Public Policy Projects
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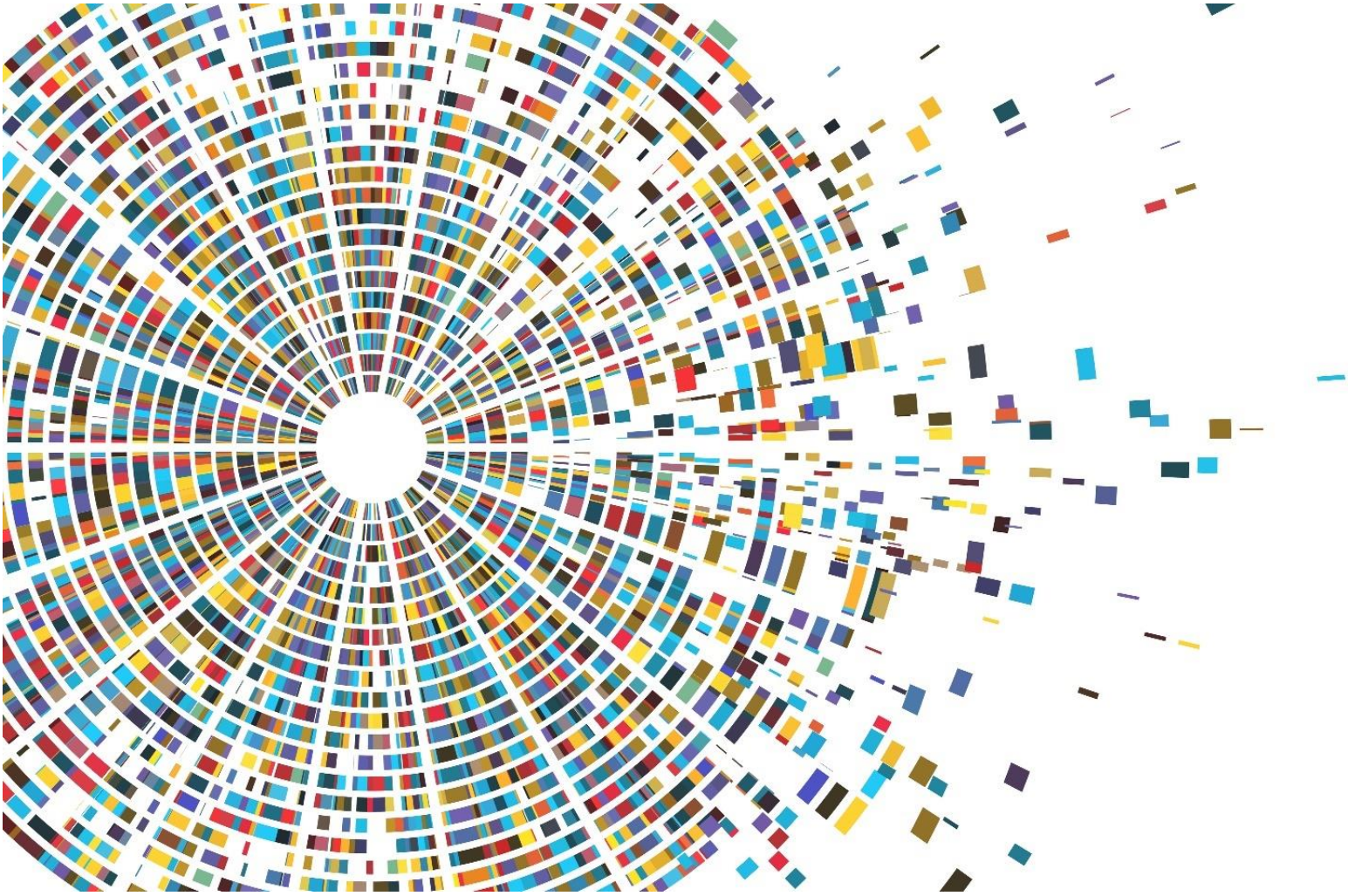
State of the Globe: Bringing the benefits of genome sequencing to the world

Roundtable Six

The Economic Benefits to be derived from participating in Genomics



This report collated the thoughts and actions addressed during the sixth roundtable of this series. The conducted discussion operated under the Chatham House rule.

