Doing well? Fulfilling the promise of precision medicine

A paper by The Economist Intelligence Unit
Contents

3 Acknowledgements

5 Forward

6 Executive summary

10 Understanding precision medicine

27 Public health: The potential and limits of precision medicine

35 The challenges of integrating precision medicine into publicly funded health systems

48 Patient-centricity: The essential complement to precision medicine

59 Turning a vision into a reality

63 Endnotes
Acknowledgements

Doing well? Fulfilling the promise of precision medicine is an Economist Intelligence Unit (The EIU) report that has been commissioned by Qatar Foundation. The findings are based on an extensive literature review and a comprehensive interview programme conducted by The EIU between March and September 2020.

The EIU bears sole responsibility for the content of this report. The findings and views expressed herein do not necessarily reflect the views of the partners and experts.

The report was produced by a team of EIU researchers, writers, editors and graphic designers, including:

Katherine Stewart, Project director
Antonia Kerle, Project manager
Antonella Bordone, Graphic designer
Emma Ruckley, Sub-editor

Interviewees

Our thanks are due to the following people for their time and insights:

Alan Balch, CEO, National Patient Advocate Association, US
Andrew Sinclair, co-lead, Australian Genomics Health Alliance
Clara Gaff, executive director, Melbourne Genomics Health Alliance
Colleen Leners, DNP, APRN, FAAN, FAANP, director of policy, American Association of Colleges of Nursing
Daryl Pritchard, senior vice president, Personalised Medicine Coalition (PMC)
David Taylor-Robinson, professor of public health and policy, University of Liverpool
Don Brown, founder & CEO, LifeOmic
Gemma Bilkey, researcher, Department of Health - Western Australia
Genya Dana, head of healthcare transformation, World Economic Forum
Geoffrey Ginsburg, director, Centre for Applied Genomics & Precision Medicine, Duke University
James Morrow, general practitioner, NHS
Kawaldep Sehmi, CEO, International Association of Patient Organisations
Kelly Gebo, chief medical and scientific Officer, NIH All of Us Program
Laura Blackburn, head of science, PHG Foundation
Marc S. Williams, professor and director emeritus, Geisinger Genomic Medicine Institute
Matthew Bellgard, director of eResearch, Queensland University of Technology; Chair, APEC Rare Disease Network
Milan Radovich, associate professor of surgery, Indiana University School of Medicine
Muin J Khoury, founding director, Office of Genomics and Precision Public Health, US CDC
Nahla M. Afifi, director, Qatar Foundation - Bio Bank
Nancy Kass, professor of bioethics and public health, Johns Hopkins University
Philippa Brice, external affairs director, PHG Foundation
Richard O’Kennedy, vice-president for research, Hamad Bin Khalifa University; vice-president for research, development and innovation at the Qatar Foundation
Ronald Bayer, professor of sociomedical sciences, Mailman School of Public Health, Columbia University
Said Ismail, director, Qatar Foundation - Qatar Genome Program
Sally Davies, master of Trinity College, Cambridge, former Chief Medical Officer for England
Sandro Galea, dean, Boston University School of Public Health
Stefania Boccia, professor of hygiene and public Health, Università Cattolica del Sacro Cuore, Rome
Takeya Adachi, research assistant professor, Kyoto Prefectural University of Medicine, Strategic Outlook toward 2030: Japan’s research for allergy and immunology
Victor Dzau, president, US National Academy of Medicine
Walid Qoronfleh, director of research and policy, Qatar Foundation - World Innovation Summit for Health
Qatar Foundation (QF) is a non-profit organization made up of more than 50 entities working in education, research, and community development.

Now in our 25th year, the mission of Qatar Foundation is to drive regional innovation and entrepreneurship, foster social development and a culture of lifelong learning, and prepare our brightest minds to tackle the biggest challenges facing our world today, and those that tomorrow will bring.

In everything we do, we strive to unlock the most precious resource of all—human potential. Education City, our flagship initiative, spans more than 12 square kilometers and hosts branch campuses of world-leading universities, a homegrown university, mainstream and specialized schools, and other research, scholastic, and community centers.

Together, these elements make Education City a unique model of academic and research excellence, pioneering a new approach to multidisciplinary, global education, and enabling breakthroughs that benefit Qatar and the rest of the world.

Aligning with our goal of catalyzing global conversations about the choices and challenges facing health policymakers around the world, Qatar Foundation is delighted to sponsor *Doing well? Fulfilling the promise of precision medicine* by the Economist Intelligence Unit.
**Executive summary**

Precision medicine is on the cusp of facilitating revolutionary improvements in how healthcare is delivered. This Economist Intelligence Unit white paper, sponsored by Qatar Foundation, looks at the promise of precision medicine, what it is currently delivering, and the challenges associated with its wider application in large health systems.

**Key findings**

**Precision medicine is best understood as the possible outcome of four ongoing developments.** Recognising that an agreed definition remains elusive, this paper conceptualises precision medicine as the potential outcome of four interwoven, data-related enablers: (1) the increasing volume of data available to health systems; (2) vast growth in the kinds of data that are relevant to health systems; (3) the increasing ability to store data in such a way that permits easier access to relevant information; and (4) the quantum leaps in analytic technology that make it possible to draw greater insights from this information.

**Hopes are high.** This granular information is expected to give us a much more detailed understanding of how an individual patient’s body works, what represents a health risk for that person, the peculiarities of a given pathogen or tumour affecting that patient, and how any treatment might affect both patient and disease. These insights should allow medicine to move away from its reliance on trial and error, enabling delivery of the right intervention (whether curative or preventative) at the right time.

This is expected to benefit all healthcare stakeholders: patients will have quicker access to the treatments they need, and will be able to avoid the risks of taking incorrect medication; health systems will reduce waste and improve outcomes; payers will receive better value for money; and the overall health of populations will improve.

**Current advances are limited but remain highly promising.** There are already a number of important examples of precision medicine in action. Thanks to a better understanding of tumour genetics, more effective treatments are now possible for several cancers, notably those of the lung and breast. In the field of rare disease, genomic sequencing is cutting diagnosis times for a large number of patients. Pharmacogenomics—the study of how a person’s genetics interact with particular drugs—is a growing field, and genetic sequencing is being used to recognise


pathogen mutations. However, the impact of precision medicine is limited beyond these efforts. To date, progress has largely been concentrated in genomic medicine, and this trend is expected to continue for the foreseeable future.

**Proof of value remains a pressing issue.** Given the possible breadth of applications for precision medicine, it is challenging to determine whether the field as a whole is cost-effective. Some interventions may be; others may not. Data indicates that whole-genome sequencing for rare disease diagnosis and the sequencing of tuberculosis pathogens to determine mutations are both worth the cost. However, cost-effectiveness studies for precision interventions are rare, and there is a lack of consensus on how to decide what level of spending is worthwhile.

**The controversy around precision public health highlights fundamental issues that must be resolved if precision medicine is to become more widely integrated into health systems.** The concept of precision public health has caused significant controversy in the public health field. This controversy centres around three questions that must be resolved before precision medicine can be used widely throughout the healthcare sector:

1. How likely is it that precision approaches will add value, compared with standard practice today?

2. ways that are misguided or harmful?

3. Is precision medicine really something new, or is it business as usual with slightly better tools?

Careful consideration of these questions is necessary to prevent avoidable mistakes as precision interventions are rolled out in any health system. Despite the controversy, there are some positive examples of precision tools being used for public health purposes. Two of the leading COVID-19 vaccine candidates use messenger RNA, and detailed mapping has been used to monitor and predict the spread of diseases such as cholera, as well as risk factors for those diseases. In Yemen, this mapping likely saved lives during the cholera epidemic in 2017.

**Those seeking to incorporate precision medicine into healthcare systems will need to address a diverse and complicated range of issues.** Innovation in healthcare systems is notoriously difficult. Integrating precision medicine into standard care will require the creation of new care pathways and new kinds of interventions, all of which will require different infrastructure. In most health systems, this process is only in the initial stages. Those wishing to expedite the process would benefit from considering the following issues.

**Securing stakeholder commitments:** Organisations that have made the greatest progress towards incorporating precision medicine share the following characteristics: strong leadership; payer buy-in, enabling
funding of the necessary investments; and patient awareness and understanding of precision care, facilitating general acceptance.

Proving value: Advocates of precision medicine in healthcare systems lack the necessary data to demonstrate that it delivers improved outcomes that justify the cost. New health technology assessment procedures are needed that can consider the wider costs and benefits of precision interventions, as current approaches often cannot capture these complexities.

Developing a workforce capable of precision medicine: Even high-resource healthcare systems lack the necessary specialists to facilitate greater use of precision medicine, notably geneticists, genetic counsellors and data specialists. Non-geneticist clinicians often lack confidence in their knowledge of genomic interventions (the cutting edge of precision medicine), and experts warn that medical curricula do not currently cover this field well enough.

Building the necessary infrastructure: Precision medicine relies on data, but information within health systems is often fragmented and not readily useable. Furthermore, laboratories often lack the capacity to take on the substantial additional testing required to expand precision medicine, even in wealthy countries.

Creating an appropriate regulatory framework for precision medicine: Precision medicine does not always fit easily into existing regulatory procedures. Leading drug approval agencies are trying to find better ways to assess the safety and effectiveness of precision diagnostics and drugs, a growing number of which have been approved as a result of this effort. However, no country has fully addressed the challenges of using artificial intelligence within healthcare.

To be successful, precision medicine must be delivered in a patient-centred way. Patient-centricity involves working with patients as co-creators of healthcare and health research, which involves a conversation of equals. Clinicians will need to help patients understand the implications of precision tests, the relevant data and the treatment choices. Both sides can then determine together what the patient values most in terms of the outcome(s) of any intervention. Similarly, health systems will need to conduct ongoing research in precision medicine in partnership with patients to ensure that patient views on what data is relevant, and what issues should be studied, are taken into account.

Adopting patient-centricity can help to address some of the pressing ethical issues surrounding precision medicine. The nature of precision medicine, and particularly genomic medicine, raises several important ethical issues, including:

Data gathered for one genomic test may reveal information about a completely different condition, raising questions about whether to inform patients and their families of these “incidental findings”. This issue is further complicated by the fact that an
individual’s germline DNA remains the same throughout their life, which means that incidental findings may not become apparent until years after the original test.

Data gathered from such tests would normally be added to databases to support future research. Patients can typically opt out of this, but if many choose to do so, precision medicine will not advance. Even though the data is anonymised, there are no guarantees that future algorithms will not be capable of de-anonymising data. Indeed, for some kinds of test data, de-anonymisation is already possible.

Historically, most medical research has been conducted in populations where certain groups—often young males of European ancestry—are over-represented, compared with their share of the population. Relying on these databases might lead to unsafe recommendations for people from other groups.

Patient-centricity is an important part of any solution to these issues. For example, the possibility of incidental findings can be discussed in a patient-centred conversation before a test is conducted, with the goal of identifying what the individual would want to be told in the event of such findings. Similarly, carefully explaining to patients the value of health databases, and working in partnership with them on research related to precision medicine, can help health systems to obtain more and better information for the entire population.
Understanding precision medicine

Precision medicine has the potential to transform healthcare. By moving away from trial and error towards more targeted, accurate diagnoses and treatments, people should be able to live longer and healthier lives and social outcomes should improve, all with less wasted time, money and energy. This is what medicine has always aspired to, but has not yet been able to deliver.

While there is understandable excitement about the promise of precision medicine, delivery will not be straightforward. Innovation within health systems is challenging at the best of times, and the nature of precision medicine means that substantial process, training and infrastructure changes will be needed. These changes will be challenging even in the most hospitable environments. At the same time, all stakeholders—including clinicians, patients, payers and the broader community—will need education to undergird the effectiveness of this kind of healthcare.

This paper looks at the promise and current limitations of precision medicine, the barriers to its implementation in public health systems, and the areas where policymakers – indeed, all stakeholders – must focus their efforts in order to realise its potential.

A transformation that defies precise definition

There are several competing definitions of precision medicine. The idea “might sound simple, but it is not. If you ask people within the field, you will get different answers,” explains Dr Walid Qoronfleh, director of healthcare research and policy at the World Innovation Summit for Health in Qatar. There are also differences in terminology, with some using the term precision medicine (particularly
Doing well? Fulfilling the promise of precision medicine

in the United States) and others using the term personalised medicine. While there have been attempts to distinguish between precision medicine and personalised medicine, a recent analysis described the differences as “ambiguous”.

One of the most commonly used definitions comes from the European Council, which prefers the term personalised medicine and describes it as follows: “A medical model using characterisation of individuals’ phenotypes and genotypes (e.g. molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention.”

A commonly used definition of precision medicine comes from the US government’s 2015 Precision Medicine Initiative, which describes it as “an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person.”

For the purposes of this paper, we use the term precision medicine and conceptualise it as the potential outcome of four interwoven, data-related enablers: (1) the increasing volume of data available to health systems; (2) vast growth in the kinds of data that are relevant to health systems; (3) the increasing ability to store data in such a way that permits easier access to relevant information; and (4) the quantum leaps in analytic technology that make it possible to draw greater insights from this information.

