Beyond One Million Genomes

Report: B1MG Country Exchange Visits

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Summary

The 1+Million Genomes (1+MG) initiative set out the goal of enabling access to genomic data and linked personal health data across European countries. For this purpose, a federated secure cross-border infrastructure and a framework of guidelines, standards and best practices are under development, providing a major contribution for genomic medicine. Furthermore, by promoting and facilitating the adoption of genomics by healthcare systems, the 1+MG will also impact how European citizens benefit from the widespread use of personalised medicine. Open discussion and exchange of knowledge and experiences among European countries are crucial to achieving this goal.

Towards this aim, three Country Exchange Visits (CEVs) to countries with advanced genomic medicine programmes were organised in the context of the Beyond 1 Million Genomes (B1MG) project, a Coordination and Support Action supporting the 1+MG initiative. The countries selected were the United Kingdom (UK), Estonia, and Finland. These countries have implemented advanced strategies for adopting genomics by healthcare systems, which were highlighted in each CEV. The themes discussed in these CEVs, namely 'Research to clinical practice: from Genomics England to NHS', 'Genomics towards Prevention', and 'Regulating the Unknown', constituted an excellent overview on how to adopt and sustain the use of genomics in healthcare systems, and shared main challenges and solutions to inspire and motivate other countries. Additionally, during the CEVs, 13 1+MG signatory countries presented their ongoing national genomic medicine

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initiatives, providing an overview of genomic medicine developing status across Europe.

This report describes the strategies described by the UK, Estonia and Finland for genomic medicine, outlining key messages that may support other European countries to make informed choices and decisions on the best approaches to implement genomic medicine.

From the discussion between participants and speakers, and the contributions of the 13 1+MG signatory countries, it was clear countries are at different maturity stages of implementing genomics in healthcare systems. For personalised medicine to be equally accessible to citizens across Europe, countries need to collaborate closely to pace up on issues such as:

- Legal and ethical framework
- Infrastructure for secure data access and exchange
- Political engagement and funding
- Training and engagement of healthcare professionals
- Public awareness, engagement and trust

The final outcome of these visits was developing a policy brief outlining key messages and recommendations for the adoption of genomics by healthcare systems.

1. Why Country Exchange Visits

Seeing the tremendous potential of access to genomic and linked phenotypic data to effectively advance the implementation of Personalised Medicine, in 2018, Europe launched the Declaration 'Towards access to at least 1 Million Genomes in the EU by 2022'. The Declaration was so far signed by 24 EU countries, the UK and Norway. This initiative set the goal of establishing the infrastructure, legal and ethical framework, and phenotypic and genomic standards to allow cross-border data sharing of genomes, impacting research and medical practice.

This genomic medicine challenge is global. This is because the more data (genomic and phenotypic) is collected and accessible, more information and functional inferences can be drawn which have medical relevance. The successful implementation of genomic medicine has clear benefits for patients, citizens and society. It needs access to enriched genomic-phenomics databases, which means the highest possible number and diversity of individuals included. A successful genomic medicine programme in a European context would require that all signatory countries reach a level of commitment and implementation maturity that will allow for secure cross-border exchange of findable, accessible, interoperable and reusable (FAIR) data, with benefits to citizens and patients.

For any healthcare system, the use of genomic data for personalised medicine requires extensive adjustments including, but not limited to, the development of technical infrastructure, competencies and ethical, legal and social issues (ELSI)

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frameworks, for acquiring, storing, sharing, interpreting, and delivering genomic information. In addition, healthcare systems need to ensure efficacy benefits, economic viability, and equity in access. Due to important asymmetries in the maturity of genomic medicine programs across Europe, as well as a diversity of healthcare system infrastructures, processes, and legislation, close cooperation between countries is necessary to overcome these challenges.

In this context, the B1MG Project WP5, '[Delivering Personalised Medicine Cross-borders: Implementation in Healthcare Systems and Societal Impact](https://b1mg-project.eu/work-packages/wp5)[1]', organised three Country Exchange Visits (CEV) to European countries with well-developed programmes promoting the use of genomics by healthcare systems, namely the United Kingdom (UK), Estonia and Finland (**Figure 1**). The aim was to promote knowledge exchange on challenges and solutions, policies and practises for adopting genomics by healthcare systems, and disseminate key messages and recommendations for European countries (**Figure 2**).

