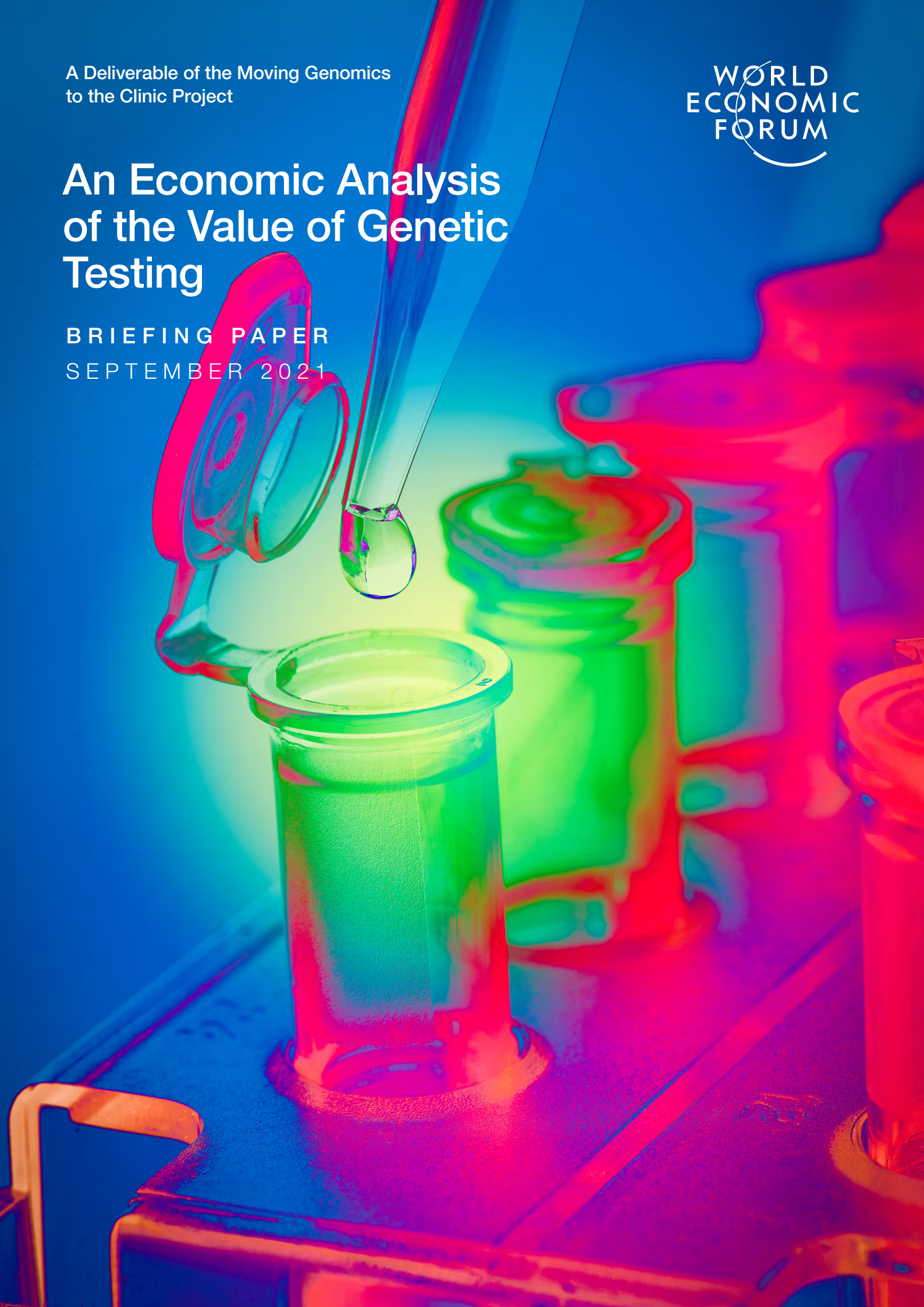
A Deliverable of the Moving Genomics to the Clinic Project

WORLD ECONOMIC FORUM

An Economic Analysis of the Value of Genetic Testing

BRIEFING PAPER

SEPTEMBER 2021



Introduction

Precision medicine has been defined as "an approach to disease treatment and prevention that seeks to maximize effectiveness by taking into account individual variability in genes, environment, and lifestyle".[1] This approach – finding the right treatment for the right person at the right time – is currently medically possible using a range of integrated tools, notably translational science, big data sets, targeted therapeutics and genomics.