The power of data

Data has always played a role in medicine, and evaluating the potential medical relevance of inherited characteristics is also established practice. Geoffrey Ginsburg, director of Duke University’s Center for Applied Genomics and Precision Medicine, explains that “often people believe that all the answers lurk in the genome, but family history has been a tried and true way to look at risk of disease since long before we had access to people’s genomes.” Clinicians are also familiar with aggregating a range of data for insight. The Framingham Risk Score, for example, first appeared in 1998 and is used to estimate the ten-year probability of developing coronary heart disease based on gender, age, blood pressure, cholesterol levels and smoking habits.

The advances made possible by precision medicine lie in its capacity to enable medical practitioners to access and evaluate more specific and detailed information about their patients, and to then tailor interventions accordingly. Even in modern medicine, the clinician is constrained by the bounds of current medical knowledge. Clinicians often have to rely on generalities when diagnosing patients due to a lack of individualised data, placing a presenting patient into a general category with others sharing the same apparent illness (which itself might be one of several conditions at the molecular level). As a result, doctors often have to fall back on interventions that sometimes work but too often do not.
James Morrow, a general practitioner with the National Health Service (NHS) in Cambridgeshire in the United Kingdom, explains that medicine has traditionally taken a sort of “blunderbuss” approach, with trial-and-error applications of interventions. These interventions have often been shown to work in only a small minority of the general population, which means that they sometimes result in “complete misses or collateral damage”. Milan Radovich, associate professor of surgery at Indiana University’s School of Medicine, describes this as “the tyranny of averages. All of medicine is based on averages.” Studies of pharmaceutical effectiveness illustrate the problem: a 2015 Nature commentary reported that, in the United States, the top ten selling drugs helped only 4-25% of people taking them. This is better than nothing but leaves the majority of those with such prescriptions no better off. “It is really important to be able to treat people more precisely,” Dr Morrow concludes.

Dr Qoronfleh describes precision medicine as a new and holistic approach that will lead to “better care, better value, better health and better social outcomes”. Colleen Leners, DNP, APRN, FAAN, FAANP and director of policy at the American Association of Colleges of Nursing, agrees, explaining that precision medicine is “a radical shift in how each of us can receive the best care possible based on our unique makeup”. The capability to harness more and better information will be central to this radical shift. Genya Dana, head of healthcare transformation at the World Economic Forum (WEF), notes that “the way different people define precision medicine is extremely variable, but there is collective agreement that data is a pretty fundamental piece of the puzzle. Precision medicine is very much driven by data.” In the words of Donald Brown, the founder and CEO of LifeOmic (a health software company), “biology and the life sciences are becoming information sciences.”

Four data-related enablers will make precision medicine possible, allowing for more fine-tuned risk assessments, diagnoses and interventions: the volume of available data, the nature of that data, the ways in which that data is stored, and the ways in which it is...
analysed. Each of these enablers is discussed in more detail below.

The volume of available data

The first enabler is an increase in the quantity of information generated within health systems. Although medical systems have always collected data, the quantity of collected data is increasing exponentially. According to Dell EMC, the pool of data held by healthcare organisations worldwide increased by 878% between 2016 and 2018. In the longer term, IDC, a market intelligence firm, projects that the volume of information within the health sector will rise at a cumulative annual growth rate of 36% between 2018 and 2025, well ahead of the global rate for all data (27%).

Although not all data is relevant or useful, an increase in the quantity of available data means that there are greater opportunities for clinicians to build a more detailed picture of their patients’ health.

The nature of available data

This increase in the quantity of available information is driven in part by an expansion in the kind of data that is potentially relevant to health. For instance, increased knowledge of the health implications of a single gene (genetics) or a combination of genes (genomics) within individuals, pathogens and tumours has reshaped medicine, with important results. Dr Marc Williams, director emeritus of the Geisinger Genomic Medicine Institute, notes that our “understanding of cancer is going from an organ and tissue-specific one to a molecular one, which has led to tremendous innovations”. There have also been advances in the speed of genetic testing, and the cost of this testing has fallen. With Next-Generation Sequencing, laboratories can now sequence an individual’s entire DNA (Whole-Genome Sequencing) or only those parts that produce proteins (Whole Exome Sequencing) within a day. In 2003 it cost around $50m to sequence the entire DNA of a single human being; today it costs around $1,000 (and that price has stayed largely constant since 2015).

While this genomic data holds great promise, Victor Dzau, president of the US National Academy of Medicine, points out that “sequencing is only one of piece of information to drive the precision of prediction.” At the molecular level, other kinds of data are likely to shed light on matters that are relevant to an individual’s health, including epigenomic data (the study of changes to heritable characteristics that do not involve DNA), proteomic data (the study of the collection of proteins in an individual), microbiomic data (the study of all the bacteria, viruses, fungi and protozoa living in an individual) and metabolomic data (the study of all small molecules within an organism). Alone or in combination, these factors could conceivably affect susceptibility or immunity to disease, reactions to medication and even quality of life.

Information on lifestyle is also likely to be essential to understanding various aspects of
Doing well? Fulfilling the promise of precision medicine

...a person’s health. Many individuals are already collecting this data themselves, and are happy to share it. According to a 2019 Pew survey, 21% of US adults have a fitness tracker or smart watch, and of these, 53% think it is acceptable for the makers of fitness apps to share their data with researchers looking into the link between exercise and heart disease.12

The growing volume and breadth of information that is relevant to health is prompting governments around the world to create large databases of medical data, such as the All of Us programme in the United States and the 100,000 Genome Project in the United Kingdom. The All of Us programme casts a wide net, seeking to combine DNA samples, electronic health record (EHR) data, information from wearables and survey responses from 1m people. It has a particular focus on previously understudied groups within the population, such as ethnic minorities, women and older individuals. Since enrolment began in 2018, the programme has reached about a quarter of its hoped-for participants.

The UK project is focused on collecting whole genomes from patients with cancer and rare diseases, and from the family members of patients with rare diseases. It was able to reach its goal of 100,000 participants in 2018, six years after it took its first sample. China, Estonia, Saudi Arabia and Turkey are also aiming to collect repositories of genomic data on 100,000 people. Other countries have projects of differing sizes.13 Qatar, for example, plans to eventually collect information and other molecular data from all of its residents, which will be matched with medical records. Richard O’Kennedy, vice-president for research at Hamad Bin Khalifa University and vice-president for research, development and innovation at the Qatar Foundation, reports that they are initially concentrating on Qatar’s permanent population and have already collected around 20,000 samples.

Dr Kelly Gebo, former chief medical and scientific officer for the All of Us programme, current professor of medicine at the Johns Hopkins University School of Medicine and practising physician, explains that rather than being national versions of the same exercise, “each [of these programmes] is slightly different in their objectives.” In the United

---

In our DNA

Cost of sequencing a single whole human genome (in USD)

Source: National Human Genome Research Institute
States, for example, the focus is on creating a large database that will help researchers learn how biology, lifestyle and environment affect health. In the United Kingdom, the aim is to gain genomic-related insights into specific conditions, while in Qatar the goal is to integrate genomic data with healthcare records for direct use in clinical contexts. Dr Gebo adds that the people working on these different programmes share expertise and best practices, as each initiative ultimately seeks to leverage better, more detailed health data to improve medical outcomes.

**Data storage**

As Dr Brown explains, “most health information systems were not designed for this era of precision medicine. Data has been tucked away in hard-to-use repositories.” However, there have been advances in how to store the growing array of available health data, with an emphasis on ensuring accessibility and usefulness. One important advance is the widespread adoption of EHRs. According to a 2018 survey, 96% of general practitioners in the European Union had some sort of EHR for their patients; the most recent equivalent figure for the United States is 86%, based on 2017 data. EHRs were originally intended to help integrate care and improve administration, but researchers have started to demonstrate that, with the correct safeguards in place, aggregated EHR data can inform large-scale studies, especially when specialised disease registries may not be available.

Finding ways to store and share information remains a work in progress (as discussed later in this paper). However, in the long term, the ability to store and access large amounts of data is likely to be more important to precision medicine than the database projects that governments are currently undertaking. This is acknowledged in France’s Genomic Medicine Plan 2025, which aims to develop national capacity to sequence 235,000 genomes per year. This goal may be superseded by technological progress, as the Global Alliance for Genomics and Health estimates that 60m people will have their genomes sequenced annually as part of regular healthcare by 2025.

**Running along**

Projected number of whole genome sequences run per year for cancer and rare disease

---

Source: Ewan Birney et al. 2017
These numbers will soon far surpass the current largest databases of molecular data. It has happened before. In Nature in 2012 an international research consortium published the results of an effort to provide the most detailed map of the diversity of human DNA. It contained just over 1,000 genomes. 

Data analysis

The final data-related enabler of precision medicine is rapid improvement in data analytics, particularly artificial intelligence (AI). Without this, much of the rest would be of limited use. As Dr Williams explains, “human cognitive capacity is not increasing. With precision medicine, you are dealing with way more variables. You are going to have to use assistance from computer systems.” With this technological assistance, clinicians are expected to gain access to extensive insights that were previously hidden in healthcare data. Indeed, Dr Qoronfleh believes that “as healthcare becomes more digital, it will decode biology. This is the future of medicine.”

Technology will play two key roles in precision medicine: finding links between the attributes of patients with health risks, diseases, and the outcomes of prevention or treatment interventions; and alerting clinicians to the health implications of specific information learned about one of their patients. Just as a blood test outside of normal parameters is flagged for the ordering clinician, EHR software could signal a potentially problematic combination of health data.

The application of AI in medicine remains very much in the early stages, making it challenging to discuss what medical AI will look like in practice. While there are a number of pilot projects, a Nature Heredity review this year found “few examples of Big Data being leveraged in healthcare despite the opportunities it presents for creating personalised and effective treatments”. A 2020 report by the University of Cambridge and the PHG Foundation, a health policy think tank, explained that while “AI is contributing important incremental improvements in clinical genomics analysis including phenotyping in rare diseases and cancer, and variant analysis and interpretation,” the “vast majority of AI activity in genomics is within the research phase.”

The case for precision medicine

Improvements in data collection, storage and analysis will help to facilitate the use of precision medicine, but what are the benefits
of this approach? With precision medicine expected to improve healthcare in a number of different ways, we discuss possible gains at the patient, health system and population health level.

**Patient-level gains**

Precision medicine is expected to provide patients with more accurate and detailed individual diagnoses, enabling the selection of the most effective treatment for the given set of circumstances. Dr Morrow adds that eliminating inappropriate options will be just as important: “Precision is as much about protecting patients from adverse effects of therapies as targeting beneficial ones. We need to avoid doing harm to people.”

Earlier diagnoses are also likely. As Dr Brown explains, “Alzheimer’s, Parkinson’s, cancer—precision medicine could allow us to spot these much earlier. The earlier you can spot a problem, the more quickly you can deal with it.” This may mean that diagnoses start to overlap with recognition of heightened risk, a benefit that polygenic risk scores may soon exploit (discussed later in this paper). Indeed, one of the great hopes is that prevention could become increasingly personalised, enabling people to understand how their own DNA and other molecular attributes may affect their individual health risk profiles.

**Health system gains**

At the health system level, Dr Qoronfleh points out that by providing access to more accurate, evidence-based information, precision medicine will give medical practitioners a better sense of the effectiveness of their interventions, as well as the return on investment for care pathways and protocols. “You can make better decisions which leads to better patient outcomes,” he explains, “because you are shaping your strategy based on information and knowledge.”

**Population health gains**

The role of precision medicine in public health remains a matter for debate (discussed in more detail later in this paper). However, it is possible that precision medicine will have important benefits at the population health level if it is incorporated into national policy and health strategy. While promising, the extent to which these gains can be delivered for patients, healthcare systems and population health will depend on how precision medicine is translated from theory into practice.

**Current progress: Promising but still limited**

Precision medicine has the potential to radically shift the practice of medicine. Dr Dzau notes that discussions about precision medicine tend to involve “a complex mix of science, aspiration and hype”. In practice, the gains have been less than revolutionary so far.

Nobody is downplaying some important advances. However, as Dr. Leners explains,
“precision medicine is not an unattainable futuristic goal. It is already happening in certain situations,” where important advances have been made. According to Dr Williams, the areas that are “furthest ahead” are oncology and rare disease, with some more limited progress in pharmacogenomics and pathogen identification.