[1] https://b1mg-project.eu/work-packages/wp5

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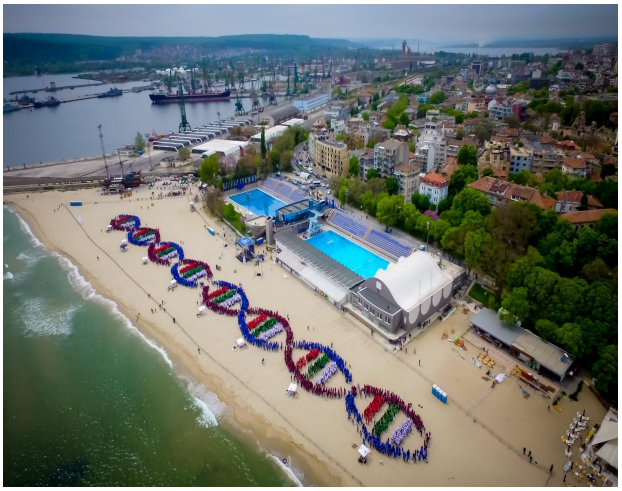

Figure 1. The three country exchange visits took place online. In the absence of a group photo, this image, presented by the Bulgarian delegates Dr. Zhasmina Koeva-Balabanova and Prof. Radka Kaneva, illustrates both the theme of these country visits and the commitment to work together on genomics (this image is property of the Medical University of Varna, Bulgaria).

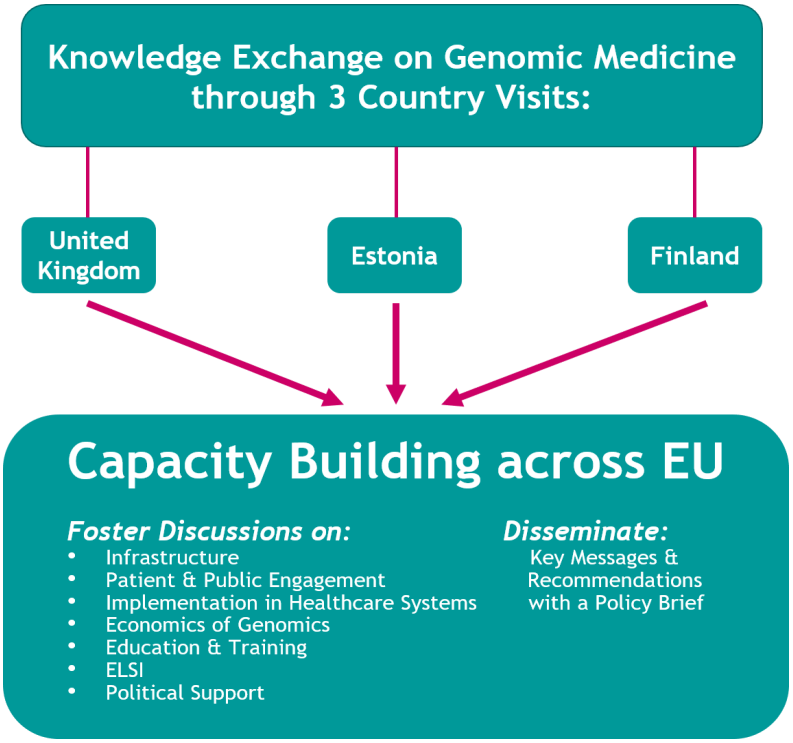

Figure 2. Outline of the roles of CEVs and Policy Brief in the context of the B1MG Project.

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2. Description of Country Exchange Visits

2.1. United Kingdom – Research to Clinical practice: from Genomics England to NHS

2.1.1. Introduction

The CEV to the UK took place on 23-24 March 2021, and the theme was 'Research to Clinical practice: from Genomics England to NHS'. Throughout the visit, participants had an opportunity to learn about infrastructure, including political support and funding, addressing and fostering sustainability, training, collaboration, patient awareness and engagement, implementation of governance, health economics of genomic medicine, and implementation into healthcare systems.

The visit had contributions from the host country (UK), including the devolved nations. In addition, several signatory countries reported on their efforts of implementing genomic medicine, namely Germany, Italy and Norway (Table 2). The full contents of this CEV are available on Minutes[2], Recordings[3] and Slides[4].