Genomic data is central to a precision medicine approach to healthcare; by using computational and statistical methods, it is possible to decode DNA into its base sequences to visualize its functional information as data, enabling researchers, bioinformaticians and clinicians to decode the characteristics of a person's DNA.[2] These insights can be leveraged to make personalized medical decisions for an individual by comparing their DNA to a "reference" genome.[3]

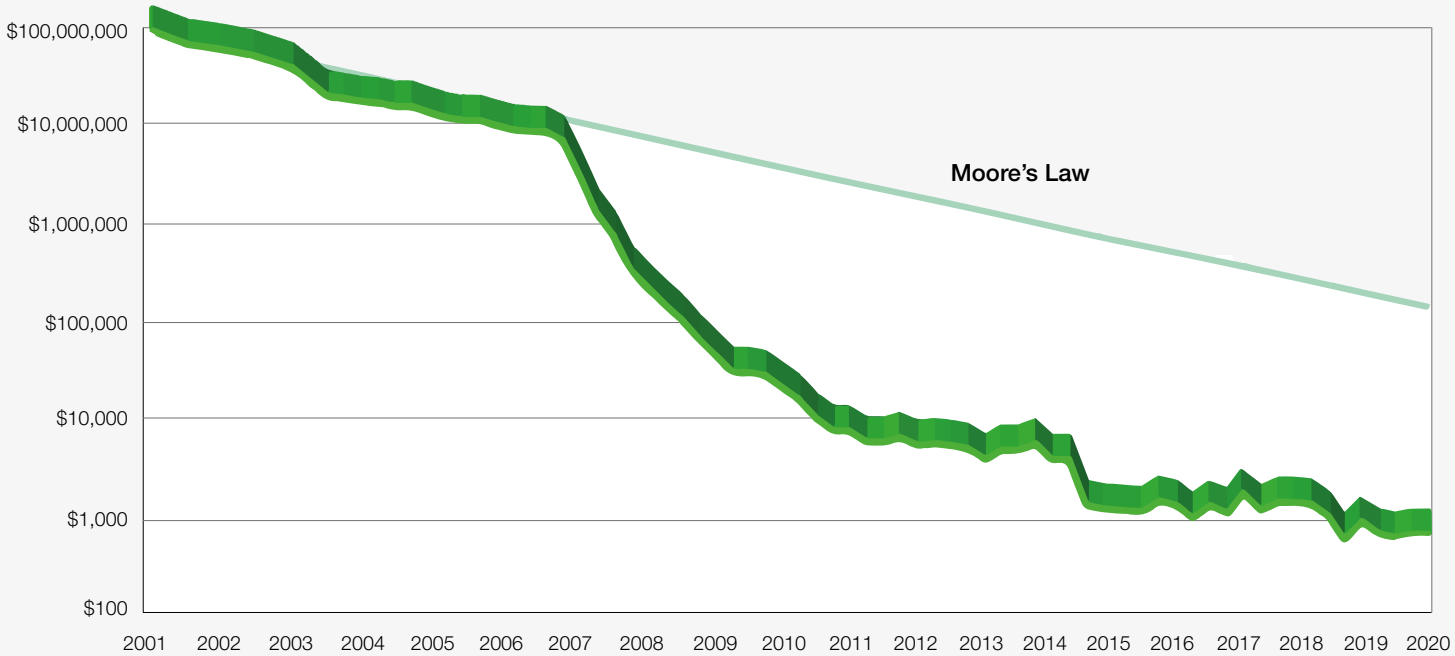
The results of genomic testing may be useful in diagnosing and assessing the severity of disease, predicting a patient's risk for developing a type of disease and illuminating the likelihood of passing on a disease to children. However, for the full potential of genomic testing to be realized, it needs to be integrated as part of routine clinical testing in clinical pathways.

