understanding of disease mechanisms and pathophysiology with highly specific diagnostic, therapeutic and/or preventive measures to improve clinical outcomes in selected patients or populations. Everyone is familiar with certain aspects of precision medicine based on the ability of vaccinations to prevent feared infectious diseases of the past, such as smallpox and polio. By understanding the causative infectious agent and by “educating and activating” the human immune system, precision medicine has been able to conquer many serious life-threatening infectious diseases.

Modern precision medicine continues to deliver cutting-edge breakthrough therapeutic, diagnostic and preventive tools against cancer, due to our increasing mechanistic knowledge of what makes different types of cancer “tick”. By understanding that a mutation in a cancer cell leads to an uncontrolled enzyme, the drug imatinib (known initially as Gleevec® in the United States and as Glivec® in all other countries) has revolutionized the treatment of certain leukaemias and other cancers, based on targeting the upregulated enzyme in the cancer cell. This drug, as well as other remarkable examples of targeted therapy, have returned patients to normal lifespans, and access is easier worldwide now that patents have expired on several such breakthrough drugs. Precision vaccines against hepatitis have decreased the incidence of liver cancer, once the most common cancer in the world. Also, thanks to recent Nobel Prize-winning work, there is a vaccine against the viruses that cause cervical cancer (the human papillomavirus). Making cancer a less common and less feared disease is an admirable goal, which precision medicine can accomplish. The ability of precision medicine to help with emerging infectious diseases is also becoming more apparent during the 2020 COVID-19 pandemic. We know from host genome work that some people are much more likely to suffer severe symptoms, even in the absence of underlying health conditions. Being able to find these people through simple testing would enable them to be vaccinated preferentially or triaged for medical attention at the first signs of illness. The ability to use precision medicine in the response to COVID-19 is going to be important given that any vaccine is likely to be in short supply, at least initially. This shows that while the remarkable advances in understanding infectious diseases and cancers have led to revolutionary changes in patient management for a few targeted diseases, the impacts have broad relevance to global health and many aspects of health and wellness.

The World Economic Forum formed the Global Precision Medicine Council (the Council) to identify and evaluate challenges to the implementation of precision medicine in different settings, countries, cultures and socioeconomic environments. The benefits of precision medicine in terms of superior outcomes are increasingly clear, but there are challenges to the equitable and widespread dissemination of precision medicine tools, technologies and solutions. The Council aims to help shape the global narrative on policy and governance for precision medicine in a constructive way that learns from prior examples of both success and ongoing improvements. Since the need for healthcare and medicine is universal, this is an ideal example of a critical ecosystem in which technology, tools and concepts cross sovereign borders, without clear or effective accepted international governance to guide the optimal use and dissemination of these technologies in different global settings.

Over the past year, the Council has identified examples of policy and governance gaps that stand in the way of implementing precision medicine approaches. After identifying such gaps, the Council collected illustrative examples of solutions or analytical frameworks to overcome these gaps with the goal of supporting global implementation and acceptance of precision medicine. In so doing, the Council aims to contribute positively to the global debate and activity by framing solutions that may be scalable and useful in many settings, as well as by identifying ongoing challenges that remain resistant to solutions in order to focus new creativity on finding appropriate paths forward.

This document presents the vision for understanding and creating solutions to overcome the challenges of gaps in policy and governance that currently exist to advancing a precision medicine approach.



## Council process

### **Step 1: Identifying the policy and governance gaps that impede the implementation of precision medicine**

The Council members determined that it would be helpful to construct a set of broad categories of gaps in policy or governance that impede the implementation and acceptance of precision medicine. Key governance gaps to implementing a precision medicine approach are:

- Data sharing and interoperability
- Ethical use of technology
- Patient and public engagement and trust
- Access, delivery, value, pricing and reimbursement
- Responsive regulatory systems

### **Step 2: Curating and assessing case studies to illustrate potential solutions in overcoming challenges from gaps in policy and/or governance**

For each of these categories, the Council formed working groups to identify examples of challenges due to gaps in policy and governance that impede equitable and widespread dissemination of precision medicine approaches. Five working groups, corresponding to the five key governance gaps listed above, identified the relevant organizations, structures and/or decision-making processes to highlight. The working groups then found illustrative and informative case studies. These case studies were chosen either because they illustrated how certain solutions have been operationalized to overcome some of the gap(s) that block precision medicine implementation, or because they identify some of the pitfalls to be avoided.

This paper represents the initial vision statement from the Council. It is meant to serve as a document to start the conversations towards even more substantive discussions in the search for meaningful long-term solutions and impact.



## Governance gap 1: Data sharing and interoperability

Data systems that can capture volumes of standardized research, and clinical and patient-reported information enable data sharing for new discoveries and clinical applications that allow for precision medicine approaches to healthcare. There are leading examples of data sharing solutions across industry, clinical providers, insurance carriers, national health programmes and many other stakeholders. Yet many of these initiatives have differing standards and often lack interoperability or scalability, which hinders the broad use of data by multiple parties. The lack of interoperability and standards is not necessarily intentional, but rather emerges from independent initiatives with myopic goals. Creating guidelines for data standardization, technical modalities and governance principles could allow for greater collaboration amid differing incentives and objectives in data sharing models. Case studies in particular illuminate the value of standardizing structured data, ensuring data interoperability, and increasing patient participation and involvement.

### Focus area 1: Demonstrating value in the standardization of disparate data to determine genotype and phenotype relationship

To understand the biology linking genes to observable traits that can enable a personalized approach to diagnosis and treatment requires the analysis of many different types of data originating from different sources. Standardization of data and moving from health data collected from one individual to collections from populations can further enable the volume of data needed to identify new genes and causal, pathogenic variants driving disease and improve diagnosis and precision treatment options at a population-level scale. As the incentives and objectives of stakeholders are not always aligned, the upfront investment required to build the data infrastructure and governance to achieve this aim is difficult to secure. There is little research on the return on investment of sharing data, despite the moral good of providing targeted, personalized answers to individual patients. The full breadth of benefits and comprehensive return-on-investment of sharing genomic data in order to deliver a precision medicine approach to healthcare has not been thoroughly investigated given the lack of data available. A recent [paper](#) published by the World Economic Forum entitled *Global Data Access for Solving Rare Disease: A Health Economics Value Framework* explores the metrics that need to be tracked to comprehensively measure the economic value of genomic data sharing for a rare disease use case.

### **Case study 1.1: Undiagnosed Network (UDN) by United States National Institutes of Health (NIH)**

On average, it takes five to seven years to diagnose people living with a rare disease.<sup>1</sup> To help shorten this length of time, often referred to as the diagnostic odyssey, the United States National Institutes of Health (NIH) created the Undiagnosed Program (UDP) in order to diagnose the most difficult *undiagnosed* cases.