2.1.2. Implementing Genomics into the NHS

The UK's Genomic Medicine programme was established in 2012, with notable political support to embrace the goal of implementing genomics into routine clinical practice in the National Health System (NHS). In 2013, Genomics England (GeL)[5] was formally launched with government funding to sequence 100,000 genomes from NHS patients (the 100,000 Genomes Project[6]) affected by a rare disease (RD) or cancer, and their families. In 2016, a new Sequencing Centre was opened by the Prime Minister, and in 2018, Genomics England reached the goal of sequencing 100,000 genomes. In that same year, NHS Genomic Medicine Service (GMS)[7] was launched to prepare the NHS for the implementation of genomic technologies to provide consistent and equitable access to genomic medicine. In 2020, a ten-year strategy (GENOME UK – The future of healthcare)[8] was launched to create the world's most advanced genomic healthcare

[2] https://docs.google.com/document/d/1jsymgO9UaJT8ZQoBKJCcGtKhKaq5ui0iNU2hmvASSOo/edit?usp=sharing
[3] https://www.youtube.com/playlist?list=PLweO8RYcVPDOWDmFxRHdEGlNsMEubMK5k
[4] https://drive.google.com/drive/folders/1QL_3kyCIUZKxlPx4fpxIiT1ls-Q9z6Pn
[5] https://www.genomicsengland.co.uk/
[6] https://www.genomicsengland.co.uk/initiatives/100000-genomes-project
[7] https://www.england.nhs.uk/genomics/nhs-genomic-med-service/
[8] https://www.gov.uk/government/publications/genome-uk-the-future-of-healthcare

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system. The pillars of the Genome UK strategy are patient trust, engaging stakeholders, supporting industry, establishing, and keeping the national infrastructure for data and analytics, and workforce development.

Genomics England (GeL) vision, as pointed out by Mark Bale, GeL, is that everyone benefits from genomics in healthcare[9]. GeL supports the NHS through sequencing services, and the system is based on an infinity loop, linking the health care system with research, each feeding the other with data and insights. An example of the advantage of the implemented genomic infrastructure in the UK is the rapid sequencing of 20k genomes of Intensive Care Units (ICU) COVID-19 patients, which constitute a valuable dataset usable for future studies on cancer and other diseases. It is important to reflect on how the UK can network with other countries.

The 100,000 Genomes Project, presented by Chief Scientist for GeL, Sir Mark Caulfield, was used to improve research capabilities, reduce NHS costs of genomic medicine and bring equitable benefits to patients, and ultimately catalyse genomics as an NHS service[10]. The project, focused on RDs and Cancer, will now embrace other areas and diseases, including pharmacogenomics and newborns 'Generation Genome', with early diagnosis before the 5th birthday. Sustainable financing is assured by the core NHS budget, allowing consistent and equitable care for 57 million people in 2021.

Genomic Medicine Centres (GMCs) were established to bring together researchers, clinicians and patients under one platform and help accelerate the genomics initiative in the country. They are responsible for identifying and recruiting participants and for clinical care following results, in an end-to-end process linking analysis of results to clinical outcomes, all within an ISO accredited pipeline. A key aspect of this process is patient-clinician contact, with clinicians being frontline healthcare workers empowered to make decisions about what is relayed to the patients. The chosen federative approach to data centralisation (in a cloud) and a centralised biorepository and sequencing service allows data access control, protection and regulation. The infrastructure set up to engage this project involves NHS GMCs covering England, Wales, Scotland, and Northern Ireland.

NHS Scotland Genetics was built in place with strong genomic research and clinical practice in cancer and RDs. A close relationship with University/teaching Hospitals was established, creating four genomic centres and empowering the sequencing capacity of Universities by investing in equipment. As explained by Zosia Miedzybrodzka from the University of Aberdeen, to overcome the different legal systems in England and Scotland, data governance and consent processes had to be separated, though allowing data sharing, which is only possible after data is de-identified[11]. Future development of Scottish genomic medicine requires improved regulatory framework regarding

[9] https://www.youtube.com/watch?v=0mLIiZCp3vg
[10] https://www.youtube.com/watch?v=RxCuZAxaEhg

[11] https://www.youtube.com/watch?v=fQG1IB3Ypk0

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data sharing and use, sustained funding, and ensuring that the final system allows data reanalysis and gene-agnostic analysis.

Data from the 100,000 Genomes Project was crucial for setting up multidisciplinary teams to work on data interpretation in Northern Ireland (Shane McKee, from Belfast Health and Social Care)[12]. As phenotype is key to diagnosis, the combination of phenotypic and genome data is crucial to building a robust infrastructure that allows going from clinical presentation to genomic diagnosis as quickly and efficiently as possible. The binder and enabler, tightening all together, is informatics, with Artificial Intelligence (AI) helping to query the genome/phenome intelligently. Building a data platform that allows data to flow in a federated and secure way is at the basis of the ongoing project GenOCEANIC, which uses open Electronic Health records (EHR) standards. It aims to use pheno-geno data to deliver clinical benefits to society.