Since the Human Genome Project – an international, collaborative research programme to map the human genome that took 13 years and cost $5.34 billion[4] – was completed in 2003, the price of genetic testing has continued to drop precipitously (Figure 1). Today, sequencing costs can be as low as $1,000 and can be delivered in days or weeks instead of years,[5] a remarkable reduction outpacing even Moore's law.[6] This decline in cost and turnaround time and a growing body of evidence of individual and health system benefits have greatly bolstered interest in genetic testing globally.

Based on current estimates, the global genomic sequencing market is expected to grow from its previous $10.7 billion valuation in 2018 to $37.7 billion by 2026. Thus the genetic testing market is predicted to experience a **compound annual growth rate of 19.1%** for 2021-2026.[7]

As genetic tests continue to be more accessible, there are a variety of use cases to investigate. This briefing paper highlights advances in three domains – **rare disease, cancer and population health** – in which genetic testing is unlocking new treatment pathways to save time, lives and resources. It also offers a reflection on future directions in the field of **carrier screening**, a set of genetic tests that can tell one whether they carry a gene for certain disorders.

FIGURE 1 **Cost per human genome sequence in the USA, 2001-2020**



Source: Jennings, Katie, "How Human Genome Sequencing Went From $1 Billion A Pop To Under $1,000", *Forbes*, 28 October 2020

1 Rare disease testing

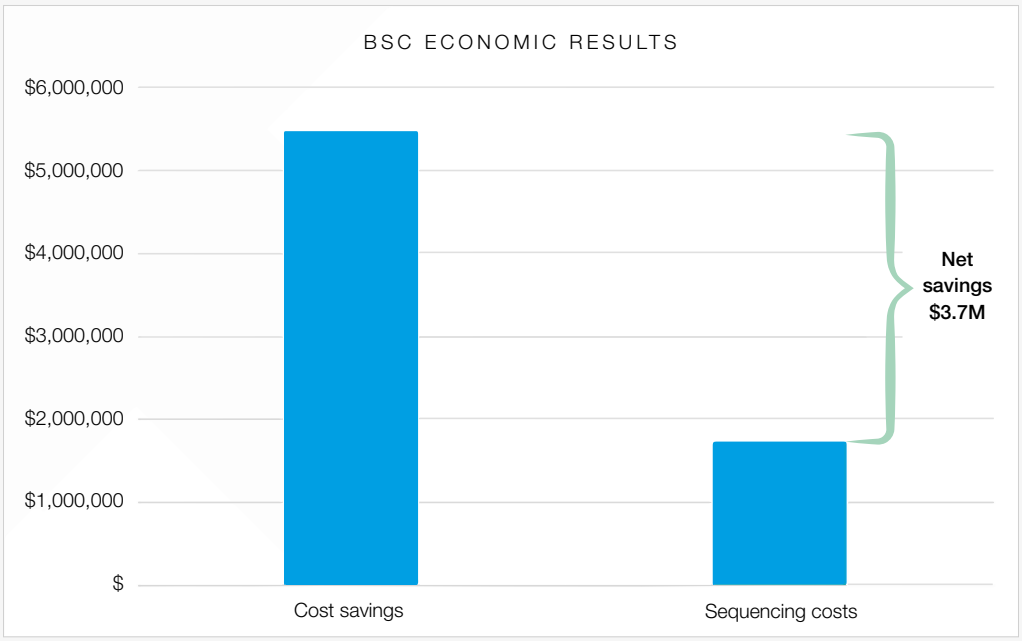
Approximately 300 million people worldwide suffer from a rare disease, defined as conditions that affect less than 1 in 2,000 citizens.[8] While 80% of such disorders are caused by genetic factors, appropriate genetic testing and diagnosis still presents a challenge. The quest for a diagnosis – commonly referred to as the diagnostic odyssey – takes an average of five years according to data from Europe, the United States and Japan.[9]