The genus of this body of work was to explore how to bring the benefits of genome sequencing to the world and an important factor in this was to explore how the lack of diversity in the dataset has the potential to exacerbate the health inequalities that we know exist. If genomics and genome sequencing is the best opportunity to prepare for the next pandemic (and indeed for other transmissible diseases), as well as optimise the protection and preservation of population health and individual health and yet genomic data continues to fail in reflecting the diversity of the global population, will it fail in bringing those benefits equally to everyone?

Roundtable 5 considered these issues in detail and also highlighted the related issues of the need for greater diversity of participation in the wider genomics ecosystem – increased diversity in research communities, the need for greater, more meaningful community engagement, and the need for more capacity building were key themes which were brought out of our discussion. Access the report of that session here:

PPP-Global-Genomics-RT5-Report.pdf (publicpolicyprojects.com)

The sixth roundtable focused on how to articulate the economic benefits of genomics. If genomics has significant potential benefits, we need to be able articulate the economic benefits of focusing on such a programme so that those who hold the purse-strings, wherever they may exist in the genomics ecosystem, can better understand why it is economically advantageous to give this priority when there are so many competing economic demands. If the Human Genome Project, and the sequencing of the human genome, represented the greatest single achievement in the field of life sciences and showed great promise for, in the words of President Bill Clinton, "making life better for all citizens of the world, not just a privileged few" how can we ensure that it is not solely those economies that can afford to invest significantly over multiple governments that get to reap the economic benefits by growing a thriving genomics ecosystem? Is the creation of jobs and companies and tax revenue the only way of demonstrating economic benefit? What about the wider health economic benefits – the costs that can be saved by deploying genome sequencing to provide more targeted interventions more accurately and quickly; the reduced care burden or the ability for people to return to work more quickly or to not become sick in the first place? How do we quantify these?

If the question were posed "Are whole-exome and whole-genome sequencing approaches cost-effective" it might be surprising to note that there are only a handful of such economic evaluations, and no such work has been undertaken in the context of Africa. Some research (including with respect to Genomics England) is ongoing and the results are imminent. The purpose of the session was to hear different perspectives on how to articulate the benefits of genomics and genome sequencing – what has worked and that has been challenging? And to explore whether the challenges are the same or different in high-income and low-to-middle income countries.

The RT6 Briefing Paper referenced Ambroise Wonkam's estimate that the Three Million African Genomes Project (3MAG) will cost $450m a year for a decade. Where is the money going to come from to enable important projects such as this to progress? There is a huge opportunity for

collaborative efforts to drive change – both between countries, between individual researchers and organisations and between those who make profit and those who don't. The genomics ecosystem needs all these elements if it is to achieve its potential.

The key themes and questions this roundtable sought to address and discuss were as follows:

1. Why is it important to articulate the economic benefits that can be derived from genomics?
2. What do we mean by economic benefits?
3. In creating a global genomics network, can international collaboration ensure that no one or few jurisdictions monopolise and disproportionally reap the financial and economic rewards?
4. Are economic benefits purely monetary or can they be reflected through investment in equipment or people for example?
5. Is it possible to demonstrate the cost savings that genomics could bring in the future? How can we help policy makers understand the wider opportunities and benefits that genomics can bring?

Why is it important to articulate the economic benefits that can be derived from genomics?

There was a recognition that there is a need to articulate the economic benefits of genomics so that publicly funded investment can be derived or maintained, whether in high or low-to-middle income countries (LMICs). The appetite for public sector investment in genomics is not, however, consistent and there can be particular challenges for LMICs whose governments have relatively small capacity for investment and many competing priorities. Not all governments have given investment in genomics priority. This may necessitate greater involvement of other funding sources including the private sector if genomics programmes are to be developed at scale (eg 3MAG).

There was consideration of why and how some governments support investment in genomics. This has been the case over multiple governments in jurisdictions such as the UK, Canada, Australia and Thailand and is just beginning in jurisdictions such as Hong Kong. Some jurisdictions are positioning genomics as a driver for economic growth. For other jurisdictions, for example across the continent of Africa, there seemed to be limited understanding of the benefits that could accrue. Is genomics and personalised medicine seen as a luxury or for rich people or countries? Should it be positioned as personalised public health? Should there be a greater focus on areas such as pharmacogenomics (PGX) or harnessing data to make more panels for screening?

Is it right to try to simply demonstrate a cost saving to the health system by utilisation of genomics? There were differing opinions on this, some saying that was likely to be the easiest way to get government buy in.