The All Wales Medical Genomic Service (AWMGS)[13], presented by its Managing Director Clive Morgan, involves a National Clinical and Laboratory service with Whole Genome Sequencing (WGS) capacity, clinics across NHS Wales, and centralised/hosted in Cardiff[14]. AWMGS provides services on cancer, prenatal diagnosis, RD and pharmacogenetics. As part of the Wales government plan to establish precision medicine, the Genomics Partnership Wales (GPW)[15] was created, coordinating activities from AWMGS, NHS, patients and public groups and higher education institutions, among others. The Cardiff centre was made a hub for research and innovation (joining academia, industry, and NHS) and service provider for genomic medicine (diagnosis and therapy). Building patients' trust is key in bringing genomics into healthcare routine in Wales, with initiatives like Genomic cafes and Genomic champions contributing to attaining that goal.

There is still a lot of political commitment underpinning the NHS genomic strategy, leading to the establishment, in 2020, of the Genome UK. Its main pillars, underpinned by dialogue with the public and the healthcare workforce, are diagnosis, PM, research, and prevention. As explained by Alexandra Pickard, Head of Genomics, Genomics Unit, NHS England and NHS Improvement, the NHS long-term plan[16] for the next 10 years is to focus on genomics, namely to sequence 500,000 genomes by 2023-2024, extend access to molecular diagnostic testing for patients with cancer and cardiovascular diseases, improve outcomes for inherited high cholesterol, and drive the research agenda to ensure that patients can benefit from linking patient needs (clinical care) and research and innovation interests[17].

The NHS and the 100,000 Genomes Project benefitted mutually from each other. The NHS made key contributions to the 100,000 Genomes Project through the 13 GMCs and

[12] https://www.youtube.com/watch?v=iCFWoNwRz4Q
[13] https://medicalgenomicswales.co.uk/
[14] https://www.youtube.com/watch?v=ODtDa1DoBRw
[15] https://genomicspartnership.wales/

[16] https://www.longtermplan.nhs.uk/publication/nhs-long-term-plan/
[17] https://www.youtube.com/watch?v=1z1rLiBw0Lw&list=PLweO8RYcVPDOWDmFxRHdEGlNsMEubMK5k&index=11&ab_channel=ELIXIREurope

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by creating direction, leading transformation and building readiness. In contrast, the 100,000 Genomes Project set the foundations for the NHS genomic medicine service. The partnership between NHS and GeL remains crucial for the success of the implementation of the GenomeUK. The National Genomic Testing Service is at the centre of this partnership, allowing the infinity loop of interconnection of clinical/healthcare and research within genomic medicine and new tests to the testing directory, which is key to moving forward to personalised medicine. Patients are the centre of all decisions and services of the genomic medicine service and are given the choice of making informed decisions on being part of the research program.

2.1.3. Patient participation

The investment in public dialogue has been huge since the beginning of the UK´s genomic medicine initiatives, ensuring patient and public involvement and seeking trust in genomic medicine.

Making justice to GeL's motto 'Every data point has a face', the Participants Panel, as the voice of patients and families, is involved in every decision regarding what data is used for and who is searching for it. This ensures patients 'trust in what is happening in between taking their samples and reaching results and outcomes', as explained by Jillian Hastings-Ward, the chairperson of the Participant Panel at GeL. The Participants Panel is represented at the GeL[18] Access Review Committee, Ethics Advisory Committee, Discovery Forum and GeCiP Board (Genomics England Clinical Interpretation Partnership). All of this ensures the best patient experience and benefit, guarantying that every patient's question is properly addressed and answered. The Participant Panel also contributes actively to public discussion and awareness of genomic medicine.

The Patients Panel has also been involved in the NHS GMS since its creation, and the process of communication and involvement is being set up at the moment. The equivalent to the Participants Panel in GeL is the National Genomics People and Communities Forum in the NHS GMS, where the Panel will be represented. Reversely, the Participants Panel will also host representatives from the Forum, among other groups from the NHS GMS.

2.1.4. Capacity building

Workforce development is one of the pillars of the Genome UK strategy. Christine Patch, Clinical Lead for Genetic Counselling and Caldicott Guardian at GeL, was involved in developing the Genetic Counselling profession in the UK and contributed to training these healthcare professionals in Europe[19].