A variety of studies in multiple countries and across multiple age groups and presentations of rare diseases have shown cost savings and cost effectiveness from genomic testing for rare diseases.[10,11] Among these, **rapid whole genome sequencing** (rWGS) has emerged as technology that can achieve faster, better and cheaper results in paediatric intensive care units, drastically improving the lives of patients and their families. With proven clinical and economic benefits, whole genome sequencing programmes in different parts of the world are leading the charge in a new standard of care for some of the sickest children across the globe.[12]

Recently, investigators from Blue Shield of California (BSC) and Rady Children's Institute for Genomics used claims data from BSC and results from Project Baby Bear (PBB)[13] to show the potential healthcare dollars saved when this test is properly used within the context of a private payer model (Figure 2). In Project Baby Bear, 94% of eliminated healthcare costs came from reduced inpatient days. Because BSC largely reimburses services based on a patient's time in the hospital, the significant impact that rWGS has on length of stay would have had a major impact on reimbursement for the PBB cohort. For the 31 patients whose clinical management was changed by rWGS, it was determined that between 462 and 606 inpatient days were avoided. This led to between $7.7 million and $9.6 million in reduced charges from the five hospitals that participated in PBB.

If BSC reimbursed this care at the same rate as the matched control patients, BSC would have realized between $4.6 million and $6.3 million in gross savings due to reduced inpatient stays alone. When distributed across the 178 sequenced patients, this would have resulted in an average $30,748 decrease in BSC payment per patient. When accounting for the $1.7 million in testing costs, this would have yielded between $2.9 million and $4.6 million in net savings for BSC.

FIGURE 2 | **Potential healthcare savings from effective rapid whole genome sequencing utilization**



Source: Data provided by Blue Shield of California and Rady Children's Institute for Genomics

These savings are likely the tip of the iceberg as the annual cost of only a subset of rare diseases in the United States alone has been evaluated at nearly $1 trillion, this cost being many times higher than cancer and other notable common disorders.[14] Diagnosis is the portal to the best and most cost-effective medical care. The true economic size of this iceberg, and the corresponding opportunities for cost savings and effectiveness, will continue to be vastly underestimated until rare diseases are better coded for and tracked in health, and other, systems.[15]

2 Cancer testing

Cancer is the trailblazer for genomic medicine. Genetic testing has been used to identify inherited and acquired mutations responsible for cancer, especially in the realm of tumour sequencing. This allows for personalized medicine that tailors treatment to each patient, positively impacting the well-being and survival rates of cancer patients.

Lung cancer is the second most diagnosed cancer, but the leading cause of cancer deaths worldwide.[16] Understanding the various genetic pathways that lead to lung cancer has also given rise to **targeted treatments** with the goal of only attacking cancer cells to minimize potential side effects from damage to normal cells and tissue. As such, testing for these mutations is an important part of the diagnosis and treatment process. Approximately 40-50% of lung cancers exhibit a targetable gene mutation[17] with appropriate targeted treatment resulting in increased progression-free and overall survival (the length of time during and after the treatment of cancer that a patient lives with the disease but it does not get worse).[18]