**Oncology**

Within oncology, non-small-cell lung cancer and breast cancer have seen the biggest advances, although biomarker testing has been integrated into standard care for neoplasms at some other sites too, including melanoma, chronic myeloid leukaemia and gastric cancer.22 Lung cancer, in particular, shows what personalised medicine can do: survival rates (while still low) have increased four to five times for those diagnosed as late as stage IV, if EGFR or PD-L1 mutations indicate that certain specific medicines may be effective.23

Much of this progress has been recent. In late 2018 just 11 genetic mutations within any neoplasm indicated use of a specific treatment,24 but in 2018 and 2019 the US Food and Drug Administration (FDA) approved 103 new molecular entities, 36 of which could be described as personalised medicines. Of these, 14 are for some form of cancer.15 However, advanced health systems are not necessarily adopting these innovations at scale. A recent study from Germany found that, of those patients diagnosed with the kind of lung cancer for which new treatments might work, only 27% were tested for the relevant biomarkers.26

**Rare disease**

There has also been rapid progress in rare disease—a term that refers to between 6,000 and 7,000 conditions that affect very few people. Although the precise threshold for being defined as a rare disease varies by country, the European Union’s definition (one case per 2,000 people) is the most commonly used. Most rare diseases appear far less frequently in the population, with around 85% of known rare diseases affecting one person per 1m population. However, the sheer number of these diseases means that about 6% of the global population has at least one
such condition.27

The vast majority of rare diseases are genetic conditions, which has allowed precision medicine—and in particular, genomic medicine—to transform the field. The impact is not so much on treatment, although there has been progress there. Fifteen new molecular entities approved by the US FDA in the last two years have been for treatment of a rare disease.28 The greatest impact has been seen in the area of diagnosis, a process that typically takes many years of frustration for patients with rare diseases (see the box on a precision shortcut for the diagnostic odyssey).
Matthew Bellgard, director of eResearch at the Queensland University of Technology (QUT) and chair of the Asia-Pacific Economic Cooperation (APEC) Rare Disease Network, notes that “rare diseases rapidly expose gaps in large health systems and highlight the need for a close alignment between precision public health and precision medicine.” The issue is not simply a lack of treatment options; with over 6,000 identified rare conditions (defined as affecting fewer than one in 2,000 people) and with more such diseases found every year, obtaining a correct diagnosis can be a struggle in itself.

A commonly cited US study reports that, on average, the typical patient consults over seven doctors and waits 4.8 years between symptom onset and accurate diagnosis. In Australia, a similar study found that the typical patient consulted five physicians, and that the journey to accurate diagnosis took 4.7 years. For 10% of patients in Australia, the process took more than 20 years. This frustrating “diagnostic odyssey” can involve numerous referrals between experts in different parts of the health system; any number of tests; and at least a few incorrect diagnoses, leading to treatments that prove ineffective.

However, the large number of rare diseases arising from genetic mutations raises the possibility of using genomic tests to speed up the diagnostic odyssey. Two Asia-Pacific programmes illustrate what this looks like at scale: the Undiagnosed Disease Programme in Western Australia (UDP-WA) and Japan’s Initiative on Rare and Undiagnosed Diseases (IRUD). These programmes demonstrate the importance of embedding new sequencing technology within expert medical care and using data analytics to understand test results.

The Undiagnosed Disease Programme

The UDP-WA brings together a team of experts in different rare diseases at a single location, so that patients have one-stop access to care. The programme accepts patients with complex multi-system conditions who have generally had multiple specialist consultations and hospital admissions. Once a patient has enrolled in the programme and seen a genetic counsellor, an expert panel of specialists reviews the case. For a limited number of patients, the panel is able to reach a correct diagnosis based on existing information and test results. If this is not the case, the panel recommends a series of diagnostic tests. These normally include both whole-exome and whole-genome sequencing.

The panel reviews the test results and, with the permission of the patient (and where relevant, the parents), shares them with national and international partners. This provides access to, and builds the volume of, the body of international shared data on rare diseases, increasing the possibility
of finding a diagnosis for the individual in question. Contributing the patient’s data also supports future diagnoses for other people.

The patient then receives a full report. If a diagnosis is found, the case is referred to the health system for appropriate care where available. If there is no diagnosis, the patient is told of any new findings and given suggestions for further tests. In both situations, the individual living with the rare disease is also referred to relevant support groups or patient communities.

This combination of measures is not perfect, as it only diagnoses around half of the patients who take part in the programme. However, this is still a significant achievement, given that many of these patients had not been previously diagnosed.31

**Initiative on Rare and Undiagnosed Diseases**

Japan’s IRUD, which began in 2015, shows how a programme similar to the UDP-WA can be scaled up. (Japan’s population is over 120m, compared with 2.6m in Western Australia.) Anyone in the Japanese primary care system who appears to have a genetic condition but remains undiagnosed for more than six months can be referred to one of over 400 IRUD partner hospitals. These are linked with around 40 Clinical Centres, where multi-disciplinary diagnosis committees review cases.

Initially, a committee compares existing test results and clinical data with the country’s national rare disease database, in the hope that this facilitates rapid diagnosis of any known condition. Should no diagnosis be forthcoming, the team can send biological samples from the patient and family members to one of five analysis centres for genetic sequencing or any other potentially valuable test. The results are returned to the Clinical Centre and recorded in the national database. If this leads to a diagnosis, the information is communicated back to the referring primary care clinic, which provides appropriate treatment and counselling.32

By mid-2018 the IRUD had made more than 1,000 diagnoses (around 37% of patients who went through the programme) and identified 18 new diseases.33 Although a higher rate of diagnosis is always the goal, the estimated number of undiagnosed rare diseases in Japan is just over 37,000.34
which means that the IRUD has made a significant contribution. The project’s next phase, IRUD Beyond, will increase international data-sharing on rare disease and use genetic insights from the diagnosis of conditions to inform research on potential treatments.

Both the UDP-WA and the IRUD are available through public healthcare systems. Although a number of countries have similar programmes, including the United States, South Korea and Canada, their wider expansion will depend on whether they provide value. Clara Gaff, executive director of the Melbourne Genomics Health Alliance, explains that there is “concern from governments that precision medicine will markedly increase healthcare costs.”

The data should reassure policymakers. While cost-effectiveness studies do not exist for the IRUD and the UDP-WA, Dr Gaff’s organisation has tracked relevant information for the nearly 4,000 patients it treated between 2015 and 2019. It found that, in general, “genetic testing can provide more answers, at lower cost per diagnosis, than a standard investigation.” Substantial savings also come from having to conduct fewer tests, as well as the ability to begin treatment more quickly. Dr Gaff and her colleagues recently published research that showed that for 80 ill infants tested, the average cost per quality-adjusted life year (QALY) gained from the intervention was around US$5,900. (This included the higher cost of reproductive services, because parents of the diagnosed children were much more likely to feel sufficiently reassured by the news to have another baby.)

Takeya Adachi, former programme officer at the IRUD, reports that perhaps the best evidence of success is the impact on healthcare beyond the field of rare disease. Dr Adachi is now taking a leading role in Strategy 2030, Japan’s ground-breaking new strategy for allergies and immunology, which seeks to use precision medicine to target small populations with similar mechanisms to address their conditions. Dr Adachi notes that the “IRUD was mentioned in the strategy document as an example of good practice. Even outside of the fields of oncology and rare disease, many researchers, companies and patients are realising its importance and success.”
Pharmacogenomics

Pharmacogenomics—which uses genomic data to indicate how a given drug will affect an individual—is another promising avenue for precision care. Roughly 20 genes have been identified as having a clinically relevant impact on over 80 medications, in fields including cardiovascular disease, mental health and cancer. Taking this information into account can have a substantial impact on patient care. In one study of patients with depression, doctors checked genomic data before choosing recommended medications. This led to greater patient adherence a year later, as well as cost savings of over $1,000 per person per year.\(^{37}\) Dr Gebo reports that clinicians in the United States are increasingly checking for these genetic markers before prescribing. Various pilot projects for using this testing in the community have taken place, largely in North America and Australia, but the practice has not yet become widespread.\(^{38}\)

Pathogen identification

Genomics could also be used to identify pathogens more precisely. NHS England, for example, is using Whole-Genome Sequencing to test bacteria in all new cases of tuberculosis in order to determine drug resistance.\(^{39}\) Dame Sally Davies, master of Trinity College, Cambridge, and former chief medical officer for England, reports that this practice has reduced the testing turnaround time by six weeks, allowing more rapid prescription of the most effective medication for each case.

The near future is still genomic

These early applications of precision medicine in the fields of oncology and rare disease are no accident; they reflect both the extent of medical need and the current limits of science. Dr Adachi explains that these two pioneering fields have three common characteristics: the severity of the conditions, many of which are fatal; the frequent lack of effective treatments; and the availability of genomic sequencing. “This is not necessarily performed in precision medicine,” he explains, but in both oncology and rare disease “you can easily imagine how to use it.” The same can be said for pharmacogenomics and pathogen identification.

Despite the breadth of possible data that may be useful for precision medicine, in current practice the field largely relies on genomic information. A recent academic review of projects that describe themselves as precision medicine found that 84% only collected biospecimens—something done predominantly in genetic research. Of the rest, 42% combined biospecimens with EHRs.\(^{40}\) Andrew Sinclair, co-lead of the Australian Genomics Health Alliance, explains that while “genomics has impacted everything, the other ‘-omics’ haven’t quite caught up.” Dr Williams agrees, noting that “things like the microbiome and proteome are ultimately going to be really important, but there is no evidence for added value [currently], only additional cost.”

The integration of data beyond the genomic
into precision medicine is unlikely to be rapid. Dr Williams explains that our understanding of these other areas is less advanced than genetics, which means that “a lot of discovery still needs to take place.” As this occurs, however, it will become more difficult to find patterns, because while DNA (at least germline DNA) remains fixed throughout an individual’s life, data on one’s microbiome and lifestyle can change rapidly. This data is also more costly to obtain on a routine basis. Dame Sally Davies believes that pulling clinically valuable insights out of such data “will be difficult. It will need machine learning to bring it all together, but in general it is not around the corner.”

This does not mean that the ultimate goal of multi-data precision medicine is untenable. Dr Dzau reports that “most of us would agree that science will eventually get us there.” He notes that recent advances in science and medicine—such as the rapid development of COVID-19 vaccine candidates, driven by advances in genetic sequencing and vaccine technology platforms—would previously have been unthinkable. However, he adds that he is unable to pin down “how soon” the full promise of this new approach will be achieved, particularly given the long record of incorrect predictions in the field.

As a result of this uncertainty, expectations about how precision medicine will expand in the near future tend to reflect new uses of genomic information. The field of cardiology is predicted to see advances because, as Dr Williams explains, it “has a high burden of disease with single gene origins which affect a substantial number of folk”. Progress is also likely in the genetic screening of neonates. Indeed, Qatar already performs such screening for 28 disorders. Dame Sally Davies also expects increased use of polygenic risk scores to stratify populations in large-scale screening programmes and provide better clinical management. Pilots of polygenic screening are already being conducted for breast cancer surveillance, although substantial work remains to be done. Dame Sally Davies adds that another promising avenue is the “fast, effective diagnosis of pathogens”, which can now occur in a matter of hours rather than days.

It is also likely that genomics will play some
role in prevention. Dr Williams reports that Geisinger Health in the United States had conducted exome sequencing of nearly 145,000 of its patients by 2020 through its MyCode programme, notifying care providers if one of roughly 60 reportable genes is found. Since then, two major Boston hospitals have opened preventative genomics clinics: Brigham and Women’s Hospital and Mass General.

As these advances demonstrate, precision medicine is far from just hype; new tools—some of which are life-saving—have already appeared and will continue to emerge. Nevertheless, it is still far short of what its advocates promise it will deliver. For now, precision medicine’s biggest impact is likely to involve wider clinical applications of genomic medicine that address a range of previously unmet challenges. Using a range of integrated data to build a highly detailed picture of individual health remains some way off.

Is precision medicine worth it?

Will precision medicine deliver better care than the current standard, and in an affordable way? In other words, is it cost-effective? Unfortunately, the answer to this critical question remains unclear. Certainly, the potential for savings in health systems is huge. A 2015 article in The Lancet projected that if personalised prevention could reduce the incidence of heart disease in the United States by just 10%, this alone could save $114bn over the ensuing five decades. However, such projections illustrate gains that might be available, rather than what technology is currently able to deliver. Evaluating cost-effectiveness is also challenging because precision medicine will work very well in some cases but is unlikely to be practical in others. The same is true for other medical approaches. For example, while surgery is cost-effective for acute appendicitis, almost certainly it is less appropriate for a mild headache.

So far, the evidence showing the cost-effectiveness of precision medicine is mixed. Certainly, some interventions in general, and on specific populations, have a good evidence base (see the box on rare diseases). However, Dame Sally Davies notes that while good cost-effectiveness evidence is available for “some mutations and treatment, I don’t think it really exists beyond limited scenarios”. Laura Blackburn, head of science at the PHG Foundation, agrees: “Saying precision medicine saves money is a comment that gets thrown around, but I have not seen much evidence.”

A global review of cost-effectiveness articles on precision medicine interventions that have been published in academic journals also paints an ambiguous picture. Of the publications included in the review, 28% were either inconclusive or found the intervention not to be cost-effective. The point at which a given intervention was deemed cost-effective also varied markedly. In some US studies, an intervention that cost less than $200,000 per QALY gained was considered
cost-effective, which is more than five times more expensive than the standard threshold used by the UK’s National Institute for Health and Care Excellence. The review concluded that “Due to the many factors which influence cost-effectiveness and the varied thresholds of willingness-to-pay applied, the cost-effectiveness of [precision medicine] remains unclear.”