As one example, in Thailand, the health economic evaluation of using genetic testing as a preventative tool for Stevens Johnson Syndrome/TENS was demonstrated and has effectively reduced cases from 1300 per annum (2019) to 300 (2021). The 2019 figures represented the highest number recorded per population in South-East Asia and was clearly an issue to be considered given that other countries had introduced a genetic test to reduce this problem. The pilot test in Bangkok took place in 2013 and it

was established that the cost benefit of this test meant that it was put into the main health insurance package for Thailand once it had been established that there was adequate service availability around all of Thailand in 2018. Utilisation of genetic testing like this is not common in countries like Thailand yet PGX is a focus in South-East Asia – medical problems that can be tackled straight away with genomics interventions such as this is seen as being cost-effective in terms of a new intervention in the health system. This is how Thailand is demonstrating, through incremental ways, the wider economic benefit which is what financial colleagues are interested in.

In Australia there is also an evaluation of projects from a health economics perspective, but it was identified that there was not a single way to do this given that funding comes from different sources for different things (State funding vs Federal Government funding) and can be considered from a short term vs long term perspective. As an example of this, acute care within the Australian system was cited as most of the benefit of an acute care test is a cost saving to the State Government with respect to health, but it is not really demonstrating a saving to the Federal Government unless you look long term. There was a recognition that these perspectives needed to converge if programmes such as this were to be funded. Separately analysis of wider programmes with respect to, for example, mental health, were approached from a more economic perspective as opposed to the work on specific conditions that utilised the health technology framework that drives a health economic assessment.

A counter view was also proposed was that it was important to look at genomics in the context of total societal cost not just narrow health system costs and a simple quality adjusted life years gain analysis.

The discussion clearly identified that there was a recognition that the economic benefits of genomics need to be articulated but no consensus on how. Each jurisdiction seems to be approaching this from a slightly different starting point.

What do we mean by economic benefits?

The discussion explored several different ways of articulating economic benefits.

In Canada, for example, Genome Canada have a 20-year legacy of adopting a cross-sectoral approach to genomics and articulating the cross-applicability of genomics. Right in the founding of Genome Canada the vision was that it would be an organisation and network of regional genome centres that created capacity in Canada for genomics excellence but not only in human health (which is important and accounts for about 50% of the focus) but also in relation to agriculture and agrifood and natural resources, all of which are areas of particular strength for Canada. However, it can be hard to quantify the benefits beyond those which citizens, taxpayers, politicians, and policy makers recognise, such as jobs and value creation. However, other benefits are important.

In the last Federal Budget in February genomics has been positioned as a key economic driver for Canada's future – it is an innovative sector. The Canadian COVID-19 Genomics Network (CanCOGen) and its role through the public health crisis has enabled a discussion with policy makers about what else genomics can do in other areas of Canadian challenge. Genomics is positioned in the economic growth spending not healthcare spending. There will be (assuming no change of strategy following forthcoming elections) a pan-Canadian Genomics Strategy, and genomics is seen both as an innovative

sector and a key platform technology (like AI and Quantum) which needs to be developed to drive economic growth. This is a really important step.

Further, a significant focus has been placed, deliberately, on talent development and creating through training programmes and education systems opportunities for careers and a skilled workforce providing the next generation of talent which is diverse and multidimensional. Using talent development as a measurement tool is critical rather than narrowly looking at jobs, IP and commercialisation (albeit these are also important). It is also important to recognise that there are other impacts that drive growth but are related to lowering cost or bringing another asset to the table, for example, in natural resources using genomics to help drive lower carbon emissions (important for a green economy) or driving more agricultural productivity, greater crop resilience in climate resistance agriculture and improved food security, particularly in remote areas where food costs are prohibitive. This is about creating a national conversation about the benefits of genomics, not just counting jobs created etc.

It was also identified that as a funding agency Genome Canada has always included socio-economic benefit analysis as part of their funding process, whatever sector is involved. This means that they are gaining new methods to measure the economic/environmental/education/legal/social impacts and benefits of genomics. However, all these individual indicators need to be collated on a macro level – and not just in Canada, but globally.

In Thailand, genomics has also been positioned as a driver for economic growth as part of the strategy for the Eastern Economic Corridor and is very much supported by the Thai Government. In part this stemmed from 3 senior ministers in the cabinet 3-4 years ago having a medical background who were very forward-looking with respect to genome sequencing and how this is an advanced technology that would enable Thailand to change the way it treats its patients and keep up with the world.