As more is learned about the biology of lung cancer, mutations that drive this disease will continue to be identified. Thus, data suggests that performing a broad panel test for many mutations can be a cost-effective way to precisely identify the correct treatment for a patient. Broad panel tests are generally available and are of interest to providers as a versatile solution to complex genetic testing. One retrospective review identified lung cancer patients who received broad panel testing versus narrow panel testing (fewer genes tested). Although patients who received broad panel testing may have had higher costs upfront due to the cost of the test, their overall cancer care cost was significantly lower,[19] findings that have been supported by other studies. Furthermore, the cost of adding additional genes to broad panels is not significant after a certain point, lending further credence to their use.[20,21,22]

3 Population health testing

Population health is increasingly relevant for today's healthcare systems.[23] The overall approach aims to improve the health of an entire population via the improvement of physical and mental health outcomes as well as the well-being of people within defined populations while addressing wider determinants of health to reduce health inequalities. Increasingly, genomic testing is being applied to population health with remarkable results. Genomic testing is an exemplar of precision public health that is using all available data to more efficiently and effectively target interventions to the most vulnerable and the most at need.[24,25]

Liver cancer is one of the most common cancer types globally, and notoriously difficult to treat in its mid to late stages. China is home to nearly 50% of new liver cancer cases and deaths worldwide.[26] China's disproportionately high death rate is due to approximately 80% of cases being diagnosed at the late stage when treatment options are either limited in effectiveness or prohibitively expensive. Among China's high-risk population,[27] 87 million people are hepatitis B virus carriers, an affliction that greatly elevates one's risk of developing hepatocellular carcinoma (liver cancer).[28]

Using liver cancer as a model, Genetron is now working with the Wuxi Municipal People's Government (Jiangsu Province) to offer early liver cancer screening as a public health benefit to high-risk individuals in the city.

Population-based genetic screening for liver cancer requires a simple blood draw, markedly reducing complexity from traditional methods (e.g. CT/MRI scans) and increasing specificity and sensitivity for early-stage cancers versus current methodologies (e.g. Type-B ultrasound and alpha fetoprotein tests).[29,30]

Comparable to the positive spillover effects of governments offering free COVID testing, community-based population health testing offers tremendous advantages. The short-term effect is raising public awareness of testing through a combination of marketing campaigns and word-of-mouth influence. By gradually normalizing knowledge and access to publicly sponsored early screening, a greater percentage of high-risk citizens will opt into the programme at their local clinic/hospital. Ultimately, the detection distribution of liver cancer diagnoses will shift to earlier stages, greatly increasing the five-year survival rate and removing costs from the healthcare system.

4 Carrier testing

Carrier genetic testing (CGT) is a type of genetic testing offered to individuals to determine the risk of their offspring being born with a genetic condition. It is usually sought by couples seeking to start a family. Carrier screening can include life limiting conditions as well as medically manageable conditions, and has grown in popularity within the preconception and prenatal disciplines.