To be efficient to patients, Genomic Medicine needs a specialist workforce, namely clinical geneticists and genetic counsellors. The 100,000 Genomes Project was built on these existing professions, but the NHS contributed additional funding to genetic counsellors' training. Although there

[18] https://www.youtube.com/watch?v=Uz4QkptUqGI

[19] https://www.youtube.com/watch?v=t_A9rrTgvMA

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is no 'one size fits all' when speaking about the genomic medicine workforce for each country, it is important to engage and involve existing clinical scientists, doctors, and nurses to work on genomic medicine.

An example of such involvement is a relevant tool that was developed with the NHS and the 100,000 Genomes Project: a simplified consent process within the healthcare context. Before signing the consent, patients discuss several issues with specialised healthcare professionals. This ensures that patients are offered the chance and have time to make an informed decision, to join the National Genomic Research Library (NGRL)[20] (a partnership between the NHS and GeL that allows integration of research into clinical care).

In terms of Education, the Genomics Education Programme (GEP)[21], created in 2014, has provided an array of online courses for upskilling the existing workforce, and includes resources for increasing the public knowledge about genomic medicine. Another training resource created within the GEP was the Competencies Framework[22], with eight high-level competencies, a tool that guides and supports individuals and organisations into best practice and development.

As a take-home message highlighted by Christine Patch, for Genomic Medicine to work, it has to involve and include professionals across the entire workforce, not just the genomic workforce. The partnership between the 100,000 Genomes Project and the NHS, and collaboration across the entire workforce, was crucial to embed Genomic Medicine into the NHS and to enable the NGRL.

2.1.5. Key discussion points from participants and speakers

During the two-day UK CEV, there was a large involvement of participants in discussion with speakers. The discussion was mainly focused on practical approaches and solutions regarding specific issues related to implementation of genomics into healthcare system in the UK, as described below:

[20] https://www.genomicsengland.co.uk/patients-participants/data/
[21] https://www.genomicseducation.hee.nhs.uk
[22] https://www.genomicseducation.hee.nhs.uk/wp-content/uploads/2021/06/Facilitiating-genomic-testing-competencies-final.pdf

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Host country: United Kingdom	
Involving the healthcare community from the beginning avoids creating new infrastructure and lowered initial resistance. This also helped get political support. Also helpful in getting political support was the involvement of the prime minister, driving top-down pressure. For GelE successfully achieving its goals, partnership with the NHS was crucial for sustainability and equity. The UK started with RD, and the knowledge built, namely from PRS, can now be used in other areas, like common complex diseases. Collaboration with Biobanks is important. Gathering phenotypic data from different sources is difficult and hinders its match with genetic/genomic data. It is important to channel investment to overcome these difficulties, integrate all data into HER of patients, and allow clinicians to use them. In summary, it is important to work towards federated data. The low diagnostic yield (20%) is not backlashing investment in genomics. This comes rather from inertia than from any opposition. Having patients willing to share data for the benefit of others is very important, but trust in the system is critical. Clarifying that 'sharing' of data means access to data for analysis not data "distribution" is crucial to build trust. Shortage of clinical geneticists impairs the implementation of genomics in healthcare. It is thus important to identify skills needed in healthcare professionals and devise adequate training programs, thus ensuring that there is enough human power to run genomics in healthcare. Also, involving, and crediting health professionals is important to incentivize them to work in this field. UK developed Education resources might be shared with other EU countries. On data usage and storage: it is crucial that robust measures are in place to avoid uncontrolled and unapproved data release. Agreements are in place to ensure that police will not request access to data. In addition, data for example on blood cancers is not used to search for bone marrow compatible donors and call people unexpectedly. Regarding communication of results and updates to patients, it is important to know how willing they are to remain in contact. It is important that every patient and family have a contact point. On how to organise and request specific genetic testing, the UK has a Genetic Test Directory and a national standardised system for request and consent, and for results interpretation and treatment recommendations. Regarding sharing information on clinical variant interpretation, for example for publishing purposes: data is not shared but information can be, as long as permission is granted.	There is general agreement on the lack of data and models that demonstrate the economic impact and value of cross border access to genomic data and of genomic sequencing in healthcare at National level. It is important, for example, to know if WGS is cost-effective both for the healthcare system and for others, like the pharma industry. The UK has already some data, suggesting starting socioeconomic evaluation for those models by collecting data on test sensitivity and cost-effectiveness. Regarding economic evaluation of genomics in health, investing in working together (NHS, GelE, industry) to investigate and make solid cases on cost-effectiveness of genomics is important to then make solid proposals to the proper ministries to integrate tests/treatments into the healthcare system and promote wide and equitable access to citizens. Private industry is still not perceived by the public as trustworthy. To overcome this, patients should be involved in conversations with industry and industry should clearly demonstrate its commitment to transparent and compliant access and usage of data. Involving industry is important, namely because they are the ones developing treatments and drugs. To facilitate this, industry and research should not be distinguished regarding access and usage of data, if they are both abiding by the 'air lock' rules. WGS introduces a major system change, as it does not come with a single diagnostic. It requires political leadership, investment through funding and public support. It opens the path to PM, as interventions will become individualised and not directed at groups of patients/diseases. COVID pandemic valued science, promoted technological innovation and readiness of healthcare systems, and promoted collaborations and dialogue, thus creating momentum that could be used for promoting actions conducting to effective implementation of genomics into healthcare. However, it is important to keep people's expectations real. Regarding introduction and implementation of new technologies within the NHS, advice is to have a unified directory and a framework for evaluating that so that changes, i.e., tests can be changed based on Health Economic evidence and more. However, this is not enough. It is important to use the "Infinity Loop" path to foster research and improve clinical care in a feedback way. Regarding citizen engagement, surveys are a good way to involve citizens in the discussion and create awareness. In addition, initiatives can be local, with an excellent example coming from the Onelondon (onelondon.online) initiative.