Dr Ginsburg notes that while the value proposition for precision medicine for payers remains “ill-defined”, it is only one part of the puzzle: “We are in the early stages of building the value models for patients, providers, health systems and countries. We need to look through all these different lenses because various stakeholders may have different views on value.”
Public health: The potential and limits of precision medicine

Another terminological muddle

Some of the most intense discussion regarding the wider applications of precision medicine has occurred in the field of public health. This has highlighted a number of issues that are likely to require careful consideration as precision medicine moves beyond (relatively) straightforward genomic conditions to address more multi-factorial challenges.

It is useful to begin by defining public health. According to the World Health Organization (WHO), public health encompasses any "organised effort by society, primarily through its public institutions, to improve, promote, protect and restore the health of the population through collective action. It includes services such as health situation analysis, health surveillance, health promotion, prevention, infectious disease control, environmental protection and sanitation, disaster and health emergency preparedness and response, and occupational health, among others." While public health does not exclude activities at the individual level, its main focus is on the population as a whole or defined sub-populations.

Defining precision public health is more challenging. "Most thoughtful people in this space recognise that the definition of precision public health is not so clear," explains Sandro Galea, dean of the Boston University School of Public Health. One particular point of contention is the nature of the link between precision medicine and precision public health. This was evident in a 2018 edition of *Frontiers in Public Health* that focused on precision public health.
contended that “precision medicine and precision public health are independent” while another argued that precision public health “sits at the nexus of precision medicine and public health.”46 Further complicating matters, Dr Gemma Bilkey, from the Department of Health in Western Australia, explains that “people sometimes use the two terms interchangeably, but they represent different (though complementary) entities.”

Muin Khoury, founding director of the US Centers for Disease Control and Prevention’s (CDC) Office of Genomics and Precision Public Health, believes that “criticism [of the very idea of precision public health] may arise from differing understandings of what constitutes precision public health.” Dr Khoury describes precision public health as “next-generation public health.” It is, he says, about asking “how the emerging abundance of data and its associated predictive analytics can contribute ... by including more extensive information in public health assessment of disease burden, facilitators and barriers to evidence-based intervention implementation and outcome measures, as related to person, place and time.” He adds that this data is not exclusively genomic and could include “biomedical, socio-demographic, environmental, geographic and other information”.

For the purposes of this paper, we conceptualise precision public health as the application of the tools, technologies and approaches of precision medicine to the long-standing tasks of public health, where doing so might prove useful to public health goals.

What might this look like in practice?

In public health, the tools, technologies and approaches of precision medicine have been implemented in specific areas, rather than across the entire field. Progress has been slower than in the field of medicine, with much of the literature still discussing possibilities rather than concrete projects. Nevertheless, precision public health interventions are starting to appear.

Research has been conducted to explore how advances in genomics could be applied to a number of public health tasks, notably screening and infectious disease surveillance. As discussed earlier, research is investigating how to use polygenic risk scores for certain cancers in screening programmes, and sequencing is being used at the health system level to identify drug resistance in tuberculosis in the United Kingdom. Smaller programmes have also used genomic sequencing to identify outbreak sources and track transmission of MRSA, Ebola, HIV, Yellow Fever and the Zika virus.47 Most recently, precision medicine tools have been used in various ways in response to the COVID-19 pandemic.
The COVID-19 pandemic is the dominant healthcare issue of 2020. Responsibility for responding to the pandemic falls squarely in the field of public health, and precision tools are playing a key role.

Work involving the genomics of the pathogen is playing a dominant role in precision public health responses to COVID-19. The US CDC's web-based Public Health Genomics and Precision Health Knowledge database maintains a dedicated Coronavirus Disease Portal of relevant published scientific literature, online news and reports. This portal already has over 7,400 entries. As of 8 September 2020, it characterised 68% of the site’s content as genomic, defined as “the use of pathogen and human genomics and advanced molecular detection methods in discovery, clinical and public health investigations involving COVID-19.”

The highest profile genomic public health activities involve the search for a vaccine. Two of the leading candidates, Moderna’s mRNA-1273 and Pfizer’s BNT162b2, use mRNA technology—a novel approach that has never led to a human vaccine before. The vaccine implants RNA into recipients’ cells, causing the affected cells to make specific elements of the virus but not the whole pathogen. The person’s immune system then learns to attack these as foreign intrusions, in theory priming it to respond quickly if infected by the whole virus. This approach has helped to increase the speed of vaccine development beyond anything possible in the past.

Pathogen genetics have also played a significant role in disease surveillance in two important ways. First, they have been used to monitor whether the virus is mutating in a manner that might vary its severity or vulnerability to vaccines or treatment. Through this work, researchers have found that COVID-19’s DNA is slowly changing. For example, the D614G mutation—so called because of a change in the amino acid at position 614 in the virus’s spike protein—has gone from being relatively rare to nearly universal in samples of the virus. It remains unclear if (and how) this change will affect pathogen severity, prevention or treatment.

This genetic monitoring should warn public health officials about potential changes in the virus well before they become apparent in affected people.

Second, genetic variations in the virus have allowed better surveillance of how the disease is spreading. In the early stages of the pandemic in the Netherlands, analysts used whole-genome sequence analyses and other epidemiological techniques to understand and estimate transmission within the community. This gave policymakers better information as they contemplated workplace and school closures.

At a more global level, Nextstrain, a project of the Fred Hutchinson Cancer Research Center in Seattle, is using minor mutations in samples of virus...
DNA to track how the disease has spread worldwide. Although the project has not published examples of policymakers using such data, its daily updates make it a viable tool. Analysis of the results can also help officials understand what works (and what does not) when considering responses such as travel restrictions.52

Important precision public health research is also taking place without any genomic element. For example, in the early stages of the pandemic, before rapid testing was available, AI was applied to CT scans for case identification purposes.53 Other uses arose as this became less necessary. In some instances, the precision intervention has involved analysing a range of information simultaneously. In Atlanta, for example, the mayor decided to roll back the city’s reopening (after lockdown) after seeing the joint effect of the number of new infections, the percentage of positive infection test results and the availability of hospital beds.54

Precision analysis may also help to explain why certain people, or people in specific locations, appear to be more susceptible to severe cases of the disease. For example, two recent studies—one from Italy, the other from India—indicate that higher levels of air pollution increase the chances of getting the disease and of dying from it.55

Data analytics may help to explain one of the most worrying trends of the pandemic: the higher death rate among ethnic minorities in various countries. Research is underway to investigate whether this disparity may reflect a difference in susceptibility because of attributes in host DNA.56 Alternatively, it may be related to depressed social determinants, as hypothesized by Dr Khoury, founding director of the US CDC’s Office of Genomics and Precision Public Health. If that is the case, he explains, “Precision public health represents a tool that could be developed by using more localised analytics, to help assess the differential risk and burden of disease and death suffered by sub-populations such as ethnic minorities and rural communities. It could then gear and tailor the decision-making and policy responses that will be needed as we move forward.”

The higher death rate could also be due to a combination of social and physical causes. A recent (not yet peer-reviewed) UK study published in MedRxiv found that, among other causes, lower socio-economic status and non-European ancestry both increased COVID-19 susceptibility and severity, but in a statistically independent way.57 Only through precision analytics can we understand what explains these race-based differences in the current pandemic, and therefore how to prevent unnecessary deaths in some groups in the future.

These are just a few examples of how precision medicine tools and technologies are being used in the fight against COVID-19, highlighting both the current role and potential future role of precision public health in enabling more effective pandemic responses.
Academic research that applies data analytics to other kinds of information in the field of public health is also increasingly common. A study in Western Australia, for example, looked at the impact of heat waves and found that age, socio-economic status, and whether one lived in an urban or rural area were likely to affect whether people required medical attention as a result of hot weather. Similarly, a large number of increasingly sophisticated efforts have looked for ways to deal with outbreaks of seasonal influenza, including the use of mobile technology and Internet search information for disease reporting and tracking, as well as genomics for vaccine selection.

Two of the most advanced examples of precision public health involve the use of analytics and geolocation for risk surveillance. A 2018 article in the New England Journal of Medicine and a 2019 article in Nature Medicine published very detailed maps of Africa showing progress against diarrhoeal mortality and towards greater levels of breastfeeding, respectively. Both demonstrated that while the situation had improved in recent years, changes differed greatly both between and within countries. This greater understanding of where health risks are situated should allow more precisely focused interventions.

In at least one case, geolocation of risk almost certainly saved many lives. In 2017 Yemen faced the world’s largest cholera epidemic since records began. The following year, the UK’s Department for International Development used data analytics to help identify likely places of outbreak, drawing on rainfall predictions, temperature forecasts, population density figures and local information on the quality of clean water infrastructure. The algorithm projected with 92% accuracy where cholera would break out. This allowed organisations on the ground to engage in local education campaigns and preposition medical supplies before the disease appeared.

Advocates discuss a number of possibilities for precision public health in the future. The most commonly discussed possibility is so-called precision prevention, where the identification of genetic risk could be used to tailor interventions for small sub-populations and even individuals. In 2018, as part of a broader, five-year, £20.5bn prevention programme, the UK government announced that it would be funding research into the use of genetics and AI "to prevent people becoming patients through personalised advice and intervention". To date, this remains an unfulfilled ambition (beyond the long-established ability to alert those with certain genetic mutations to higher cancer risk).

The causes of controversy

While some see great promise in the potential of precision public health, others view the idea with scepticism. The ongoing debate highlights three important questions that will need to be answered if precision public health is to become more widespread.
How likely is it that precision approaches will add value, compared with standard practice today?

Perhaps surprisingly, critics and advocates of precision public health have much in common when it comes to the question of value. Dr Khoury, for example, advocates for the expanded use of precision public health but also stresses the need for a strong evidence base to determine the value of specific precision interventions, as would be done in any other area of medicine. Where the two groups differ is in their degree of optimism about the likely aggregate outcome of such research.

It is likely that some precision public health interventions will prove themselves while others do not, and very few seem guaranteed to succeed. For example, Dr Williams—who is no critic of precision public health—notes that while polygenic risk scores have seen a lot of investment and are an interesting idea, they may not provide actionable results. He explains that certain genetic mutations, such as the deleterious version of the \textit{BRCA1} gene, can increase one’s likelihood of cancer by roughly 10%, but the “difference in polygenic risk scores [across the population] is much more modest. Where is the bar where you would change surveillance?” A broader concern is that data that becomes available may not necessarily be useful. Google inadvertently demonstrated this when it attempted to harness user search information about symptoms to track seasonal influenza outbreaks—an effort \textit{Wired} magazine described as an “epic failure.” This is not to say that all precision ideas will not work. To date, however, the higher profile ideas have yet to prove themselves.

Critics also warn that efforts focused on personal prevention may be ill-considered. David Taylor-Robinson, professor of public health and policy at the University of Liverpool, notes that even with a wide range of evidence to draw upon, “the extent to which meaningful individual prediction is even possible remains unclear. The inconvenient truth in the risk-prediction industry is that we are predicting outcomes for groups of people like our patient; we are not predicting
the outcome for an individual.” A further complication is that most non-communicable diseases (NCDs) are multi-factorial, which means that genomic insights alone would have limited predictive value (particularly as our understanding of other molecular-level data is currently far less advanced).

It also remains unclear if risk information at the individual or small-group level will be of much benefit, especially where the solution is behaviour change. Dr Taylor-Robinson cites several studies demonstrating that, in other contexts, knowledge of health risks does not greatly affect behaviour. Dr Williams has seen better outcomes—for example, over half of patients in a study at Geisinger changed behaviour when told of individual genetic risk. However, the large number of people who are overweight or obese in developed countries, despite the well-known risks, suggests that patient education will not prove universally successful, even with individualised data.

Does a precision approach change our understanding of what public health means in ways that are misguided or harmful?

The second question about precision public health is whether the approach itself is fundamentally misguided. Here, differences in opinion largely reflect different understandings of how precision public health works in practice. Those who are most sceptical tend to see precision public health as dominated by a focus on biomedical issues (in particular, genomics), in direct contrast to public health’s traditional emphasis on socio-economic matters. Dr Taylor-Robinson, for example, expresses concern that precision public health seems to be “very much driven by the genomics angle, as far as I can tell,” while Dr Galea takes issue with “a notion that technology is a be-all and end-all solution to the problems which face public health, when problems like clean air, a fair economy and gender equality are poorly served by technology”.

Dr Galea believes that this focus has a substantial opportunity cost: “When tools take over and they become the end rather than the means, we make mistakes. It will be a net loss for all of us if there is a distracting investment in these approaches at the expense of others.” Ronald Bayer, professor of sociomedical sciences at Columbia University’s Mailman School of Public Health, agrees: “My main concern is that, because of a bandwagon effect, there will be a big investment in, and shaping of, research that will shift the gaze of those interested in population health so that they will focus on precision interventions.” He cites anti-smoking efforts as an example of where this would have negative effects: “The way we control the major morbidity and mortality arising from tobacco is by limiting smoking. They are not going to be resolved by precision medicine.”