It was also posed that it was important to look at genomics in the context of total societal cost and not in terms of narrow health system costs and a simple quality adjusted life years gain analysis (which is often the approach of guideline regulators). But how should this be approached?

In the UK the initial acid test for whether the £300m of taxpayers' money that had been spent on genomics was a success would be whether the health system would adopt it at all. To address this a national test directory was developed (these were not guidelines and there would be no reimbursement if other tests were used). This was done because in an early phase of Genomics England's data it was shown that children born after 2003 spent a median of 6 years not getting a diagnosis and attended at least 68 hospital appointments. This resulted in around £15,000 per person being spent on not getting a diagnosis and between 2003-2017 amounted to over £87 million being spent over a small number of cases. This analysis will be published in the New England Journal of Medicine shortly.

An important point that was made was that when we stand back and look at the facts, we are spending extraordinary amounts in pretty much every health economy but because it is embedded and buried within routine healthcare it has an invisibility to it which means that until we unpick that and pull it out, we don't realise what we can unlock. This is an important consideration globally.

For Genomics England whole genome sequencing (WGS) was the agenda although at the present time the case can only be made for a mixed economy – it is not a panacea – and other tests are needed. However, what was observed for the whole of rare disease was that people had multiple appointments, about every three months, over many years and having test by test by test by test: do one test, get a negative, do another one, and another one. If there had been the ability to do WGS there would have been a more comprehensive picture.

With respect to PGX, Genomics England looked at 76,000 genomes and 99.5% (including a range of ethnic groups representing the demography of the UK) have a risk of coming across a medicine that does not work or could do harm. In the UK there is data to suggest that 6.5% of hospital admissions are due to adverse drug reactions. In 2019 (which was the last "normal" year of reporting) the UK had 1.5m hospital admissions meaning 97,500 people admitted for adverse reactions. If one in 10 of those was a PGX reaction, there is a lot that could be done if there was proper pre-emptive testing.

The Genomics England research also showed that 25% of people have at least 4 of these gene drug pairs so over a life course the likelihood of being exposed to these highly commonly prescribed drugs is high. Money could clearly be saved on that meaning the economic argument can be made.

In the case of Hong Kong – which is right at the beginning of their journey with the Strategic Plan for the Hong Kong Genome Institute currently being written – the vision is to avail genomic medicine to all and to improve health and well-being. Hong Kong will be starting a pilot project of WGS focusing on disease and hereditary cancer. The main phase will see 18000 families being recruited. The most immediate evidence of economic benefit has been the nurturing of the talent pool. Hong Kong has now created the first consultant geneticist post in the hospital system (previously this was only in universities and the Department of Health) and they are also creating specific bioinformatics and genetic counselling roles in hospitals. Hong Kong will be following the examples of Australia with respect to having implementation flagship projects and are going to use these to reach out to champions in different specialities in medicine and create evidence, both clinical utility and economic benefits. PGX is definitely an area of interest - a previous study focusing on exome sequencing of 1000 patients identified that 99% of the population carried at least one actionable PGX variant (median is 4) but the genes involved are totally different from the data published in Europe and North America.

Some potentially surprising outcomes were also identified. In Australia, for example, a paediatrics test was funded (ie health economic benefits demonstrated) and the individual State Government released it in such a way that the individual paediatricians were encouraged to order the test. However, only 20 tests were ordered in over a year. Why was this? The funding was there – the health economic benefit had been proven - but it was not being taken up equally. This is important as it demonstrates that even if economic benefits can be demonstrated there are also issues about implementation and equity of availability, both across a State and across all the States.

In creating a global genomics network, can international collaboration ensure that no one or few jurisdictions monopolise and disproportionally reap the financial and economic rewards?

This is an area of focus for many organisations, including G2MC. It was acknowledged that there is increasing utilisation of Public Private Partnerships in the field of genomics and as a global community we need to look at this. Overlaid over all of this is the need for standardisation, a subject that has been considered in other roundtables, and the work of GA4GH is critical in this regard. Only by having a standard approach to data and having data that can communicate with other data can we derive the maximum benefit.

As an example of the benefits of standardisation, a paper will shortly be submitted on COVID-19 in the UK where multiple new loci to cause severe critical illness in COVID-19 have been identified. This work was only possible because it was possible to evaluate a small number of cases from the UK NHS ITU system and then compare them against the entire 100k Genomes Project. The desire is for everyone to be able to do that kind of comparison but if we do not democratise the data, we are going to hold the globe back in terms of implementing genomics directly into healthcare.