Due to the success of the UDP in providing diagnoses to previously undiagnosed rare disease patients, the programme expanded to 12 clinical sites across the US, including a singular coordinating centre, a sequencing centre, a model organisms screening centre, metabolomics centre and a biorepository, which make up the Undiagnosed Disease Network (UDN). The objectives of this programme are to: 1) improve the level of diagnosis and care for patients with undiagnosed diseases through the development of common protocols; 2) facilitate research into the etiology of undiagnosed diseases, by collecting and sharing standardized, high-quality clinical and laboratory data, including genotyping, phenotyping and documentation of environmental exposures; and 3) create an integrated and collaborative research community across multiple clinical sites and among laboratory and clinical investigators prepared to investigate the pathophysiology of these new and rare diseases and share this understanding to identify improved options for optimal patient management. The UDN has created a “way of working” that includes not only the standardization of data shared, but also the standardization of operations, criteria to measure success, institutional review board (IRB) interactions, communications, publications and research guidelines, alignment for clinical and research protocols, biospecimens protocols and a set of biobank guidelines.

The UDN solves close to a third of cases that are otherwise undiagnosed in their network. Across the network, 96% of patients are sequenced. Furthermore, the genomic data from the UDN is shared through ClinVar, dbGAP and PhenomeCentral. Due to the success of the UDN model, it was adopted in part by Undiagnosed Disease Network International (discussed in further detail later in this paper). The UDN is solely funded by the NIH Common Fund until 2022. To learn more, please [click here](#).

## **Case study 1.2: National Health Service (NHS) and Genomics England (GeL)**

Established in 2013, Genomics England (GeL) is a national genomics initiative under the Department of Health and Social Care in the United Kingdom tasked with collecting 100,000 genomes as part of the well-known 100,000 Genomes Project. The national effort, established with investments from the National Institute for Health Research (NIHR), the National Health Service (NHS), the Wellcome Trust, Cancer Research UK and the Medical Research Council, had four principle aims: 1) to collect genomes focused on leveraging genomics to improve diagnosis and care for people with cancer and rare disease in the NHS; 2) to create an ethical and transparent programme based on patient consent; 3) to enable new scientific discovery and medical insights specifically through the identification of disease-causing genomic variants; and 4) to fuel the development of a UK genomics industry. The programme has already resulted in identifying clinically actionable findings in 20–25% of rare disease patients (and as many as 40–50% in certain settings such as intellectual disability and retinal disease) and in cancer identified as many as 50% of the patients as having potential treatment options or available clinical trials. The programme's success led to its expansion in 2019, with the UK's ambition being to sequence an additional 5 million genomes and a commitment from NHS England to sequence 500,000 whole genomes as part of routine care for patients with a rare disease or cancer. The bioinformatics infrastructure created for the programme will be at the core of the ongoing NHS whole-genome sequencing platform. In addition to creating a platform to provide a clinical-grade, high-throughput interpretation of genomic data via a variety of interfaces and APIs (application programming interfaces), Genomics England also created PanelApp. PanelApp is a crowdsourcing tool that allows gene panels to be shared, downloaded, viewed and evaluated. PanelApp allows diagnostic laboratories, clinicians and researchers to: 1) share structured gene-disease validity assessments; 2) create and compare evidence-based virtual gene panels for genomic analysis; and 3) contribute to national and international efforts to establish consensus gene-disease relationships. To learn more, please [click here](#).

The integration of genomics is improving a precision medicine approach to healthcare; understanding how genomic variants contribute to observable traits can be accelerated by organizations, countries and other modes of data sharing to distinguish between causal variants versus low-frequency occurrences of a particular variant. To learn more, please [click here](#).

### **Case study 1.3: Australian Genomics Health Alliance**

The Australian Genomics Health Alliance (Australian Genomics) was created in 2016 from a **National Health and Medical Research Council** grant in Australia. Australian Genomics manages AUS\$55 million of funding allocated to genomics research through the **National Health and Medical Research Council** and the **Genomics Health Futures Mission**.

Australian Genomics is composed of more than 100 organizations across Australia and has the aim of building a national infrastructure for genomic data storage and access, to create national policies and processes to ethically access genomic data for research purposes, and to establish a system for diagnostic labs to share variant classifications and evidence for a first-of-its-kind national genotype-phenotype database. Countries building similar national genomic infrastructure are aware of the need for interoperability. Genomics England, the translational clinical genomic programme in the UK, recently partnered with Australian Genomics to enable remote access to its UK-based PanelApp. To learn more, please [click here](#).

### **Focus area 2: Enabling interoperability across different standards to improve diagnosis and research**

Although there are examples of national data sharing and interoperability, to understand biology and its relationship to disease requires the analysis of data derived from different populations around the world to discern the causative nature of gene variants in relation to, for example, disease risk and therapeutic responsiveness.

To enable potential partnerships, common objectives and principles for data sharing, the G20 created the **FAIR principles** in 2016. The FAIR principles<sup>2</sup> emphasize machine-actionability (the capacity of computational systems to find, access, interoperate and reuse structured data with little or no human interaction) as humans increasingly rely on computational support to deal with the increasing volume and complexity of data. The FAIR principles focus on: 1) Findability; 2) Accessibility; 3) Interoperability; and 4) Reusability.

In addition, The **Global Alliance for Genomics and Health (GA4GH)** provides an international forum and international working groups to enable responsible genomic data sharing within a human rights framework. The GA4GH created the **Framework for Responsible Sharing of Genomic and Health-Related Data** based on: **respect** for data sharing and participants' privacy preferences, **transparency** of governance and operation, **accountability** to best practices in technology,

ethics and public outreach, **inclusivity** by partnering and building trust among stakeholders, **collaboration** to share data, **innovation** to accelerate progress, **agility** to benefit those suffering with disease and **independence** by structure and governance. Many GA4GH driver projects leverage these principles and act as important use cases to spur the greater implementation of data sharing models.

### Case study 2.1: Undiagnosed Disease Network International (UDNI)

The **Undiagnosed Diseases Network International** has 23 member countries at the time of this report, uniting countries with varying genomic data policies to solve undiagnosed rare disease cases. The UDNI was founded using governance and operations of the UDN (previously mentioned) as a guide. However, in order to overcome the differences in regulation of data, privacy and data security across countries, a new mechanism was required. The UDNI leverages a technical solution for sharing anonymized rare disease patient data called **Phenome Central**. Phenome Central enables clinicians and researchers to identify rare disease patients across borders who share genomic variants. Matching algorithms work to identify atypical phenotypes, which also enables the discovery of genotype-phenotype relationships. While the list continues to grow, active members of the UDNI are Austria, Australia, Belgium, Bulgaria, Canada, Hungary, India, Italy, South Korea, Spain, Sri Lanka, Sweden, Thailand, Turkey and the United States. To learn more, please [click here](#).

### Case study 2.2: European Reference Networks

The **European Reference Networks** (ERNs) is a virtual network involving healthcare providers across the European Union. The Clinical Patient Management System (CPMS) enables clinical data sharing and facilitation of consultation between ERN members on specialized and rare diseases. The ERN is focused on body systems or “thematic issues”. Currently the platform supports more than 900 healthcare units from more than 300 hospitals across 26 EU countries. The CPMS is supported by virtual communication tools and Digital Imaging and Communications in Medicine (DICOM) viewers to facilitate the interaction between clinicians. Reporting tools allow users to generate reports for clinical purposes. Not only does this initiative standardize data collection across disease indications, but it also gives clinicians access to other clinicians with similar patients, driving standardized care and protocols across the EU.