Advocates of precision public health do not see the approach as inconsistent with
the traditions of public health, in large part because they disagree about the purported dominance of genomics and biomedical sciences. Dr Khoury, for example, has always characterised precision public health as an extension of public health, rather than an attempted replacement. He believes that “it is about much more than genetics. We should not lose sight of what we are trying to do at the population level, namely to use better and more precise data to target disease prevention and control, and to improve health and health equity worldwide.” In considering which data to use, he continues, “social determinants are integral to precision public health.”

This broader focus was reflected in the *Frontiers in Public Health* 2018 special edition on precision public health. Of the 18 articles included in this special issue, only four related to genomics (or other -omics). Of those four, two looked at questions that would need to be resolved using traditional public health approaches before such technologies could be used at scale.

It is clear that precision public health is no longer predominated by genomics (if it ever was). What continues to divide people is whether precision technologies will dominate or support work in the field in the coming years.

**Is precision medicine really something new or is it business as usual with slightly better tools?**

The third question is related to the second: if precision public health is not largely about the -omics, what distinguishes it from traditional public health approaches? Advocates argue that precision public health is distinct, in that it can provide tools to address many public health challenges more effectively. Others disagree, arguing that modern public health has been using increasingly sophisticated data and technology to understand risk and plan interventions since the birth of the field (when John Snow mapped a cholera outbreak in London in 1854). Much of today’s output, says Dr Taylor-Robinson, “is just public health with better data”. Dr Bayer adds that, in many areas, “precision public health’ represents a terminological shift, not a paradigm shift. Targeting at-risk populations has always been part of public health strategy. They now have Big Data capacity to shape our understanding of where things are occurring.” Again, he sees a danger in allowing a “powerful conceptual domination that flows from medicine” to affect the broader world of health.

It remains unclear where precision tools are most likely to add value in public health, whether they will distract from the mission and currently successful strategies of the field’s practitioners, and whether they will cause a noticeable revolution that differs from the steady evolution of capacity in public health research. Keeping these issues in mind will help to maximise our understanding of how to leverage the opportunities of precision technologies while reducing the risks.
The challenges of integrating precision medicine into publicly funded health systems

Integrating precision medicine into health systems is no small feat. As Dr Morrow notes, “for many GPs the whole concept of personalised medicine is, in many ways, alien.” Dr Dzau agrees, explaining that “the practice of medicine has to change. That is one of the biggest elephants in the room.”

Three factors exacerbate this challenge. First, healthcare systems have a particular immunity to large-scale transformation as a result of their size, complexity, high levels of regulation and large range of stakeholders. Indeed, two decades ago, the late Clayton Christensen, one of the world’s leading experts on disruption, wrote that “Health care may be the most entrenched, change-averse industry in the United States.” As recently as 2016, Mr Christensen told The Economist Intelligence Unit that this problem had still not been resolved. The number of articles on the difficulty of enacting change in healthcare shows that his observation remains accurate in the United States and many other developed countries. As Dame Sally Davies explains, “Generally, my tribe resists change.”

Second, precision medicine has made clear progress in specific areas of medicine, but it will only expand as potential benefits in other areas become apparent. “The real impediment”, Dr Dzau explains, “is that the field is not there yet”.

Finally, precision medicine will do limited good within traditional health systems. Kawaldip Sehmi, CEO of the International Association of Patient Organisations, argues that this may represent the biggest change to medicine since the founding of the WHO nearly 75 years
ago: “People haven’t appreciated the huge leap from standard medicine which this represents. We need a new, unique precision framework with the right institutions, policies, guidelines and standards.”

The expansion of precision medicine into health systems involves a highly disruptive institutional overhaul within a notoriously change-averse environment, all to create a system whose features are not yet fully clear. As Dr O’Kennedy notes, this “change has to be very carefully managed.” While a detailed manual for careful management is well beyond the scope of this paper, it is possible to identify five key areas that will require attention: stakeholder commitment, proof of value, human capital, infrastructure and regulatory environment.

Stakeholder commitment

Healthcare providers

As with any change management effort, the first challenge is securing an organisational commitment to find the best ways to take advantage of precision medicine’s promise. This begins at the top. Dr Williams observes that “the biggest hurdle is for an organisation to make the decision that this is important.” He notes that while US leaders in this field, such as Geisinger and Intermountain Healthcare, have already made this decision, “colleagues say that an important issue is to raise awareness in their systems that they need to pay attention to precision medicine.” Those not paying attention are currently in the majority. A 2020 survey of American health systems found that 70% described themselves as having low maturity in, or no use at all for, precision medicine. 70 Strong leadership characterises early adopters. For example, Dr Dzau notes that Qatar and the United Kingdom are making extensive efforts in this field, reflecting the conviction of political and health system leaders that such investments will pay extensive dividends in the long term.71

Such convictions cannot remain isolated in senior management, however. They need to percolate through the whole organisation, where many people may remain sceptical. “Culture and education are the big challenges,” Dame Sally Davies explains. Dr Qoronfleh
adds that “there is a bit of a continental divide” between those who see value in precision medicine and those who do not. There is significant literature on winning the hearts and minds of stakeholders within an organisation, and the basic principles identified in this literature apply equally to this challenge. To cite just one example, Dame Sally strongly recommends using change champions to support a better understanding of the issues at play: “You need them. They play a big role.” Other elements of best practice will also need to play a role, including developing a coherent strategic vision, building a clear roadmap for change and aligning incentives with the desired outcome(s).

**Patients**

Stakeholders outside the organisation also need to be on board, and the most important stakeholders are patients. Daryl Pritchard, senior vice president for science policy at the Personalised Medicine Coalition (a multi-stakeholder group supporting the development of precision care), notes that “you need patient empowerment rather than a paternalistic relationship with the physician. How do you get a patient involved in their care so they know they should get diagnostic testing that would drive more effective care?” (See the chapter on patient-centricity for further discussion.)

**Healthcare payers**

Healthcare payers must also be committed to change. In Europe, health systems seem well disposed to cover some precision interventions, but this reflects hope for the future rather than strong convictions about their cost-effectiveness. For example, a study of eight major European health systems found that they were willing to reimburse diagnostic tests, but that this “was seemingly done primarily to ensure access to the precision medicine and only secondary to the value they would provide”. The German government has broken new ground by agreeing to fund prescriptions for mobile phone apps, but each must prove its value in a limited time.

Payers appear more cautious in the United States. A recent survey found that while they were not averse in principle to funding

---

### Leaping hurdles? Barriers preventing adoption of precision medicine (%)

<table>
<thead>
<tr>
<th>Barrier</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reimbursement / ROI</td>
<td>51</td>
</tr>
<tr>
<td>Technology limitations</td>
<td>11</td>
</tr>
<tr>
<td>Clinical expertise</td>
<td>11</td>
</tr>
<tr>
<td>Provider leadership support</td>
<td>8</td>
</tr>
<tr>
<td>Patient accessibility</td>
<td>8</td>
</tr>
<tr>
<td>Data aggregation / storage</td>
<td>8</td>
</tr>
<tr>
<td>Viable outcomes</td>
<td>3</td>
</tr>
</tbody>
</table>

Source: Center for Connected Medicine and KLAS
precision interventions, they “will need evidence of clinical utility to support coverage and reimbursement.” Many do not yet see such evidence. Indeed, a 2020 survey of US health systems found that reimbursement issues were the dominant barrier to further adoption of precision medicine.

Dr Dzau notes that US payers will drive more rapid adoption of precision interventions in areas where their value can be demonstrated. Payers are not alone in these concerns. The lack of answers to questions about cost-effectiveness and improved outcomes represents perhaps the biggest weakness for advocates of precision medicine as they seek to win hearts and minds among health stakeholders. Ms Dana notes that this is “often the only kind of evidence a hospital administrator or payer wants to see. There is frequently not enough evidence for a lot of them to be prepared to invest in new approaches.” Dr Pritchard agrees: “Healthcare payers and providers want practice-based evidence that will improve outcomes and lower costs. Since many of these technologies are new, that evidence hasn’t yet caught up with the promise of personalised medicine delivery.” Greater use of precision medicine will require the generation of more extensive evidence of its value.

**Proof of value**

Evidence of value is clear in some instances, such as the use of genome sequencing to diagnose rare diseases. In general, however, robust studies of cost-effectiveness remain patchy. The problem is not a lack of willingness to test new interventions, but rather a lack of appropriate guidelines for doing so. Stefania Boccia, professor of hygiene and public health at the Università Cattolica del Sacro Cuore in Rome, explains that “those who want to make HTA [health technology assessment] reports for genomics or digital do not have agreed guidelines. Thus, in Europe there are very few. Without these reports, decision makers have difficulty knowing what to do.” A 2020 review by the Personalised Medicine Special Interest Group of the International Society for Pharmacoeconomics and Outcomes Research came to a similar conclusion when it looked at the developed world more broadly: “Most
evaluation processes for precision medicines remain rudimentary for addressing evolving complexity in this space.77

Precision medicine presents many new challenges for traditional HTA procedures. One of the biggest challenges is finding ways to assess the value—in terms of cost, clinical outcomes, health system efficiency and patient quality of life—of the following:

- Diagnostics in general, including the impact of result accuracy on patients and health systems
- Diagnostics when applied to different use cases, such as screening, treatment decisions or pharmacogenomics
- Interventions that integrate diagnostics and treatments
- Next-generation sequencing, which might identify multiple therapies or diseases that were not tested for
- Drugs involved in so-called basket trials, where the same medication is tested on multiple conditions that have a shared genetic attribute (to this particular challenge, add the problem of knowing which current therapy to compare the new one against)
- AI-based decision-support products78

Currently, a lack of expert consensus impedes the wider adoption of precision medicine interventions and creates substantial decision inconsistency. In 2010 the manufacturer of the precision lung cancer drug gefitinib presented the same data to England’s National Institute for Health and Care Excellence and Scottish Medicines. The former estimated the cost per QALY gained to be £35,700 and agreed to fund its purchase. The latter put the figure at £154,022 and rejected it. Although a dated example (the drug is now available in Scotland), this kind of disparity between precision assessments continues. Being able to understand the true costs and outcomes of disruptive innovation is an essential prerequisite for the wider roll-out of precision medicine.79

**Human capital**

If precision medicine is to reshape healthcare, health systems will need to develop workforce capacity, primarily through extensive workforce training and improved medical
education. Dr Williams notes that finding enough “trained genetic professionals is challenging because they are rare”, estimating that there are around 1,600 medical geneticists in total in the entire United States. A recent survey conducted in the United States (the only one for which data is easily accessible) also found that the number of geneticists is not rising. Instead, the additional work brought about by precision interventions is leading to longer wait times and higher average patient caseloads.80

Genetics counsellors are also key players in the provision of precision care. This role often combines training in genetics and nursing (in many countries, a master’s degree) and can involve various responsibilities, such as providing patients with information on the reasons for genetic tests and the implications of the outcome, as well as giving support to clinicians who have less training in genetics. Genetics counsellors are also in short supply, however. A 2018 study found that there were just 7,000 genetics counsellors spread across 28 countries worldwide, and that around 4,000 of these were based in the United States.81 The US National Society of Genetic Counsellors believes that rapid proportional growth in the number of people in the profession is addressing the shortage. However, with slightly over 5,000 counsellors in the entire United States—or around 1.6 per 100,000 people82—it is hard to disagree with Dr Williams’ description of these professionals as “rare”.

The same is true elsewhere in the world. Experts in Europe report an existing shortage that will only get worse as precision medicine becomes more common.83 Similarly, in Australia, Dr Gaff believes that as “a lot more health professionals incorporate genetic testing into care, it will not be possible for counsellors to be involved with all of those patients.” Dr O’Kennedy adds that these low numbers are not just an issue in themselves; they also send a problematic signal about job prospects. “If people are to make their careers in these areas, they need to know that there will be jobs available,” he explains.

Dr Gaff and others identify better training in genetics across the broader clinical workforce as an important part of the solution. In principle, this is not an unusual suggestion. As Dr Morrow explains, “medicine changes all the time. Every physician always needs retraining.” The problem is the extent of education that is required. Dr Radovich explains that “existing health systems are not trained to handle” genomics and precision medicine. Dr Qoronfleh reports that older clinicians in particular “don’t have the training and knowledge. It is a gap.” Furthermore, he notes that the places to which these clinicians may turn for insight also lag behind. Clinical guidelines, for example, largely continue to be based on traditional medicine. Dr O’Kennedy agrees that dealing with the very rapid changes in this field is “crucial”. “Clinicians will need constant updating and older clinicians may not have received sufficient basic training to understand some of the information and its
implications. Fear based on lack of knowledge can create major impediments to adoption.”