If national governments in Africa who have stronger health imperatives for them that means that they can't invest in genomics, we as a global community, wherever that need is in the world, need to try to stimulate public/private/charitable partnerships so that we can bridge that gap. We've seen that done in the UK. The UK Biobank and Our Future Health are Public Private Partnerships – Government put up some money, but the rest was commercially funded. It is possible to navigate that space in a way that makes the data democratically accessible, but it is important to recognise the motivation of certain commercial entities for doing this. For example, if an organisation thinks that if their drug is discovered this way it is two times more likely to get to market then there can be a huge shrinkage of costs for a relatively marginal investment in comparison to what those companies invest in failed medicines already.

The experience across the continent of Africa is relevant here, particularly in relation to programmes such as 3MAG where it is commonly accepted that governments won't be able to fund. There has been a lot of interest from the private sector but there is concern that there is an ulterior motive. What will be the costs of data sharing in this context? Yet it is recognised that private sector and funding agencies have a role to play in these big projects.

When it comes to implementation at a government level across Africa, governments might be more willing to consider harnessing data to create better panels for screening. PGX is a quick win – there are many drugs which don't work on African populations because they have not been designed for or tested on African populations in clinical trials. If there could be encouragement to do more testing in the relevant populations so governments know these drugs work and are affordable to their populations this would be positive. Demonstrating how many side-effects can be avoided or the benefits of a healthier population on cost savings to the health system should be positively received.

In terms of the application of genomics in relation to rare disease in Africa this is often overlooked as it is not necessarily seen as a priority as this would affect such a small sector of the population. HIV and TB are the big disease burdens and governments have this on their radar and would be more interested in investing in these areas when it comes to genomics. There is a similar approach with respect to investment in SARS COVID-2 sequencing and surveillance. There is an issue about priorities

and what is feasible – how many people can be reached with the lowest cost, not how many individuals can get access to personalised medicine.

This is not, however, just an issue about public sector vs private sector funding – although there is an important discussion to be had about the role of the private sector which is still seen as challenging given lack of trust – there is also an important role for other funding agencies such as NIH and Wellcome.

The global collaboration with respect to the utilisation of genomics to sequence SARS COVID-2 was cited a number of times as a game changer. Initiatives such as CanCOGen or COGUK are really informing public health and policy decisions and will have an economic impact that we cannot yet measure but is tangible in demonstrating the utility of genomics. The global collaboration in this area should be held up as an example of what can be achieved.

Positioning genomics as an economic driver as opposed to just a driver in healthcare might be the solution to driving greater government support, acknowledging that the specific strategic point will be different by country. This is a point that the WHO Science Council is considering.

One obstacle raised to making the economic case is that the public (if they even know about genomics at all) still see this as expensive and quite luxurious. And, of course, in LMICs the overall costs of instruments etc is higher.

Are economic benefits purely monetary or can they be reflected through investment in equipment or people for example?

Looping back 2-3 decades consideration was given to how investment in basic research can stimulate health and economic impact. As an example, Wellcome created The Sanger Centre in 1993 as a contribution to the Human Genome Project. The Wellcome investment was in infrastructure and skills. 10 years later when that project was completed, Wellcome doubled down and invested in infrastructure and skills in genomics, understanding the application and utility of genomics and keeping the ethos of open science in genomics.

At the Wellcome Genome Campus – which is only one location – Wellcome have invested over the last 25 years £3.5 billion in genomics and biodata. This investment has not just been in The Sanger Institute; focus has also been given to the European Bioinformatics Institute, to education, training, public engagement, data generation and storage, service of that data and provision of resources to the entire community. That initial investment was not about impact – it was about creating knowledge. And over time that knowledge has created an ecosystem.

It could be argued that investment by Wellome and the success of that investment then garnered UK government support to further investment, eg Genomics England, the UK Biobank and the 500k cohort (who are now WGS). These initiatives were built on capacity and skills that had been demonstrated by earlier investment. Our Future Health (5m cohort) and the sequencing of the UK Biobank were also funded by commercial partners.

The UK ecosystem has many key players and the Government's Genome UK Strategy brings together academic organisations, commercial organisations, Genomics England and healthcare and importantly links not just the research and the funding but workforce training, public engagement and discussions on ethics and data. COGUK have sequenced over 500,000 COVID19 genomes (probably about three quarters of all of those available in the world) but that remarkable achievement was built on 3 decades of investment and training and skills in genomics that were able to be applied to a new threat. There are direct policy implications of that work.