### **Case study 2.3: World Economic Forum Breaking Barriers to Health Data**

A federated data system is another model that allows for genomic data sharing without the physical data ever leaving its original location. A federated data system is a decentralized technology that allows for localized data control while also enabling remote queries to aggregate multiple datasets across disparate locations. The **World Economic Forum's Breaking Barriers to Health Data** project is an attempt to create a proof of concept of a federated data system for genomic data from people with a rare disease across country borders. Working with Genomics England (UK), Intermountain Healthcare (US), Genomics4RD (Canada) and Australian Genomics (Australia), the project aims to **deploy a scalable governance framework** to support the effective and responsible use of **federated data systems** to advance **rare disease diagnosis and treatment pathways**. The project centres on **three public outputs**: 1) an economic analysis of the return on investment of implementing a cross-border federated system for rare disease genomic data;<sup>3</sup> 2) a governance framework; 3) a proof of concept that explores the technical functionality involved in operationalizing a federated data system. The project is also piloting a new, user-centred approach to governance development by including the leading national patient advocacy organizations from the UK, the US, Canada and Australia and individual patient voices.

### **Focus area 3: Patient engagement and participation**

Patients and patient foundations, especially in rare and undiagnosed disease, have demonstrated instrumental participation across the health continuum from diagnosis to real-world evidence of therapeutic value.<sup>4</sup> Examples include international patient registries and natural history studies, which form the foundation of understanding the genotype of the disease phenotype and provide the opportunity to identify new causal genes and variants. Without patient organizations or patient involvement, there would be a tremendous gap in data/knowledge. Realizing this, many patient foundations are creating data and opportunities for precision medicine where there were none.

### **Case study 3.1: Simons Simplex Collection**

The **Simons Foundation Autism Research Initiative** (SFARI) was created to support and advance research for autism patients and a genotype-phenotype database that is made available to researchers around the world, lowering the barrier to access hard-to-find data. It includes 2,600 simplex families, each of whom has one child affected with an autism spectrum disorder. Unaffected parents and siblings become the seeding of a rich, deep genotype and phenotype database, with the aim of driving the biological understanding of the mechanisms behind autism. The database provides managed access to biological data to researchers worldwide.

### **Case study 3.2: Fighting Blindness and Luxturna**

Fighting Blindness, a patient organization, not only supports a registry, My Retina Tracker, but also invested in the research to develop the first gene therapy, Luxturna, for a gene essential for normal vision, RPE65. The foundation invested about \$10 million in laboratory research that made possible Spark's Luxturna, the first approved gene therapy in the US. The funding of research mitigated the risk of development and included studies to understand the role of RPE65 in vision and retinal disease, the development of animal models with RPE65 mutations, RPE65 gene therapy testing and development, and support for early clinical research at the Children's Hospital of Philadelphia (CHOP). To learn more, please [click here](#).

#### **Notation of ongoing challenges in governance gap**

The aim of the section was not to create an exhaustive list of the challenges of data sharing and interoperability but to focus on some examples of how key challenges were overcome with successful use cases. One of the biggest challenges not addressed is that data sharing and interoperability involves a discussion across a handful of countries that are capable technically of initiating such projects. Unfortunately, more than half of the world's population still have no access to genetically driven precision medicine and are not involved. Some countries that do not have the internal capabilities are working to join cross-country programmes but struggle since they lack the internal infrastructure to do so. The importance of worldwide access and of addressing these inequities is urgent. Other factors that play a role in preventing the sharing of data are the representation of data in different ways and the use of different ontologies. In addition, there are cultural challenges to move an organization from a protective and siloed data mentality to a mindset of data sharing with all relevant stakeholders.<sup>5</sup>

## Summary and recommendations

The key points that drive successful precision medicine initiatives involving data sharing and interoperability initiatives are as follows:

1. Embrace the complexity of analysis of patient data in the collective.
2. Investment in the future through committing funding to data standards and interoperability can improve individualized care and health system economics.
3. Stakeholder alignment at the level of data sharing principles, interoperability process and governance can be a foundation for groups that may have different objectives to work together.
4. Patients/patient foundations as equal stakeholders are vital in driving precision medicine initiatives.



## Governance gap 2: Ethical use of technology

Precision medicine has the potential to transform global health outcomes. To enable the ethical progress of this technology, society must seek to maximize the benefits across the population, while minimizing its costs. A challenge in doing so is that the more specialized and targeted the therapeutic option, the more expensive it becomes. At the same time, as the economic costs of genomic sequencing continue to decline, the potential benefits to be realized from sequencing and analysis to myriad populations are increasing, especially if we focus on greater inclusivity and representativeness in research populations. This creates an urgency to generate adequate consent processes and safeguards against misuse of data. Critical ethical issues to address as precision medicine comes of age include: 1) informed consent; 2) just distribution of benefits; and 3) inclusiveness and representativeness of study populations. These three areas of focus are described below, along with several real-world examples that embody each.

### Focus area 1: Informed consent

Researchers and scientists must seek richer concepts of informed consent from research participants and build upon cross-cultural and historical examples to ensure patients and participants understand the scope of the research being conducted, the implications of the trials in which they are participating, and the risks of participation, including the potential sharing and possible misuse of sensitive genetic data.

### Case study 1.1: San peoples of Southern Africa – fighting prejudice

The San peoples have been a population of research interest for decades due to their early genetic divergence from other populations. Following a 2010 **study** published in *Nature* that included the use of language perceived as insulting to the San peoples, and a failure to consult those communities about their wants and needs, the San peoples **published** their own **code of ethics** to help researchers understand how **consent** can be acquired and research can be conducted in the context of San cultural traditions.

### **Case study 1.2: Havasupai research – cultural insensitivity**

A Native American tribe, the Havasupai, participated in research ostensibly looking for the genetic underpinnings of diabetes. However, **researchers went far beyond the understood consent**, publishing papers describing the tribe's "inbreeding coefficient", a potential for increased schizophrenia risk and an analysis of the Havasupai's migration patterns over the Bering Strait, a claim that contradicted cultural traditions. Many tribes refused (and **still refuse**) to work in genetic/genomic research due to mistrust of researchers' intent.

#### **Focus area 2: Just distribution of benefits**

Research subjects are often not the direct beneficiaries of research results, and may be unable to access the benefits because of the prohibitive costs of doing so. Researchers and clinicians should develop best practices to ensure that participation in research aiming to benefit society also brings benefits to those who participate in the research itself.

### **Case study 2.1: BRCA in Lebanese women – expanding access**

The median age of breast cancer diagnosis in Lebanon is ten years younger than in Western countries, yet far less is known about the genetic underpinnings of this population. Social stigma around BRCA (BReast CAncer gene) testing and the unavailability of relevant insurance and local testing capacity has limited Lebanese women's access to the **benefits** of this precision medicine technology. To address this disparity, the **American University of Beirut Medical Center** aims to become a local and regional leader in offering BRCA testing and developing models that allow testing to be done in-country to build capacity so that samples are not processed in other nations.