The problem is particularly marked at the primary care level, where various surveys reveal low levels of self-assurance among individuals about their capacity to understand the results of—and in some cases, even order—genetic testing. A survey reported in the journal *Health Affairs* found that 86% of general practitioners contacted in New York City lacked confidence in interpreting these results. Although this percentage is unusually high, a majority of primary care providers have limited trust in their own ability to carry out key elements of precision interventions. Dr Qoronfleh is not surprised by these findings: “The hurdles include the vast complexity of the science, and the need for physicians to learn about a significant range of new tests and novel ways to counsel patients through probability-based decision-making.”

Dr Qoronfleh notes that “modernising medical curricula and medical school instruction is critical,” but progress to date has been slow. Ms Dana reports that “genomics does not get much coverage in medical curricula,” and the data bears this out. In the United States, for example, the number of genetics programmes in medical and nursing schools has been growing, but a recent expert editorial noted that “the actual number of learners in these ... is dwarfed by the number of non-genetic health-care professionals in practice.” For those already in practice, various training programmes exist across developed countries, but two extensive international literature reviews found scant evidence on how to make these programmes effective at changing clinical practice on the ground.

Human resource deficiencies also extend beyond clinicians. Dr Khoury highlights that “a critical workforce shortage ... in the application of mathematics and data science to life sciences and healthcare currently exists.” He adds that far too few people with the necessary skills are available to manage and make use of large volumes of complex data from numerous domains. Health systems that are serious about more widespread adoption of precision interventions will need to do better at finding new personnel and training current ones in the necessary skills.

Another human resource issue that is likely to prove equally important has received even less attention: how effective precision medicine will inevitably reshape patient–clinician interactions and demand the provision of resources so that healthcare providers can spend more of their already limited time with patients. Precision medicine will present substantial time challenges for clinicians, especially generalists (in the absence of sufficient geneticists and genetics counsellors). At the primary care level, for example, doctors will need to educate patients in new fields that are relevant to their care, such as genomics—areas where they frequently lack confidence. If doctors are to order genetic tests as part of their day-to-day clinical work, they will also need to devote
more time to ensuring that patients have given informed consent.\(^8\) (As discussed in the next chapter, this is more complicated than for many current medical interventions.) Finally, a learning health system—the goal of precision medicine—will also require ongoing changes to best practice in care, and at a faster rate than currently occurs.

For Dr Ginsburg, this raises an important question: “How does a generalist have a legitimate patient-centred conversation, when you have 15 minutes to assess, make a decision and get on your way? We don’t have a paradigm to really engage the patient in the ways that are needed to make precision medicine impactful for them.” Dr Morrow agrees. “The big challenge”, he says, “is that it is relatively easy to do traditional medicine because it is standardised and can almost be semi-automated. Also, at current levels of resourcing, that is what can be realistically achieved. To move to genuine precision medicine will require a more personalised approach for many of the discussions, which will require more time. It is hard to see how that will be achieved within the resource constraints of primary care.” (He adds that more accurate diagnosis and treatment may perhaps eliminate some of the time required in today’s trial-and-error approach.) This highlights that health systems adopting precision medicine will have to rethink care pathways and provide clinicians at all levels with the necessary time to carry out their revised roles.

**Infrastructure**

Precision medicine requires substantial infrastructure above and beyond what is needed to support current healthcare. In such a data-dependent enterprise, the ability to collect, store and analyse a vast array of possibly relevant information, and to then feed any insights into the health system, is of fundamental importance. Some countries have taken substantial steps in this direction, but none are there yet.

QUT’s Matthew Bellgard explains that the data necessary for precision medicine is generally “fragmented, and housed in multiple disparate data repositories, be they spreadsheets, registries, longitudinal databases or paper-
based notes”, adding that “there is an urgent need for cross-jurisdictional data governance and standards harmonisation.” LifeOmic’s Dr Brown notes that “the first hurdle [in implementing] precision medicine is aggregating all that data in some sort of useful way.” Dr Bilkey agrees: “The biggest challenge is collecting the right data and linking it to ask meaningful questions without compromising privacy. Adequate computational infrastructure is a big issue.” Developing this infrastructure, she adds, “is still a work in progress”.

Amid the excitement about precision medicine, it is worth noting that health systems and researchers are both in the very early stages of obtaining and organising the necessary data. A study published by the Organisation for Economic Co-operation and Development (OECD) in late 2017, for example, found that while EHRs had become much more common across all countries, only ten of the 28 member states had the necessary technology to support “health system quality, efficiency and performance and create a firm foundation for scientific research and discovery”.

Persistent problems include a lack of validated, high-quality data; poor interoperability in data systems, even within countries (let alone internationally); insufficient data infrastructure to gather and analyse the necessary information to better inform their own activities; and the continuing, widespread storage of healthcare information in unstructured ways, including on paper.

Even in leading areas in precision medicine, such as cancer care, data is not yet available in a format that allows analytic tools to use it reliably for complex purposes. IBM’s much-heralded Watson Oncology Expert Adviser, for example, was unable to recognise important details from patient files such as stage at diagnosis and therapy history timeline. While oncology is well ahead of other medical fields, it may still take the better part of a decade to work through the issues involved in getting reliable, well-labelled data.

One sign of this data dearth is the substantial interest that high-quality data attracts. Dr Gebo explains that within three months of the All of Us programme launching the beta version of its Researcher Workbench in May 2020, 100 institutions had signed up for access, even though genomic data was not yet available. Similarly, in May 2020, Nature’s editorial focused on a series of articles looking at genetic variation based on 15,708 individual human DNA sequences and 125,748 exomes, heralding this as “the most extensive publicly accessible analysis carried out so far” and describing the amount of data as “staggering”. These are important developments, but they are far short of the vision of nearly unlimited data, gathered from a vast range of sources.

These data issues will not fix themselves, but proof of value is required to address the various challenges. As a recent essay in NPJ Digital Medicine explained, “In spite of the widely touted benefits of ‘data liberation’, a
sufficiently compelling use case has not been presented to overcome the vested interests maintaining the status quo and justify the significant upfront investment necessary to build data infrastructure. Until this use case has been developed, the ability of precision medicine to deliver on its promises will be highly constrained.

Another essential element of precision medicine infrastructure is sufficient laboratory testing capacity, given the large number of diagnostic tests involved, and in particular next-generation sequencing. According to a study by Diaceutics, a diagnostics company, biomarker tests are only offered in enough facilities to benefit the optimal number of patients 1.5 years to 5 years after the launch of the relevant treatment. The study identifies various reasons for this. Some of these reasons involve clinicians, but others are lab-related problems, such as low levels of test availability, reliability and speed. An increasing demand for tests will also exacerbate current workforce shortages in many developed countries. The Diaceutics study concluded that “The clinical diagnostic testing landscape is broken.” If precision medicine is to become better integrated into the health system, this landscape will need to be fixed. Efforts to integrate genomic testing into NHS England provide examples of the kind of changes that are required (see the box on mainstreaming genetic testing in NHS England).
In 2017 Dame Sally Davies, then chief medical officer of NHS England, issued an annual report entitled Generation Genome, which called for the integration of genomic medicine into the service’s standard care. Such a transformation takes time. In April 2020 the NHS rolled out the Genomic Medicine Service, but health officials do not expect genomic medicine to be part of routine care until 2025. For healthcare, this is a respectable pace of change. As Dame Sally notes, “we have started really well and have a lot to be proud of, but we are not there yet.” A number of issues around “democratising” genetic laboratory testing—that is, making it part of the routine care provided to every patient, where appropriate—illustrate some of the practical considerations involved in the necessary reshaping of existing health infrastructure and practices.

Within Generation Genome, Dame Sally Davies called for a new kind of laboratory infrastructure, part of which involved expanding the kind of expertise and tools available. The report said that the required facilities would need “high-powered computing, not banks of test-tubes.” Another necessary change was more structural: a shift in the number and capacity of laboratories. At the time, Dame Sally says, a kind of “artisanal, cottage industry” of multiple facilities existed. Their locations and areas of expertise did not reflect a thoughtful distribution of resources, but rather were influenced by local funding and academic interest. She adds that this uncoordinated network is “not the way to deliver the best national genomic service. You need centralised laboratories. They are the state of the art because of throughput and cost-effectiveness.”

As with many health system changes, the interests of current stakeholders had to be addressed, including the interests of people managing existing laboratories. The result was a compromise, with the creation of seven supra-regional laboratory hubs (although some tests requiring specific expertise are conducted by a more limited number of National Specialist Test Providers). Dame Sally explains that she “would have liked to see more consolidation, but [having seven hubs] meant that we took people with us”.

Another fundamental requirement for the democratisation of genomic medicine testing has been to make clear who inside the health service can order such tests, and when. Accordingly, the National Genomic Test Directory lists the tests covered by the NHS, and the symptoms associated with ordering those tests. It also indicates the kinds of clinicians who can order different types of test. At present, the directory is largely dedicated to rare diseases and cancer, but it is expected to expand to cover more conditions in greater depth as research develops relevant assays. Although Dame Sally acknowledges the limitations—and would prefer more
whole-genome sequencing and fewer point tests—she believes that “we are one of the only countries that has such a directory. It is really special.”

With a specialist laboratory network and this directory, non-geneticists will be able to order a growing number of tests for an expanding array of conditions. In order for these new tools to provide value, the complexity of interpreting the results needs to be kept to a minimum. Accordingly, the new NHS Genomic Testing Reporting Specification requires that the ordering clinician receives a brief test outcome code, along with the detailed results. Depending on the reason for the investigation, these codes convey information such as “Diagnosis Consistent with Referral Indication”, “[Tumour] Variant Detected – Response to Targeted Therapy, Prognostic/Actionable” and “Actionable Pharmacogenomic Variant Detected”.

As NHS England’s efforts demonstrate, getting the organisational arrangements in place is often as important as the science behind the medicine.

**Regulatory environment**

Without actively seeking to enable precision medicine, healthcare regulation will almost certainly impede it. The existing and typically extensive regulations that exist in most countries are designed to support the old way of doing things. As a result, they could block possible innovations, such as using AI to identify the best treatment or basket trials for multiple cancers that share a common mutation. Government policymakers who wish to enable wider use of precision medicine will need to create an appropriate regulatory environment.

Drug approval bodies in many developed countries have already taken substantial steps in this direction. The US FDA, for example, has issued various guidelines on the diagnostic use of next-genome sequencing. It has also been looking for ways to modernise clinical trial design, including increasing the use of basket trials, umbrella trials (trials of multiple drugs, or combinations of drugs, compared side by side), real-world data, and smaller
trials with more defined populations, all of which can expedite the approval of certain precision medicines. The European Medicines Agency (EMA) has been working on similar issues, often in co-operation with the US FDA and other major regulatory agencies. Looking ahead, the EMA’s 2020-2025 strategy document lists as its top human medicine priority “catalysing the integration of science and technology in medicines’ development”. This priority largely consists of goals that explicitly and implicitly seek to support the development of precision medicine.\(^{103}\) This focus helps to explain the high proportion of newly approved drugs that are precision medications.

There are greater concerns around AI and data. In 2020, for example, a WEF report found that there “are no common frameworks for the privacy and ownership of precision health data”.\(^ {104}\) The regulation of AI within medical devices also faces a host of unresolved challenges. One such challenge is transparency, as many AI tools cannot explain why they are recommending a particular course of action (which runs contrary to medical ethics). Another challenge is continuous adaptation: as the AI learns more and its recommendations change, will they still be safe and appropriate? A third challenge is whether the data that AI uses to learn is of sufficient quality, or is representative enough of the patient being treated to provide accurate advice.\(^ {105}\)

Major regulatory bodies such as the US FDA and the EMA are wrestling with these issues, but the answers will not be easy to find. Until these issues are resolved, data analytics’ contribution to precision medicine—and with it, much of the field’s promise—will remain limited. These efforts will also be complicated by some of the thornier ethical questions related to precision medicine, which are discussed in more detail within the context of patient-centricity in the following chapter.

---

**Getting more personal**

**Percentage of FDA approvals relating to personalised medicine (%)**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2014</td>
<td>21</td>
<td>28</td>
<td>27</td>
<td>34</td>
<td>42</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>2015</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2016</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2017</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2019</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Source: Precision Medicine Coalition*
Patient-centricity: The essential complement to precision medicine

The advent of precision medicine is not the only tectonic change that healthcare has been experiencing lately. As Dr Ginsburg explains, “in general, up until the last 15 years or so, medicine has been an incredibly paternalistic profession. It is not just precision medicine; the entire field is shifting to understand the patient and his or her priorities and needs.”