We can now see the impact of previous investments – skilled workforce, health benefits, economic impact. In terms of commercial genomics in the UK there are now 154 companies with more than 500 employees. £3bn of private investment, inward investment, has been invested in these companies. The private sector plays a key role.

We have to link all of this up – in the UK Wellcome and Sanger and other research organisations work across into commercial organisations and between all of these elements there is always a dialogue with Genomics England. There is a recognition that all these elements are greater than just a sum of the individual parts. But we need that integrated strategy to fully reap the health and economic benefits of genomics.

Is it possible to demonstrate the cost savings that genomics could bring in the future? How can we help policy makers understand the wider opportunities and benefits that genomics can bring?

As noted elsewhere in this report there are challenges of unpicking some of the costs incurred in existing health economies that could be impacted by better deployment of genomics as these costs are embedded and buried within routine healthcare. However, specific examples shared serve to identify the approach that could be taken to try to unpick some of these challenges. Genomics England has been carrying out a systematic, comprehensive study with the University of Oxford Health Economics Research Centre (which goes beyond the research to be published in the New England Journal of Medicine noted above) which will be published later this year. This should serve to help other systems see the benefits and make the arguments to their governments.

Consideration was given to the recent work at Genomics England with respect to WGS for newborns. What is the cost of that vs the lifetime of benefits reached is interesting but is that sort of approach simply way beyond the reach of many jurisdictions?

The reason Genomics England are looking at this is that approximately 600 conditions were identified, 1 in 190 live births (which will be true for most western societies), knowing at birth that there is a high likelihood of a fully penetrant disease. The study looked at a targeted approach of intervention before the 5th birthday. The number of quality adjusted life years gain that can be achieved at this point is quite dramatic because at this point you are dealing with children in early life versus dealing with chronic disease in later life (where you don't have that life left to gain). If it is possible to engineer the price point for the test down and look at what would have been spent on disability without intervention, and the intervention basis is choosing an intervention that can reduce disability or avoid harm entirely, this would be beneficial.

As a specific example to highlight this point there is one child – she is now 14 but was 10 when the research commenced – who had immunodeficiency and her multiple, recurrent admissions to ITU cost the UK taxpayer £357,000. By carrying out WGS a mutation was discovered that affected the white blood cells and a curative bone marrow transplant was carried out. It cost approximately £700 for the diagnosis and £70,000 for the bone marrow transplant and now she only goes to hospital to monitor her transplant. It doesn't take many of those cases to make significant savings and this was the basis that was advanced to Government. This was the subject of the Generation Genome Report[1] and the review is intended to help those around the world make an informed decision about whether this is the right thing for them to do and to focus on interventions which can clearly make a difference and there is proven evidence of this.

Multiple examples are cited elsewhere in this report about the different approaches to demonstrating economic benefit beyond the traditional markers of job creation/intellectual property/commercialisation and it is important that policy makers are understanding of these broader impacts. Positioning genomics as a driver for economic growth beyond healthcare and articulating how that might be measured was a strong recommendation. This is an area worthy of further consideration as that goes beyond the scope of this Programme which has largely focused on human health.

Conclusion

The discussion generated through this session served to outline the economic benefits which can be derived from participating in, creating, and operating a national genomics ecosystem. However, it also provided crucial 'food-for-thought' in prompting the cohort to consider as well, the wider and more holistic socio-economic benefits which can result from genomics.

Genomics, if effectively integrated into national health ecosystems, not only has the potential to revolutionise the health of the individual, but also of the population and wider society. But should a cross-sectoral approach to genomics be encouraged more widely? Would that help position genomics as a driver for economic growth as opposed to being seen purely through the lens of healthcare? Is that even possible for many jurisdictions?

In terms of the application of genomics in the specific field of healthcare numerous examples were discussed about the wider economic impacts this can have, for example, through the reduction of hospital admissions, improved quality of life for the patient and their family, fewer more targeted interventions, ability to avoid adverse drug reactions, amongst other key themes, served to prove the wider societal value provided and maintained through genomics.

As with other roundtables the concept of the need for all elements of the genomics ecosystem to work in collaboration was highlighted. There is much to be done in this regard if we are to ensure that the benefits of genome sequencing are to truly to brought to the whole world.

[1] Generation genome and the opportunities for screening programmes (publishing.service.gov.uk)