### **Case study 2.2: Research on Anhui population without return of benefits to participants**

In 1995, researchers collected DNA from more than 16,000 people in the Anhui region of China, which led to many downstream research contracts between the non-Chinese academic institutions and industrial collaborators. Despite **prior agreements** between the academic researchers and the Anhui community, the research did not **benefit** local people monetarily or via improved research or treatment options for them. Local communities, who were generally illiterate, had been told they would receive free healthcare, a promise that never materialized.

### **Case study 2.3: Nuu-chah-nulth blood samples**

In the 1980s, the Nuu-chah-nulth (Nootka) tribe of Vancouver Island in Canada **agreed to participate in a genetic study on rheumatoid arthritis** and provided more than 800 blood samples to a genetic researcher for this purpose. The **researcher** published more than 200 papers using these samples, sometimes on stigmatized topics, without the tribe being notified or receiving benefits. In 2004, the blood samples were returned to the tribe, and the Nuu-chah-nulth formed their own research ethics committee to review all research protocols.

### Focus area 3: Inclusiveness and representation

Different populations may vary in their response to therapies based on genetic and sex-based differences. Until precision medicine reaches greater scale and is inclusive of more diverse populations, treatments developed primarily in the United States and Europe for individuals of European heritage (or male-only studies) may not be as effective for populations in other parts of the world. Researchers must seek to include diverse populations in research to enable a better understanding of the effectiveness of therapies across populations and to ensure that the benefits of precision medicine reach beyond US and European borders.

#### Case study 3.1: American Heart Association – Research Goes Red

Though heart disease primarily affects men, it is also the number one killer of women in the US. Historically, research has primarily been carried out in men, something the AHA seeks to correct with its **Research Goes Red** initiative. They have combined forces with **Verily** to bolster **inclusiveness and representation** in research and use the power of big data to understand how women's risks vary from men's risks. Verily plans to combine clinical research, surveys and technology such as fitness trackers and apps to move the research forward.

#### Case study 3.2: Pharmacogenomics Research Network – collaboration with community

The **Pharmacogenomics Research Network** (PGRN) is an academic–community partnership with American Indian and Alaska Native people living in Alaska and Montana to study pharmacogenetics that features community oversight of the project, research objectives that address community health priorities and bidirectional learning that builds capacity in both the community and the research team. **Including the community** as co-researchers can help build trust to advance pharmacogenetic research objectives that also serve the community's needs.

### **Case study 3.3: Botswana GWAS: single nucleotide polymorphisms (SNPs) associated with HIV-1C**

Most HIV research has focused on Caucasian men living with HIV-1B, but a new, **inclusive genome-wide association study (GWAS)** of 556 treatment-naïve Botswananans living with HIV found two genetic regions that are significantly associated with HIV-1C acquisition or progression in sub-Saharan Africans. These results suggest “new potential targets” for preventing and treating AIDS and indicate the potential of using genetic markers as HIV disease progression indicators in sub-Saharan Africans.

### **Case study 3.4: Maori “Warrior Gene” – dangerous assumptions**

A New Zealand researcher **erroneously claimed** the Maori (a group indigenous to the island) carried a “warrior gene”, monoamine oxidase, at higher levels than other populations. He held that the gene explained why the Maori were “more aggressive and violent and more likely to get involved in risk-taking behavior”. This type of rhetoric exemplifies the dangers of using genetic analysis to explain social and cultural differences, further entrenching stereotypes with the backing of “science”; population differences are rarely predictive of individual traits, especially social traits.

#### **Notation of ongoing challenges in governance gap**

The case studies included herein help to frame an ethical pathway forward for precision medicine that safeguards against historical missteps. There are open questions that these case studies and issues raise, such as: How do we create a more robust framework for addressing cultural differences in consent practices? How can populations that have traditionally been excluded be brought into the research community in a just way? Should those who participate be compensated for their participation? If so, how do we ensure that compensation does not become a problematic inducement that further skews the demographics of the research population? Is there a role for communal compensation?

## Summary and recommendations

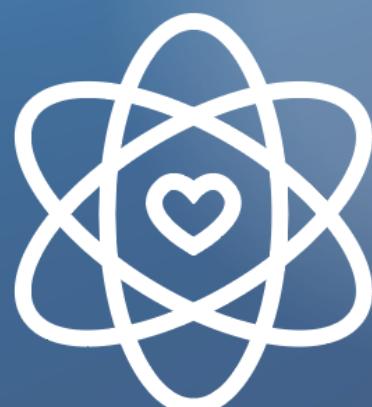
These case studies offer caution and hope for the pathway ahead to enable the ethical progress of precision medicine. Initiatives such as the American Heart Association's Research Goes Red campaign, BRCA testing in Lebanon and Botswana's genomic research on HIV provide roadmaps for how precision medicine can become more inclusive. The San peoples' code of ethics shows us that there are culturally conscious and mutually beneficial ways of engaging populations that have not traditionally been part of research if those in power are willing to listen. Collaborations with Native populations in North America suggest strategies for developing research that includes participants from the start and consciously considers what sorts of benefits may be returned to communities.

Our working group suggests the following three action-oriented recommendations for researchers, clinicians and policy-makers:

1. Identify richer concepts of informed consent that are culturally informed; help participants to better understand the scope of the research; and inform them of the risks of participation, including potential risks arising from the sharing of genomic data.
2. Develop best practices to ensure that participants also share in the benefits realized by their involvement in precision medicine research.
3. Prioritize greater inclusivity and representativeness of research populations to achieve increased effectiveness of therapies across populations and more equitable distribution of the benefits of precision medicine globally.



**TRUST**



**CORE VALUES**



**SOCIAL  
RESPONSIBILITY**

## Governance gap 3: Trust and engagement

Precision medicine is a collective global endeavour enabled by the health and genomic data of millions of people – both healthy and sick, of all ages and of all ethnicities. If people do not trust those who hold their data to act in their best interests, precision medicine will not flourish and will widen global health inequalities. Across the world, most populations, and many healthcare providers, have little or no understanding of the concepts of genetics and genomics, which may lead to distrust. While the direct-to-consumer market is booming across the globe, the use of data acquired by companies is not always transparent, which may undermine trust in health data use more broadly. Along with the global lack of genetic counsellors and trustworthy advisers, these gaps, if not addressed, place a burden on the healthcare system and will destabilize and fragment precision medicine. Here, three major focus areas have been identified: 1) understand and appropriately build societal trust in health data access and use; 2) increase awareness of genomics to the public and increase professional education; and 3) address the impact of direct-to-consumer testing.

### Focus area 1: Understanding and appropriately building societal trust in health data use and access

Confidence and trust in the way health and genomic data is being used requires more than assurance about data security or confidentiality. It cannot be gained simply by de-identifying data. Erlich et al.<sup>6</sup> showed it is now possible to infer the identity of about 60% of individuals of European descent using the genome sequence datasets built up by consumer genomics, which now number in the millions. Numerous studies demonstrate that re-identification of de-identified data is possible.<sup>7</sup> The first step in building trust begins with understanding people's concerns, which will vary from country to country.

### Case study 1.1: Your DNA, Your Say

This is an ambitious global online research project that aims to understand whether people would donate their data and for what purpose and whether they perceive any harms associated with the act of donating. It has already reached 40,000 representative public audiences from 22 countries in 15 languages. It uses short films and learning tools, followed by an online survey to capture opinion. To learn more, please [click here](#).