This shift away from paternalism has been driven by the advent of patient-centred care. Again, there are competing definitions of what is meant by "patient-centred", coupled with a lack of agreement regarding specific terminology (for example, the WHO prefers "person-centred" to "patient-centred"). A 2019 Economist Intelligence Unit study reviewed many definitions and found three common elements that are key to patient-centred care:

- Access to high-quality care
- The recognised status and authority of patients, families and carers within any health-related activity, so that they are co-creators of healthcare with medical personnel
- Processes and mechanisms built into the system to support patients, families and carers in taking on this co-creator role

Rather than viewing patients as objects of solicitous care, or even as an empowered consumers, they are seen as full and active partners with clinicians. This partnership includes decision-making about an individual’s treatment, and, to the extent possible, the co-creation of health research activities and patient input into the management.
of healthcare systems. This patient-centric approach has won the intellectual battle in most health systems and in the pharmaceutical industry; the challenge is to translate this approach into practice.\textsuperscript{107}

**Integrating precision medicine and patient-centricity**

It is important to distinguish between patient-centricity and precision medicine. Perhaps because of the lack of accepted definitions for the two terms, Alan Balch, CEO of the National Patient Advocate Association in the United States, sees a "risk that people may assume that precision medicine equates to patient-centricity, and if you are offering the one you are also offering the other". Indeed, the ideas are sometimes conflated, with people assuming that precision medicine will be patient-centred simply because it looks closely at each individual’s data or characteristics.\textsuperscript{108}

Such thinking mischaracterises patient-centricity. Mr Balch explains that patient-centred care is not just about finding a genetically or immunologically appropriate medication, but rather is a comprehensive process through which the patient and clinician collectively decide on an evidence-based course of care, informed by the patient’s unique attributes and preferences that will impact health outcomes. Precision medicine may be applied as part of this process, but the process may also lead to no medical intervention at all.

Mr Sehmi agrees, describing "a lot of confusion. People seem to forget patient engagement when they talk about precision medicine because the technology overwhelms it. The shiny part takes over, and they forget the complex human mixture of emotions and frailty that somehow does not fit in." This confusion is dangerous, warns Nancy Kass, professor of bioethics and public health at Johns Hopkins University. "Patient-centred care looks at the whole person, including habits and values," she says. "You will probably get better medical outcomes from that than from just sequencing a genome. My biggest fear from precision medicine is doctors and patients putting far too much emphasis on it as a panacea."

When both are understood properly, however, patient-centred care and precision medicine can reinforce each other. As Dr Dzau explains, "precision medicine, if done right, is totally aligned with patient centricity."

**What does this look like in practice?**

In a patient-centric approach, clinicians, patients and other relevant stakeholders share information to help reach agreement on the best way to deal with a given issue. Medical professionals typically contribute expert insights on constraints and choices—for example, the nature of a health condition or risk; different ways in which it may be addressed; and the implications of those options, such as the probability of clinical success or side effects. Patients bring details
about the kind of outcome(s) they value most, based on what is important to them. This search for value can go well beyond traditional medical matters. “I might want an Alzheimer’s Disease test, not because of any clinical action I can take, but to be able to change my plans for long-term care,” Dr Ginsburg explains.

Mr Sehmi notes that precision medicine does not fundamentally alter this partnership. Instead, it adds to the available options that are included in the conversation. Patients and clinicians should consider a precision intervention near the start of their interaction, rather than the clinician assuming that it is the best option. Dr Williams explains that at Geisinger, “the engagement piece up front is critical. You have to ask what it is that you, as a patient, want to accomplish from this care episode. Genomics is a new shiny toy in the medical armamentarium, but not every question has a genomic answer. Don’t try to impose one on a situation that does not need it.” Mr Sehmi uses the analogy of a spear: precision medical science may be the tip of the spear, but the shaft is just as important, which involves “making sure the person being treated is happy [with the option] and comes in the right frame of mind”.

Advances in precision medicine do, however, affect the role of both partners in several ways. Clinicians will require education about the general public and their role as patients. If patients do not understand how precision medicine works, they are unlikely to ask about how it might apply to their situation. Dr Morrow says that the kind and degree of expertise that patients expect from clinicians in patient-centred relationships is likely to change. Precision medicine will vastly increase the amount of available and potentially relevant data and provide a host of valuable new insights, which will simultaneously create even more extraneous information that needs to be stripped out. “The biggest challenge in translating this amazing science into a person-centred framework”, Dr Morrow continues, “is that the presentation of highly complex data has to work at a physician level and a patient level”.

At the same time, Dr Brown explains that patients will gain much greater control
over how they obtain information about themselves, independent of traditional healthcare providers. He expects that technology will allow a “decentralisation of healthcare. Rather than go to a clinic, hospital or doctor’s office, we will be able to do laboratory assessments of our bodies in our own homes and have the data analysed.” As discussed earlier, consumer wearables are also likely to provide a plethora of potentially relevant lifestyle information. Determining how to use and regulate this kind of data remains a matter of debate, but it is clear that the patient–clinician partnership will move even further away from one where the clinician decides what information matters to their conversation.\textsuperscript{109}

This does not eliminate the need for a patient–clinician partnership. In many cases, patient-provided data—including data that can only be provided by the patient—can be valuable to all parties. Dr Ginsburg cites a web-based questionnaire on family history at his clinic as an example of how patient-provided data can be used to inform and enhance patient–clinician precision medicine discussions. Once the patient has entered the relevant data about the health conditions of various ancestors and other relatives, software uses a series of decision-support rules to analyse the information and make recommendations. These are put into a report sent to both the clinician and the patient, who can then discuss the information in more detail when they next meet.

\textbf{Co-creation and collaboration}

Aligning patient-centricity and precision medicine is not simply a matter of finding the best treatment for individuals. It must also involve the co-creation of the research and analysis that is an integral part of precision medicine. The pharmaceutical industry is already seeing the benefits of working with patients as partners in drug research and development,\textsuperscript{110} and Mr Sehmi believes that the analytical tools applied to further precision medicine will also require patient involvement: “You can’t expect a patient-centred response from a computer unless you have programmed it to be patient-centred. AI and machine learning tools will often miss out cultural differences. Being culturally competent requires a lot of understanding from all those involved. Otherwise, the wrong choices will be made.”
Mr Balch adds that when AI is useful for understanding a medical situation, it should include the most robust variables that are relevant to patients. These should go beyond clinical outcomes to include data sets related to how an intervention affects issues such as employment or the ability to live independently. “There is an opportunity to wrap data collection and AI around these matters,” he continues. “Then you can move into a care-planning mode that helps patient and clinician understand when they might expect to see these types of other socio-economic barriers to healthcare access and affordability and talk about what to do.”

Dr Ginsburg does not see this breadth as changing the aims of precision medicine. Rather, it is about enabling precision medicine to do what it should always have aspired to: “At its core, it should take into consideration all aspects of the patient, including their priorities, social determinants and family history.”

Achieving this vision of patient-centred precision medicine remains a work in progress. Dame Sally Davies notes that “even where the right words are there, a lot of the time, the real partnership is not.” The issues are often not related to science. As Dr Dzau highlights, resolving questions around transparency and the democratisation of information will be crucial to achieving alignment between patient-centric care and precision medicine. This requires consideration of the potential contribution of patient-centred care when addressing ethical matters associated with precision medicine.

**Viewing ethical issues associated with precision medicine through a patient-centred lens**

Many of precision medicine’s biggest ethical issues are far from new. Informed consent and patient privacy, for example, are longstanding concerns in healthcare. However, the advent of widespread precision medicine is adding greatly to the complexity of these issues. One driver of these new complications is the permanent nature of an individual’s genetic data and the potentially vast amount of information that can be derived from it.

Said Ismail, director of the Qatar Genome
Programme, explains that “When you do whole-genome sequencing, you are not just targeting one gene or one disease. Genetically, the individual is an open book for you.”

This breadth of detail creates the possibility of incidental findings, which may become apparent at the time of the original laboratory work, or possibly years later as our understanding of genetics improves (assuming the patient’s DNA is kept on file). Where people have given their genomes on a voluntary basis to databases before they are patients, Dr O’Kennedy notes that this “represents a significant trust. It is literally a life-long commitment.” Deciding what to tell a patient about an incidental finding is not straightforward. In some cases, the patient may not want to know. For example, Dr Morrow explains that “a significant proportion of people at risk of Huntington’s Chorea choose not to have the relevant genetic test. They would rather live with uncertainty, which allows them to function and manage the risk and their lifestyles in a way that works for them.” If autonomy matters, he continues, doctors need to respect those sorts of wishes.

However, as Dr Ismail adds, “the thousands of mutations where [genes may show a risk, but] the science is not yet clear cut?” Complicating matters further is the extent of shared genetic heritage within families. As Dr Nahla Afifi, director of the Qatar Biobank, explains, “families can be affected by one person’s genetic findings. Within the same family some may want to know, some may not.” At the same time, it seems inappropriate to not be able to tell a patient that they are at high risk of a serious condition where a clinical response is possible. The European Society of Human Genetics and the American Society of Medical Genetics take different views on this matter. The latter maintains a list of genes that should be reported to the patient when found incidentally; the former stresses the need to inform the patient of the issues before the test and take into account the possibility of incidental findings when deciding whether to use a whole-genome sequence.

A change in how health systems operate in an age of precision medicine will bring further ethical challenges. Dr Ginsburg notes that these systems will need to be “learning health systems, so that in the course of care we gather data and generate evidence. They should be where care is given, and research done.” The blurring of these two activities has important implications for the meaning of consent. For example, a whole-genome sequence taken in search of information on a single condition could potentially lead to database discovery of other health related findings. As a result, Dr Afifi believes that “the main ethical concern [around precision medicine] is consent.” Even asking for consent in this context is far from straightforward. Ms Dana explains that such “information is deeply personal. If you consent to have it collected, are you consenting for your children and relatives? These are not questions normal consent processes cover.” She adds that
there are further challenges if genetic sample collection involves working in less developed regions of the world, where “often the language does not even exist for this kind of conversation. The word ‘gene’ might not exist in the local language.”

The storage of genetic data also raises privacy issues. Mr Sehmi explains that patients do not want medical data being used against them—for example, at a traffic stop or when applying for life or medical insurance. As a result of such concerns, patient information included in large databases is typically anonymised. That said, it may be possible to de-anonymise this information in the future. Professor Kass notes that “we used to say that we could guarantee the anonymity of blood samples. Now, we can’t really do that when a scientist can do certain analyses. It is not that the original researchers were dishonest. Instead, science has evolved and certain information about us is unique and in our blood.”

Informed consent also has to be obtained in a way that allows data collection from a suitable range of patients. Professor Kass explains that “certain kinds of databases do not reflect the heterogeneity of the whole population. Sometimes that is fine, sometimes not. If databases used for predictive modelling are not as heterogeneous as a population, inappropriate inferences may be made.” Part of the solution to this particular challenge is the large databases being put together in countries such as Qatar, Turkey and China. Engaging with potentially distrustful minority communities in developed countries—a perennial issue for health researchers—will be equally important.

Finally, while diversity is essential for accuracy in precision medicine, it can also complicate how health systems address ethical concerns. Scientists and religious leaders, for example, often have different attitudes towards precision genetic medicine, and attitudes may also vary across and within different religions. These attitudes are not necessarily in conflict, but they may inform different perspectives on ethical issues. Dr Qoronfleh explains that “you cannot underestimate” the importance of different faith and cultural traditions when considering questions regarding the implementation of precision medicine.

**How patient-centricity can help**

Patient-centricity does not unilaterally resolve these challenges, but it is an essential component of the solution. An enriched discussion about a given precision intervention, for example, should cover the ethical matters related to data. Patients should be told about the possibility of incidental findings prior to testing, enabling medical teams to learn from each individual in their care what he or she wants to occur if such a discovery arises. There is no reason to impose a one-size-fits-all policy here, especially when, as Mr Balch puts it, “precision medicine is about creating appropriate variations in care based on evidence.” Dr Morrow agrees, noting that respect for autonomy, except in very
rare circumstances, means letting the patient choose, even if a given decision is “at odds with traditional medical frameworks”. With so much data being held on a patient, including their wishes on matters such as incidental findings should not be difficult.

The way that any information might be stored or used should also feature in the discussion, and any privacy concerns should be addressed. Mr Balch recommends that people should have to opt in to contributing their medical information to larger databases. This approach is highly unlikely to undermine patients’ willingness to share data, as most patients are already inclined to do so. Surveys show that majorities in various countries are willing to share with researchers medical and lifestyle data that is relevant to health, although factors such as the precise nature of the information and whether the research is conducted for profit do affect decisions to an extent. Some individuals do not even wait for academics to contact them. For example, around 6,000 people have made the results of their own commercial DNA sequencing available in a public database, OpenSNP. This willingness to share data is consistent with the experience of experts interviewed for this paper. As the Australian Genomics Health Alliance’s Dr Sinclair explains, “if people are sick, they don’t care that much” about these issues.

Nevertheless, willingness to contribute data is not universal. Philippa Brice, external affairs director of the PHG Foundation, expresses the concerns of many when she notes that “we will only get [the] most from precision medicine if we can share and learn from data. If people have difficulties with data sharing, it is a potential problem.” Here, a patient-centricity can again smooth the way. Mr Balch explains that people are much more likely to share data if patients are co-creators of the research or can be part of the learning experience. “If you create a value proposition for patients”, he says, “if they understand that the data being collected are relevant to their care and can help others, people will be invested. If you put the data in a black box and they never see how it is used, they are less likely to understand the value.”