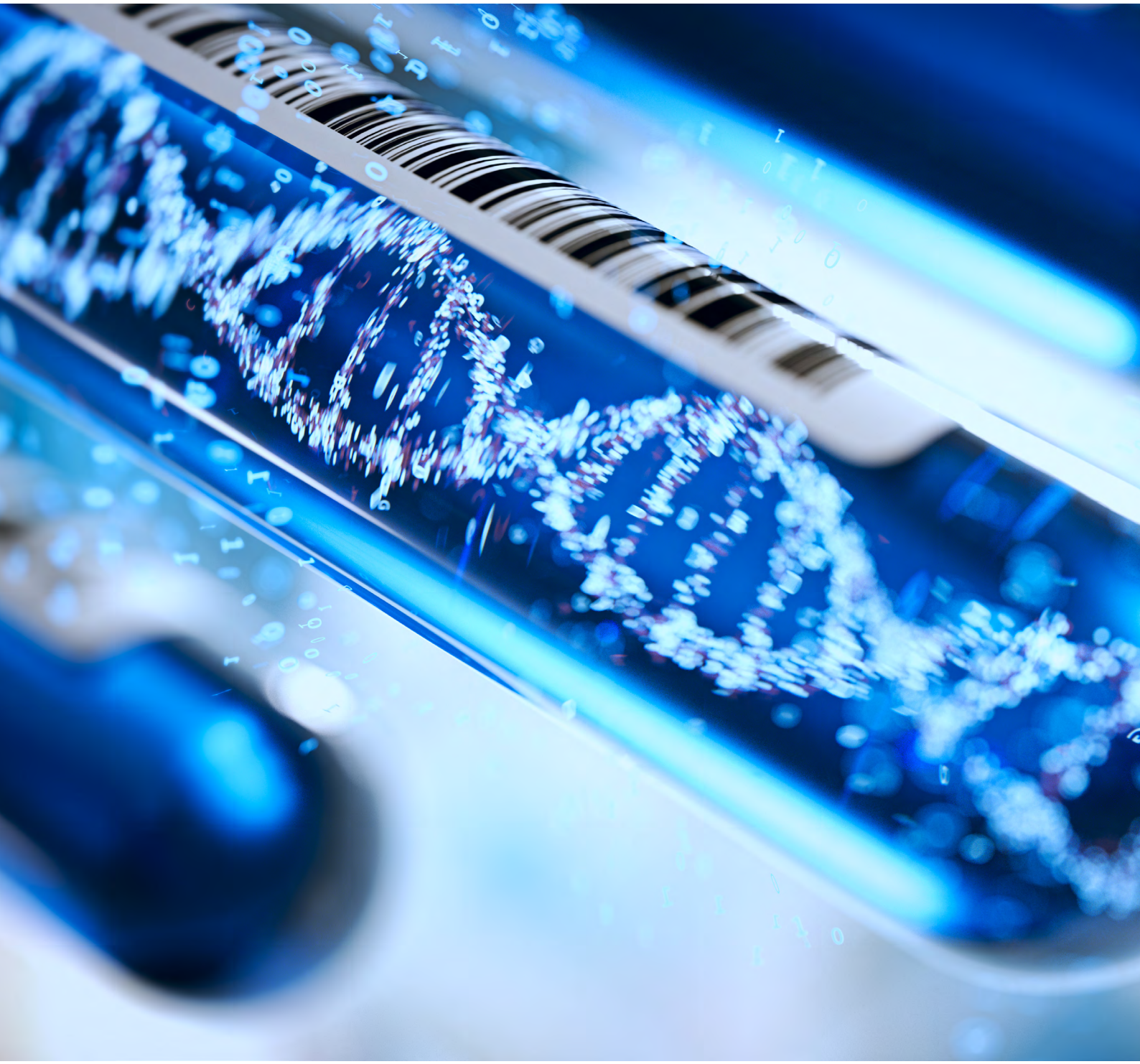
CGT on healthy individuals inherently raises questions regarding ethical use, equity in access[31] and impact on management. In the preconception setting, there is considerable disagreement on what genes or diseases should be included for CGT. For example, are the genes screened based upon a population or heritage versus the most common disease or syndromes? Additionally, there is the potential challenge of interpreting genetic, especially novel, variation in the absence of a phenotype (e.g. an affected child). While many questions surrounding CGT are not unique, some are, or are more complicated due to the pre- or peri-conception testing context. When considering CGT in the couples seeking future fertility, the primary benefit of universal offering is **patient autonomy**. Yet, while ethical dilemmas also arise around carrier testing preconceptionally, offering screening in this context has advantages for a couple considering having children in the future.

In response to the increased risk of certain conditions, some ethnic groups have developed screening programmes targeted to conditions present in their population. Carrier screening within the Amish, Mennonite and Hutterite groups in the United States places a focus on **patient education** and **genetic counselling**, with the goal of early identification and treatment of affected individuals. Historical guidelines from the American College of Obstetricians and Gynecologists (ACOG) recommended that all women of South-East Asian ancestry be screened for thalassaemia, a red cell blood disorder that can result in reduced blood oxygenation, leading to anaemia. The Dor Yeshorim programme was developed by the Orthodox Jewish community to avoid the lethal conditions common within this population. Given the community's focus on both health and family, this programme focused on determining the "genetic compatibility" of couples interested in marriage. Although the programme unabashedly describes the goal of preventing debilitating diseases, it provides an example of how targeted testing can provide an at-risk community with information to empower decision-making, maintain confidentiality, and support mental and emotional well-being.