### **Case study 1.2: Genomics England Sciencewise public dialogue**

Genomics medicine has been part of routine healthcare in the UK's National Health System (NHS) since late 2019, having established its feasibility through the **100,000 Genomes Project**. It is well known that patients and members of the public have different views about health data use, so, before the service began, Genomics England sought the views of a demographically representative group of members of the public through a deliberative exercise led by Sciencewise and Ipsos MORI. A number of "red lines" emerged.

- No "surveillance society" through access to data by police, justice, immigration or other state, political or corporate actors to stratify, penalize or monitor individuals or groups
- No data access for marketing that enables invasion of privacy or profiteering
- No data access by insurers to set personal insurance premiums
- No disproportionate benefit by commercial companies using data

To learn more, please [click here](#).

A number of organizations have become trustworthy by ensuring that governance of genomic data use and access is by people whose data is in a particular dataset.

### **Case study 1.3: Genomics England Participant Panel**

The members of the 30-strong Participant Panel are involved in every aspect of Genomics England, including access to data. They have a central role in decision-making and are widely respected. They have been critical to trust in the 100,000 Genomes Project. To learn more, please [click here](#).

### **Case study 1.4: The National Centre for Indigenous Genomics, the Australian National University, Canberra, Australia**

The National Centre is a beacon for what true community governance can achieve. There is majority Aboriginal governance. A statutory collection has been collated with repatriation of samples. This has generated reference range data (whole-exome sequencing [WES] and whole-genome sequencing [WGS]). The centre is truly community-led. Its mission is precision medicine in which "no one is left behind". To learn more, please [click here](#).

## Focus area 2: Increasing awareness of genomics

### 1. Making genomics familiar to the public

Extensive work by the Wellcome Trust's Understanding Patient Data unit concludes that the dominant issues raised by the public in relation to trust in precision medicine are "who has access to my data" and "who benefits from its use". Trust will not be increased by greater knowledge of genomic technology or genetic science. Patients are often the most trusted ambassadors for precision medicine here.

Familiarity with genomics – its socialization – appears to be increased best via exposure to the media and popular culture. General messages such as "your genes are only part of your story" or "there is a great deal that is not yet understood" are best transmitted in non-educational setting; for instance through film, TV soaps and personal stories in magazines and radio.

### Case study 2.1: Hollywood, Health & Society programme

Hollywood Health & Society (HH&S) is a programme of the University of Southern California (USC) Annenberg Norman Lear Center that provides entertainment industry professionals in film and TV with free, accurate and timely information about public health, access to healthcare and climate change and serves as a resource and a model of excellence worldwide. It recognizes that TV has the power to communicate, but it has the facts. It has launched global centres in India's Bollywood and Nigeria's Nollywood. HH&S is funded mainly by the Center for Disease Control and by the Gates Foundation. The programme also conducts studies on the impact of storylines on audiences. To learn more, please [click here](#).

### 2. Making genomics familiar to healthcare professionals

Patients need to trust the advice of their healthcare professionals. An increasing problem is that no single health professional or administrator can keep up with the deluge of information that is genomics. There is already evidence that doctors are finding gene-based testing problematic and that it may be recommended, ordered, interpreted or used incorrectly.<sup>8</sup> Professionals need new curricula and continuing professional development (CPD), plus access to constantly updated information, possibly through an integral part of test ordering.

Precision medicine is also moving rapidly into general medical, rather than specialist, care and may be delivered in primary care or by nurses. Everyone will need specialist information as and when they require it. The information should be available in their mother tongue, with signposting where appropriate to relevant patient support groups – global in the case of rare diseases or local for more common conditions. The same information should be made available to patients in simple, accessible language.

### **Case study 2.2: Health Education England Genomics Education Programme**

Ahead of the introduction of the NHS Genomic Medicine Service, Health Education England devised an extensive genomics education programme with online courses and clinical resources. Many elements such as returning genomic test results were co-produced with patients. The National Genetics and Genomics Education Centre has developed a “telling stories” strand in which patients recount their stories to help health professionals better understand genomics. To learn more, please [click here](#).

### **Focus area 3: Addressing the impact of direct-to-consumer testing (DTC) on trust**

In 2018, there were approximately 75,000 genetic tests available, with 10 new ones being introduced each day according to one study.<sup>9</sup> The DTC market, encompassing ancestry, lifestyle and health tests, surpassed 10 million genotyped customers in 2018, with 100 million anticipated by 2021.<sup>10</sup> DTC companies appeal to individual empowerment through being able to make better choices for themselves and their families. Thanks to these companies, many consumers are now aware of genomics and most DTC companies offer accessible genetic information and are highly innovative, which should be supported and encouraged.

There is, however, a lack of standardization and regulation in the DTC testing market in many regions of the world. Tests may be based on non-representative population data; for instance, North European tests marketed for South Asian populations. Companies may also under- or overestimate risk.<sup>11</sup> There may be a high number of false positives, too, which places a burden on health systems for repeat testing.

A small number of companies offer very cheap lifestyle tests, or other types of testing, but do not make clear that they will be selling the consumer’s data to any purchaser, nor that they will make it available to the police or other authorities. There is a real danger that such practices will lead to outrage in the media and will have major impacts on confidence in all areas of precision medicine. Regulation is possible.

### **Case study 3.1: The European In Vitro Diagnostics Medical Devices Regulation**

This directive becomes law when it becomes a regulation in May 2022. One consequence of this wide-ranging legislation will be that DTC illness tests (not wellness tests) will be placed in the second highest category of risk, similar to screening for infectious disease. Companies will have to prove scientific validity, be clearer about the limitations and predictive value of tests and show what patients should then do or not do. Pre- and post-test counselling will be mandatory for serious untreatable conditions such as Huntington's.

### **Case study 3.2: MyGeneCounsel.com**

**MyGeneCounsel.com** is a scalable, digital service set up by Yale academic and genetic counsellor Ellen Matloff. It provides genetic advice to subscribers, either individuals or health systems, through Living Lab Reports®. The advice is continuously updated by networks of professionals, and subscribers are alerted if there are changes to management or treatment guidelines affecting an individual.

#### **Notation of ongoing challenges in governance gap**

Challenges still need to be addressed in order to gain public engagement and trust in precision medicine. Disproportionate benefit by commercial companies is a toxic trust issue in understanding and appropriately building societal trust in health data use. There are also many aspects to the increasing public awareness of the use of genomic data in precision medicine that should be the subject of national conversations, such as the impact of test results on wider family members. In addition, there are misconceptions that need to be addressed: for example, the view that DNA taken for health purposes may be used later to incriminate someone at the scene of a crime is very widespread. Moreover, DTC results may be misinterpreted by the consumer, even where results are not medically significant, and are creating a tsunami of demand for genetic counselling within health systems. The impact on health systems is two-fold: first, the indirect costs of additional consultations and testing; second, reduced trust and confidence in the value of precision medicine from patients and physicians. The number of genetic counsellors worldwide is small, around 7,000 across 28 countries, including 4,400 in North America.<sup>12</sup> In some regions (South America, many parts of Africa and Asia and some European countries), physicians provide genetic counselling. By 2030, the world will require 18 million extra health workers.<sup>13</sup> A major global expansion of genetic counsellors/geneticists is not realistic. Thus, new approaches for genetic advice need to be developed and evaluated, with genetic counsellors taking complex cases while alternative systems for supportive lifestyle advice are sought.