Patient-centricity is also likely to help ensure that databases are sufficiently diverse and represent the population as a whole, as the All of Us programme is finding (see the box on the All of Us programme). Lack of diversity is a long-standing problem in medical research and could undermine the ability of precision medicine to help large sections of the population if it is not appropriately addressed.

Finally, in a truly patient-centric conversation, patients, their families and their carers bring with them their religious and cultural views. This allows clinicians to understand what constraints, if any, these views might impose on precision interventions, and how these might be best addressed on a case-by-case basis.
The demographics of individuals who participate in medical research do not reflect those of the general population in much of the world. The disconnect is probably most studied in the field of clinical trials in the United States. A 2018 article, for example, looked at ten trials held in the three preceding years for drugs to treat cancers that predominantly affect black people. The research found that white people were the largest group of patients represented in the research.114

Dr Ginsburg reports that this is a problem within current databases available for medical AI. “What is missing”, he says, “would be diversity. We have poor representation of ethnicities from outside of those of European ancestry.” This statistical issue has important health implications. For those whose ancestry is less represented, adds Dr Ginsburg, “the chances of misinterpretation are high.” Race is not the only issue; women and older people are also less represented in many databases.

Although the general problem of under-representation of certain groups in research has long been recognised, progress to address it has been slow. This is not necessarily an issue of researcher negligence. A study that looked at the problem for clinical trial researchers found that leading barriers to greater inclusion of a variety of racial and ethnic groups included mistrust of the process by under-represented groups, discomfort with the research process, lack of information about the study and its potential value, and the time and resources needed to take part.115 All of these issues reflect a frayed relationship between researchers and study participants, who, in the words of one respondent, are wary of being treated like “guinea pigs”.116 The study warned that no single intervention could solve the problem.

One aim of the All of Us research programme is to address this research disparity. Dr Gebo, the programme’s former chief medical and scientific officer, explains that they wish to create “a

All of Us: Bringing diversity and patient partnership together

Dedicated to diversity
Race and Ethnicity of All of Us enrollees to 24 September 2020 (%)

Source: All of Us
research platform with a wide variety of populations, including those who have not been traditionally included in biomedical research studies before. Accordingly, the programme is trying to collect data on a disproportionately high number (compared with the general population) of individuals from such groups, including ensuring that over half of its participants are from US racial and ethnic minorities and 80% are from any understudied group, such as older Americans. So far, it has met these goals.

Correcting under-representation of these populations is not simply a matter of sending circulars to minority individuals. It has required the All of Us programme to find ways to establish strong, trusting relationships with minority communities and individual participants. For example, it has worked with black churches to explain the programme to their members, and it is relying on clinicians in a number of Federally Qualified Health Centers to reach individuals from lower socio-economic backgrounds (rather than simply recruiting through academic medical centres, as many trials do). The programme also has a Tribal Collaboration Working Group, composed of tribal leaders, researchers, institutional review board members and community members, to support work with American Indian and Alaska Native populations. “If you have a trusted relationship with groups that are under-studied”, says Dr Gebo, “it will help you understand what participants are doing by donating data [i.e. the emotional commitment behind it] and they will trust the research you are doing.” This in turn will lead to greater levels of participation and engagement.

Outreach to community leaders must be accompanied by efforts to build strong relationships with the individuals involved in the study. This begins with enrolment, with most people entering the programme via in-person recruitment sites. Once enrolled, the status of participants within the joint effort is critical. Dr Gebo explains that “one of the most important lessons we have learned is the value of partnership. We view participants as partners: they help us think through questions like what data we should collect and how, what types of research questions they would like for us to address, as well as which researchers we should aim to have. There is nothing like talking with a participant who says this is what you are doing wrong and this is how to fix it.” These interactions bring clear practical gains in understanding how to structure research, but they also create a sense of purpose. As Dr Gebo notes, working with participants as partners “drives home to us why we are doing the work we are doing”.
Patient-centricty can help to address the ethical challenges associated with precision medicine by transforming healthcare from a transactional activity to a relationship between the various stakeholders, especially the clinician and the patient. In doing so, it can engender trust. Without this, says Dr Dzau, precision medicine will not deliver on its promises. “The public and patients need to feel that they own this approach. It is so important to gain their trust,” he explains. Dr O’Kennedy agrees: “Trust is essential when you are looking at this. It is something we all have to learn more and more about.” This highlights that patient-centricity is not a complication for those seeking to use precision medicine; rather, it is an essential part of making it work.
Turning a vision into reality

The possibilities of precision medicine are compelling. Rapid changes in the volume and nature of available data, and in our ability to store, access and analyse that data, could collectively move healthcare towards what has always been an unstated and unattainable aim: delivering the right intervention to the right person (or population) at the right time. Achieving this would mean that patients receive far better treatments, health systems become far more effective and populations become far healthier.

Precision approaches are already bringing real benefits. In some cases, doctors have a much greater ability to prescribe the correct drugs right away, rather than using trial and error to determine which option (if any) works best. Previously undiagnosed rare diseases are being identified, and patients with potentially fatal cancers are now experiencing greater life expectancies, and in some instances cures.

Aid workers have even been able to predict and prepare for cholera outbreaks.

While it is important to acknowledge and celebrate this progress, one must also acknowledge the limitations in the field. To date, precision medicine has tended to deliver gains in very specific areas, primarily where genomics play an extensive role in how bodies, tumours and pathogens act. The promise of individualised care, informed by a wide range of molecular and lifestyle information about a specific person, remains a distant goal. So, too, does the broader transformation of medicine from what can be an art of trial and error to a precise science.

The broader integration of precision medicine into healthcare (beyond specific genomic applications) will happen quickly, but it will require a supporting infrastructure that differs from existing health system infrastructure.
in most countries and in various ways. No manual exists for those seeking to bring about this change, but experience to date suggests that the following recommendations will be useful to keep in mind.

First, those who are interested in enabling the expanded use of precision medicine need to remain focused on why they are pursuing this goal, even as they struggle with the “how”. As the debate around precision public health illustrates, two broad questions are central to determining whether the effort to use precision approaches is worthwhile. They are, in some ways, two sides of the same coin.

- **Is the effort worth the added value that precision medicine may bring, compared with current practice?** The answer to this question is likely to vary across different areas of healthcare, and over time. In some areas, the answer will be a resounding “yes”, but in others the potential benefits may be small. This suggests that precision medicine will be introduced in a piecemeal manner, at least initially. As more and more fields gain access to newly created infrastructure and enhanced workforce skills, it is likely that an increasing number of beneficial uses will become apparent.

- **If precision medicine represents a significant shift within a specific medical field, is that change misguided?** Even without precision medicine, modern healthcare has been highly successful in meeting the needs of patients and populations. The sector’s aversion to risk is a change management challenge, but it has laudable roots. “First, do no harm” is inculcated into clinicians in part because most can cite examples of innovations that fell flat. Too great a focus on precision medicine has the potential to undermine what current arrangements already provide, and any innovation needs to avoid hurting effective processes that are already in place.

Second, efforts to increase the use of precision medicine must address a wide range of practical issues, including those listed below.

- **Securing commitment:** Advocates of precision medicine within health systems and healthcare organisations will have to dust off their change management textbooks. The most pressing need is to secure the commitment of top management, the organisation as a whole, and other key stakeholders such as patients, payers and regulators.

- **Proving value:** At present, there is insufficient evidence to demonstrate that precision medicine provides improved outcomes in cost-effective ways. Any new way of doing things has to be able to show hard evidence of its advantages over existing approaches, not merely to win over sceptics but to justify greater deployment. HTA bodies in particular will...
Doing well? Fulfilling the promise of precision medicine

need to develop agreed ways to measure such value.

- **Developing relevant expertise**: Medical schools and health systems need to train up more clinical geneticists and genetics counsellors. An understanding of genomics, and eventually other aspects of precision medicine, also needs to be inculcated in the medical workforce.

- **Providing clinicians with appropriate time and resources to engage in precision medicine**: Current resourcing levels reflect what is needed to deliver traditional medicine. The necessary investment to roll out precision medicine must include the required time and money for revised clinical pathways and clinician–patient interaction.

- **Getting data into shape to provide the necessary insights**: The vast amount of data that already exists within health systems—along with any relevant information produced outside of those systems—remains largely unready to provide the insights on which precision medicine will rely. Large health systems, healthcare providers, information technology companies and regulators will need to continue efforts to turn today’s disparate information into something that is genuinely useable at a large scale.

- **Strengthening laboratory testing infrastructure**: In many countries, the diagnostic tests that are currently central to precision interventions are not being rolled out quickly enough. Laboratories are frequently stretched and understaffed. Health systems and laboratory service providers will need to build centres of excellence to ensure speed and quality.

- **Putting in place regulation that reflects how precision medicine is done**: Regulation needs to keep people safe in a way that does not block innovation. Leading drug approval agencies have been taking steps to achieve this for precision medications, and this kind of change must continue. Health system regulators will also need to wrestle with how best to regulate AI tools.

- **Working with patients as full partners in all the changes that are needed to bring about precision medicine**: Patient co-creation will focus precision medicine on the issues that can provide the most value to patients. It is also likely to reduce the ethical challenges that will arise from the new kinds of healthcare data and analytical tools that become available. This will require both new attitudes within health systems and more extensive basic education of the population about how precision medicine works.

We are still in the early stages of learning how to implement precision medicine and understanding what this will look like in practice. All relevant stakeholders need to
ensure that they develop the appropriate and necessary foundations for precision medicine in order for this radically new way of doing things to deliver on its promises.
Endnotes

1 Definitions of precision medicine are discussed later in the paper.

2 The term precision medicine has been used more frequently in US discussions in recent years, following its adoption in a 2011 National Academy of Medicine study. In preferring the term precision medicine, the authors sought to avoid any connotations of individualised treatment arising from use of the word “personalised”. However, it should be noted that they used an older definition of personalised medicine to describe precision medicine. See: National Research Council, Toward Precision Medicine, 2011, https://www.ncbi.nlm.nih.gov/books/NBK91503/pdf/Bookshelf_NBK91503.pdf


6 These enablers have long roots in medicine. Indeed, amid the rapid innovation occurring in the field, it is important to remember how much of today's progress is part of a longer evolution and reflects aims that clinicians have always shared. As Marc S. Williams, professor and director emeritus of the Geisinger Genomic Medicine Institute, explains, “precision medicine is medicine.”

7 For example, the works of ancient Greek medical writers such as Hippocrates and Galen are replete with case studies drawn from interactions with patients. See: Trygve Nissen and Rolf Wynn, “The history of the case report: a selective review,” Journal of the Royal Society of Medicine Open, 2014, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4012665/. Indeed, a recent analysis of a medieval medical pharmacopoeia, the Lylce of Medicynes, found that despite knowledge constraints, doctors from the period took a rational approach to fashioning treatments, some of which were successful. See: “Data-mining medieval text reveals medically bioactive ingredients,” MIT Technology Review, 1 August 2018, https://www.technologyreview.com/2018/08/01/141220/data-mining-medieval-text-reveals-medically-bioactive-ingredients/


17 For further discussion, see Amy Nordo et al., "Use of EHRs data for clinical research: Historical progress and current applications,” Learning Health Systems, 2019; Martin Cowie et al., “Electronic health records to facilitate clinical research,” Clinical Research in Cardiology, 2016.


20 The 1,000 Genomes Project Consortium, “An integrated map of genetic variation from 1,092 human
Doing well? Fulfilling the promise of precision medicine


14. For details see Takeya Adachi et al., “Japan’s initiative on rare and undiagnosed diseases (IRUD),” European Journal of Human Genetics, 2017, https://www.nature.com/articles/ejhg2017106


© The Economist Intelligence Unit Limited 2020
Doing well? Fulfilling the promise of precision medicine

© The Economist Intelligence Unit Limited 2020


The history of the term precision public health may explain some of this concern. When the term was first used in Western Australia in 2013, it involved the provision of genetic sequencing to help diagnose many patients with rare diseases,56 straddling the grey area between individual medical care (diagnosis) and public health (epidemiology). Similarly, the US CDC’s efforts in precision public health grew out of its work on public health genomics.57 Fears about a focus on genomics and AI have been further exacerbated by public figures describing precision public health exclusively in such terms. (For example, see the UK health minister’s comments when announcing a precision prevention initiative.)58


57 The editors of which were mostly from the Western Australian group involved in introducing genomic sequencing to screen for rare disease.


78 Economist Intelligence Unit, The digitisation of the German health system and value-based care: Opportunities and limitations, forthcoming.
Centrer for Connected Medicine and KLAS, Top of Mind for Top Health Systems 2020, 2020,
Doing well? Fulfilling the promise of precision medicine

© The Economist Intelligence Unit Limited 2020


Ibid.


https://www.england.nhs.uk/publication/genomics-testing-reporting-specification-v1-0-for-2020-21/


© The Economist Intelligence Unit Limited 2020


While every effort has been taken to verify the accuracy of this information, The Economist Intelligence Unit Ltd. cannot accept any responsibility or liability for reliance by any person on this report or any of the information, opinions or conclusions set out in this report. The findings and views expressed in the report do not necessarily reflect the views of the sponsor.