Conclusion

The use cases presented in this paper are only the tip of the iceberg in the realm of genomic and precision medicine. As the cost of such tools continues to drop in tandem with the development of evermore effective sequencing methodologies, the prospect of truly "moving genomics to the clinic" for a wide variety of uses will, inexorably, become reality.

Several barriers remain to widespread adoption, however. While these challenges can be addressed, the speed with which genomic tools percolate into healthcare systems will be set by the choices of the community, policy-makers, payers, physicians, scientists and genetic counsellors, among many others. There is an urgent and increasing need for these stakeholders and decision-makers to facilitate timely and equitable access.



Contributors

Authors

Lynsey Chediak
Head, Partnerships, Rarebase, USA

Anne Claussen
Vice-President, Cancer and Other Serious Illnesses Transformation, CVS Health, USA

Katherine Dunn
Associate Advisor, Intermountain Healthcare, USA

Kirsten Farncombe
Scientific Associate, Toronto General Hospital Research Institute, University Health Network, Canada

Jason Flanagan
Genetic Counselor, Sanford Health, USA

Panos Kanavos
Deputy Director, LSE Health, London School of Economics, United Kingdom

Raymond Kim
Clinician Scientist, Princess Margaret Cancer Centre, University Health Network, Department of Medicine, University of Toronto, Canada

Konstantinos Lazaridis
Executive Director, Center for Individualized Medicine, Mayo Clinic, USA

Christy Moore
Program Manager, Clinical Genetics, Blue Shield of California, USA

Jeff Niu
Innovation and Experience Lead, Product & Strategy, Genetron Holdings, People's Republic of China

Maria Raimundo
Senior Account Manager, Beta-I, Portugal

Shirisha Reddy
Medical Director, CVS Health, USA

Caoimhe Vallely-Gilroy
Global Head, Digital Health and Therapeutics, Merck, Germany

Bryce Waldman
Strategy and Business Operations, Invitae, USA

Christina Waters
Senior Advisor, Congenica, United Kingdom

World Economic Forum

Cameron Fox
Project Lead, World Economic Forum LLC

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Madison Arenchild
Manager, Strategic Programs, Rady Children's Institute for Genomic Medicine, USA

Gareth Baynam
Clinical Geneticist, Genetic Services of Western Australia, Australia

Tiffany Boughtwood
Managing Director, Australian Genomics Health Alliance, Australia

Alicia Cock-Rada
Oncogeneticist, Cancer Institute Americas, Colombia

Andrea Corazza
Head, Brussels Liaison Office, Public Policy and Government Affairs, Biogen, Belgium

David Dimmock
Medical Director, Rady Children's Institute for Genomic Medicine, Rady Children's Hospital, USA

Kevin Doxzen
Hoffmann Fellow, Arizona State University, USA

Arthur Hermann
Principal Policy Consultant, Kaiser Permanente, USA

Dany Matar
Strategist, Strategic Partnerships, Color, USA

Kathryn Phillips
Professor and Founder, University of California San Francisco (UCSF) Center for Translational & Policy Research, UCSF School of Medicine, USA

Cecilia Schott
Vice-President and Global Head, Precision Medicine, Novartis, USA

Eli Townsend-Shobin
Director, Diagnostics Pathways, Biogen, USA

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World Economic Forum
91–93 route de la Capite
CH-1223 Cologny/Geneva
Switzerland

Tel.: +41 (0) 22 869 1212
Fax: +41 (0) 22 786 2744
contact@weforum.org
www.weforum.org