## Summary and recommendations

To address our identified governance gaps, action in the following areas needs to be developed:

1. A global engagement campaign that is clear, evidence-based, culturally sensitive and joined up should aim to gather evidence on public opinions and concerns and should share good engagement practices across countries and systems.
2. A global governance agreement should set out the red lines for access to sequence data gathered for health purposes. We suggest that no use for a surveillance society by police or state and no use for discriminating against minorities should be a global norm. Governance should have meaningful inclusion by those who have contributed data.
3. A framework for transparent distribution of benefit should be developed.
4. Education for all levels of healthcare professionals should be urgently increased.
5. The spread of accurate information through storylines in TV and film should be encouraged to enable better conversations within families.
6. A global resource of constantly updated knowledge for patients should be developed, appropriate to regions and freely available to low- and middle-income (LMIC) countries.
7. DTC testing should be standardized at a global level, with better regulation at a national and international level.
8. There should be transparency about the use of data gathered by DTC companies, with a global ethical code of conduct to which companies should sign up.
9. New models of providing advice in relation to precision medicine testing should be developed through online genetic counselling and other new services.



## Governance gap 4: Access and fair pricing

Although precision medicine should be accessible to all people, access is unfortunately controlled by pricing, reimbursement and unclear definitions of “value”. This is creating disparity in terms of where and to whom precision medicine tools are available and where precision medicine tools are likely to be developed. With increased molecular understanding of disease, and novel techniques such as gene-editing and stem-cell therapy, we have the potential to improve and maybe even cure select subtypes of disease. Many of these “breakthrough” therapies receive accelerated regulatory approval to speed patient access. Surrogate endpoints are used as proxies for clinical outcomes that do not always provide a complete understanding of a drug’s effectiveness and safety. The lack of a complete evidence package makes it extremely difficult for healthcare stakeholders to untangle the potential promise and value of these therapies, creating challenges in terms of putting precision medicine into clinical practice. Beyond therapeutics, core technologies, such as diagnostic tools and patient registries, are fundamental for precision medicine. These resources are available today and if implemented correctly could accelerate the development, accessibility and delivery of precision medicine in an equitable manner. However, governance policies, or lack thereof, are blocking their implementation. Here, we detail four separate focus areas and policy examples related to pricing and access that are affecting precision medicine and provide recommendations for change. Collectively, these policies can create an ecosystem that fosters and rewards innovation to improve health and healthcare for all.

### Focus area 1: Ensuring evidence of safety and effectiveness throughout fast-track drug life cycles

The lack of evidence-based data and transparency in fast-track drug approvals deprives clinicians, patients and healthcare system stakeholders of vital information that can help improve outcomes and avoid adverse medical events. At present, post-market trials or studies are often delayed, are not always robust, often do not happen at all and sometimes fail to confirm the clinical benefit predicted in pre-market trials. This creates challenges in physician prescribing, establishing meaningful outcomes-based contracts and ensuring fair payment for precision therapies based on performance.

### **Case study 1.1: Fast-tracked drugs have limited real-world efficacy evidence**

In the United States, the Federal Food, Drug, and Cosmetic Act (FFDCA) enables pharmaceutical manufacturers to get Food and Drug Administration (FDA) approval on an expedited basis when a drug: (1) intends to treat a serious condition; (2) generally provides a meaningful advantage over available therapies; and (3) demonstrates an effect on a surrogate or intermediate endpoint that is reasonably likely to predict clinical benefit. Because the accelerated pathway allows marketing based on endpoints that merely predict clinical outcomes, the FDA can require post-market clinical trials or studies to verify safety and effectiveness. Despite the FDA's intentions for more robust post-market analysis, this has failed to occur or to be reported. For example, between 2008 and 2013, 67% of oncology drug approvals were made on the basis of a surrogate endpoint. In a four-year-plus follow-up period, 86% of these drugs still had unknown effects on overall survival or failed to show improved survival.<sup>14</sup> A study in *The BMJ* found that approximately 25% of post-market studies are not reported publicly, regardless of their completion.<sup>15</sup>

### **Focus area 2: Need for a national patient registry**

In the US, patient data is fragmented across different healthcare sites and systems of care, without the ability to easily, accurately and effectively combine disparate records. Thus, clinicians often do not have access to a patient's prior interactions with the healthcare system, including previous tests and screenings or patient interventions. This leads to inefficiencies, redundancies and an overall failure to deliver optimal care.

### **Case study 2.1: Lack of national patient identifier system by HIPAA**

In 1996, the United States' Health Insurance Portability and Accountability Act (HIPAA) legislation called for the development of a national patient identifier system that would give each person in the US a permanently assigned, unique number to be used across the entire spectrum of the national healthcare system. This identifier would allow the healthcare system to more easily and accurately match different patient records and documentation of patient tests and interventions with one another to create a comprehensive, longitudinal record of care and outcomes. Unfortunately, citing privacy concerns, Congress has prevented the Department of Health and Human Services (HHS) from implementing the national patient registry. This is a disservice to patients, as data generated in the present (and collected over time), would better document patient history and could support the development of new precision medicine tools.

### **Focus area 3: Patentability of biomarkers**

Although biomarkers and algorithms are the cornerstone of precision medicine, leading to advanced modes to detect and treat disease, they are not eligible for intellectual property (IP) protection in the US and in other parts of the world. IP is often a prerequisite to obtaining the funding needed to develop these biomarkers into patient care. Thus, despite widespread consensus on the promise of biomarkers to accelerate precision medicine, the pace of innovation is sluggish, due in part to shaky IP protection and lack of economic incentives.



### **Case study 3.1: Section 101 of US patent law**

Estimates suggest IP comprises more than 38% of the United States' GDP and represents 80% of the market value of publicly traded companies (US Commerce Department, 2016). Inventions using biomarkers and algorithms stand to benefit all of society. Innovators and investors in the diagnostic space expect IP protection for their discoveries. In the US, biomarkers and algorithms are considered "products of nature" and "abstract ideas" and are thus not patentable under Section 101 of US patent law. Notable Supreme Court and Federal Court cases such as Mayo vs. Prometheus (2012), Association for Molecular Pathology v. Myriad Genetics (2013), Ariosa vs. Sequenom (2015), Esoterix vs. Qiagen (2016) and more, have established jurisprudence that even if an original patent is granted to a diagnostic innovator, the IP rights will not be upheld in court, and will likely be dismissed under section 101. This has led to significant economic costs for the original inventor. These legal decisions have led to many investors completely shunning investment in diagnostics, slowing innovation.

### **Focus area 4: Global standards for new diagnostic pricing models**

During the approval process for precision medicine diagnostics, experts need to evaluate the rationality of pricing based on the value of the innovative technology. Existing pricing models that include "cost-plus" or code stacking are not suitable for many innovative products. Globally, there remains a challenge to set appropriate pricing for this new era of diagnostics.



### **Case study 4.1: Advanced diagnostics pricing in China**

One of the most significant and fastest-growing areas of the Chinese healthcare market is advanced diagnostics. Public hospitals represent ~80% of this market, which consume most of China's medical resources. At present, the pricing approval process to bring these tools to public hospitals is long (two to five years), meaning it is unable to keep pace with innovation. The approval process itself is unclear, leading to mixed-quality reviews of new products. For example, it is difficult for innovative diagnostics to get approval without market inspection, but because unapproved products are blocked from major hospitals there is de facto no market inspection. Lack of pricing standards further impedes the review and application of new products. Precision medicine diagnostics should be able to enter the market quicker and receive feedback from relevant medical experts with clear pricing expectations.

#### **Notation of ongoing challenges in governance gap**

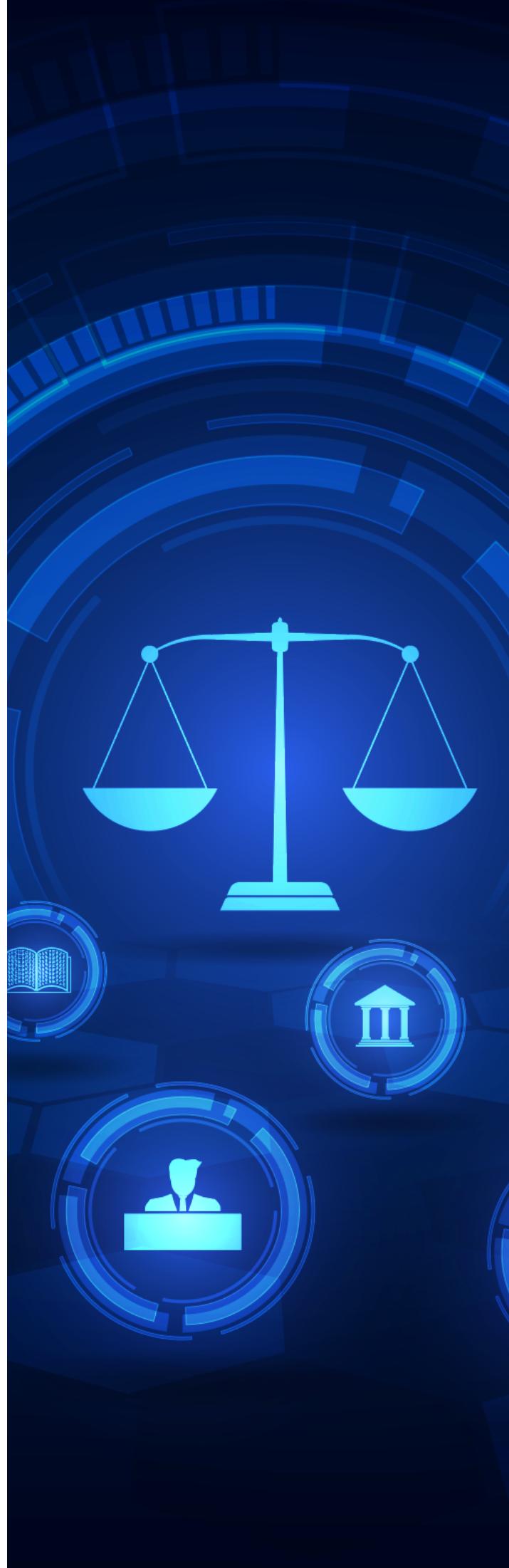
The case studies included herein help frame the challenges associated with existing policies that affect access and fair pricing for precision medicine. There is a strong desire to make new therapies available to patients as soon as possible. With accelerated approvals, how do we know if the treatments will truly be effective? How should we price these innovations if we don't understand the true value? By failing to monitor patients throughout their lifetime, what insights into health and disease are we missing? Without IP protection and new pricing models, how do we incentivize the development of innovative diagnostics that can lead to better health?

#### **Summary and recommendations**

Policy-makers and regulators should consider modernizing precision medicine approval and pricing processes for therapeutics and diagnostics, as well as establishing new modes to track patient journeys. Specifically, we recommend:

1. Meaningful and timely post-market trials or studies on fast-tracked therapeutics for regulators. Manufacturers should be required to publicly report post-market trial and study results, and the FDA should post them alongside the drug information.
2. Establish national patient registries to more accurately track and monitor changes along an individual's health trajectory. This will inform new insights into health, disease and interventions.

3. Reset global IP norms to explicitly block IP of bona fide products of nature (genes, proteins, metabolites), but provide protection for novel means of detecting, quantifying and correlating biomarkers with meaningful clinical phenotypes.
4. Establish new global pricing models for advanced diagnostics. Global standards must be established so that patients everywhere have access to the best diagnostics.



## Governance gap 5: Responsive regulatory systems

Access to precision health data is accelerating due to a transformation in the logistical and financial costs of generating, interpreting and making use of that information. This information is already beginning to redefine the way in which we deliver healthcare across populations, from identifying conditions earlier in their progression to avert high-cost and high-impact healthcare events, to changing the nature of the healthcare system's interactions with individuals over their lifetime. However, as precision health data including genomics has become much more widespread in care, global regulators have not evolved to keep pace and ensure an appropriate and reasonable balance between broadened access for individuals and modern privacy and data ownership rights. What is the regulatory and ethical framework that enables this information to be the most effective, useful and scalable across populations globally?

### Focus area 1: Data privacy and data ownership

There are no common frameworks for the privacy and ownership of precision health data. It should be assumed that patients own their health data in most jurisdictions. While genetic and precision health information is fundamentally health data – and should be treated as such, regardless of its application – governments, institutions and companies have proceeded in the generation and use of precision data without consistent privacy and security protections. Precision health data should be treated with the same rigour in terms of privacy safeguards as other health information – whether in the context of existing regulatory frameworks such as the US's **Health Insurance Portability and Accountability Act**, the EU's **General Data Protection Regulation (GDPR)** or other strong regulatory frameworks globally. For instance, GDPR establishes that all health information should be treated as sensitive data under a consistent framework – whether generated by end users or by healthcare professionals. Consistent protections will help lessen the treatment of genetic and precision health data as precious exceptions within current healthcare practices and speed the introduction of this technology into healthcare.

### **Case study 1.1: Teamsters and employer-sponsored precision health programmes**

The **Teamsters Health and Welfare Fund of Philadelphia and Vicinity** is a not-for-profit organization providing participating members of the Teamsters Union in the United States with healthcare benefits. In 2019, following growing member demand for improved access to genetic testing, the fund elected to provide genetic screening and precision health services in collaboration with Color, a health technology company, to all of its members and dependents at no out-of-pocket cost. Within the first six months of offering the programme to its members, the fund saw 20% participation – nearly 10 times the average uptake of other benefits programmes within US union populations.<sup>16</sup> The enrolment was driven in part by two core principles: access to clinical-grade testing that would drive members back into the healthcare system, and clear education, communication and consent about the use of members' genetic data. Members are educated about any of the fund's receipt of data for healthcare billing purposes and the fund's commitment to non-discrimination on the basis of that information.

### **Focus area 2: Obligations to patients**

There is a stronger need to acknowledge the obligations to patients in the course of generating and using their genetic and precision health data. In a growing number of examples around the world, individuals are well equipped to make decisions about the use and dissemination of their data, with appropriate disclosure of information. First, there is a growing imperative to return results to participants in research-driven sequencing efforts. While this need was previously hampered by complicated logistics or a lack of clinical community consensus, research programmes today – whether driven by investments from the pharmaceutical industry, academic programmes or otherwise – are facing a growing demand from participants to benefit in the immediate term from their contribution to research efforts. Second, when data is being generated from individuals, there is a need for transparency of the objectives and purposes of that data collection – whether for healthcare, research, data sharing or other purposes. Finally, there is an obligation for transparency of financial incentives in obtaining precision data, as with any other healthcare information; regulatory governance must support a transparent disclosure of the financial flows supporting the generation of the data (e.g. for commercialization to a sponsoring pharmaceutical company, for internal research or otherwise).

### **Case study 2.1: The All of Us Research Program**

One of the most ambitious biomedical research efforts ever undertaken, the **All of Us Research Program**, will sequence 1 million individuals across the United States with the goal of accelerating health research and enabling individualized prevention, treatment and care. The programme has balanced a focus on recruitment and research from populations that have been historically under-represented in clinical science and genomic medicine with a commitment to providing value and impact back to participants. All of Us is **providing participants with clinically valid results** from their genetic sequencing, as well as **access to trained genetic counsellors**, to help participants and their families understand the impact of the results on their health. This broad-based return of results may establish a new paradigm of large-scale genomic research programmes that acknowledges shifting expectations from participants to learn something from their contributions, and the opportunity to have an impact on individuals' health today in parallel with long-term research efforts.

### **Case study 2.2: Singapore's National Precision Medicine programme**

Singapore's National Precision Medicine programme is an expansive effort to further the applications of precision health data and genomics across the healthcare ecosystem – for scientific advancement, population health impact and broader economic development.<sup>17</sup> The ten-year programme establishes a common infrastructure for engaging patients and participants and transparently supporting parallel applications of their data for research and clinical applications. Realizing the expansive applications of genomic and precision data across the broader healthcare ecosystem, Singapore has worked in tandem to strengthen frameworks for non-discrimination protections within Singapore. In 2020, it is focusing on removing most exceptions for discrimination for life insurance policies for nearly all genetic/heritable disease conditions.

### **Focus area 3: Acceptable applications of precision health data and issues surrounding direct-to-consumer testing**

One of the most critical regulatory gaps today relates to potential discrimination based on genetic information. For instance, many countries do not have appropriate protections to prevent discriminatory premiums or insurance policies for individuals who have a genetically identified heritable condition. This lack of protection fails to acknowledge the rapid acceleration in access to genetic information (including through patients'/consumers' own choices) and the ever-expanding areas affected by the impacts on health.

Similarly, the lack of consistent protections for participants in health-related DTC testing is damaging the broader environment in terms of the appropriate applications of genetics. Security breaches, law enforcement action and downstream monetization of data are not typical use cases of data from traditional healthcare, yet have become relatively common within the DTC space.

### **Case study 3.1: Genetic Information Non-Discrimination Act (GINA)**

The Genetic Information Non-Discrimination Act (**GINA**) was enacted into law in the United States in 2008 to protect Americans against discrimination based on information found in their DNA. The law bars health insurers from using genetic information in determining coverage or premiums and prohibits employers from making decisions based on DNA tests of their employees or potential employees. Public confidence that divulging genetic information will not lead to unintended harm will help advance precision medicine and the necessary biomedical research that undergirds it.

### **Notation of ongoing challenges in governance gap**

These case studies demonstrate a new model that is evolving, while also highlighting additional areas for further exploration:

- What are the appropriate regulatory frameworks for health information from direct-to-consumer (non-physician-ordered) genetic services, where trained providers are not involved in clinical care delivery?
- How else can stakeholders diminish the exceptionalism of precision health data in routine care, given the potential of the technology to affect the care and outcomes of large populations as costs decline (e.g. the appropriate role and regulation of informed consent)?
- How should intellectual property frameworks for genetic information evolve, as advances in more novel genetic algorithms progress into clinical care and population health management (e.g. polygenic risk scores)?



## Summary and recommendations

The four key takeaways of the working group's study of broad-based precision health data include:

1. Regulatory frameworks should first and foremost consider and prioritize the value to participants/patients – supporting the return of results to patients, strong privacy/data protections and clear articulation and transparency of data flows.
2. Institutions should be rigorous in deploying precision health data at scale – clinically and with regards to regulatory frameworks.
3. Global regulators must explicitly target potential discriminatory uses of precision health data given the potential benefits to individuals and public health systems from the data.
4. Entities supporting precision health data should be transparent to individuals about their intentions in collecting their precision health data and the downstream uses of that information.

# Conclusions and next steps

In this initial vision statement, the Council has attempted to draw attention to a set of policy and governance gaps that it is crucial to address so that the benefits of precision medicine can be accessed efficiently and sustainably by the maximal number of people worldwide.

By identifying five very broad (and not completely mutually exclusive) categories of policy and governance gaps, the Council has attempted to impose some structure on the discussion to make it easier for different countries and constituencies to address these gaps.

This vision statement sheds light on a number of areas that clearly impede the implementation of precision medicine to different degrees around the world. In some countries, a mismatch between the costs and available resources limits access, but as technology progresses, the costs should decline. Certainly, as sophisticated therapies exit from patent protection, advanced therapeutic agents become generics, which can be produced more like public goods at lower costs. The costs of computing power and storage have also dropped dramatically, of course, and this opens up the potential to create a broad-based infrastructure that fully supports large-scale international collaborations and comparisons of approaches and outcomes from precision medicine-focused tools and technologies.

In constructing this vision statement, the Council chose to illustrate challenges that have been met in different ways through a selection of case studies. Additionally, it was possible to identify a number of continuing challenges that resist simple solutions, as well as pitfalls to avoid when closing these gaps. These examples can be used to focus efforts in the most positive ways while avoiding past mistakes. For example, cultural insensitivities have led to a great risk of mistrust among vulnerable populations, and this can be addressed through education and public sensitivity as well as regulation.

Since governmental and socioeconomic systems differ dramatically in terms of healthcare across the world, the solutions to these gaps will be diverse. Policy experts can use these frameworks to bridge gaps with solutions that are most likely to work in their own countries.

The work of the Council to date is the first step towards developing a robust international collaborative environment in which to understand the many challenges and to test solutions that bridge current policy and governance gaps.

In this way, the benefits of precision medicine can be expanded in accordance with practical principles, local mores, government structures, regulatory environments and the efficient use of resources. By detailing relevant present policies and understanding the gaps, together we can envision the future and help to make substantive steps towards operationalizing it on a global scale.

We hope that next steps may be taken locally to complement the ongoing collaborative structure offered by the World Economic Forum. Ideally, some of the lessons of the illustrative case studies that overcame gaps in policy will be extrapolated to other gaps.

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# Endnotes

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