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2.1.6. Main conclusions and takeaways

This CEV was successful in showing how the UK managed to make genomic medicine work within the healthcare system, with some key points contributing to UK's success in this matter, namely by securing political support and funding, ensuring a trustful framework, informing patients and trained healthcare professionals, and fostering fruitful partnerships between research, healthcare, and the industry (**Figure 3**).

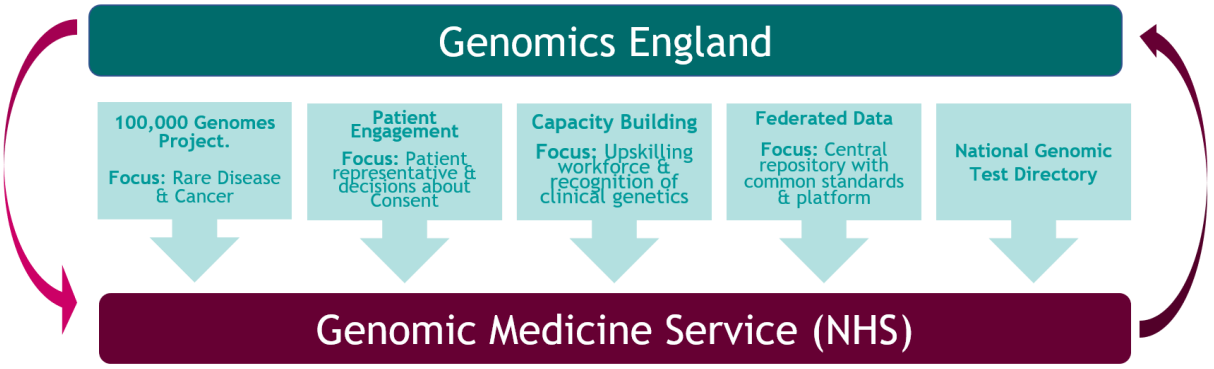

Figure 3. Main features of the UK strategy to implement genomics into healthcare.

Overall, the main takeaways from this CEV's host country on infrastructure, patient and public engagement, implementation into the healthcare system and health economics were:

Infrastructure

- Genomics initiatives require political support and sustained funding. In that respect, the 1+MG Initiative is encouraging discussion and bringing together different stakeholders. Although the UK is advanced in its implementation of the genomic strategy, further development needs data sharing with neighbouring European countries, making it important for the UK that the 1+MG Initiative helps all countries to align strategies quickly.
- Standardisation (e.g., ISO & GA4GH) is vital and it is recommended that common standards and guidelines are set among countries engaged in future cross-border data sharing.
- There are UK's shareable learnings across Europe, such as the GeL pipelines, a governance framework and ELSI requirements.
- Use cases, such as RDs, can be used to highlight diagnostic odyssey and emphasise the need for genomic sequences, thus contributing to pressure the system to accelerate progress into using genomics for personalised medicine.
- Countries can learn from GeL solutions re-engineered pipelines to accommodate other diseases, such as cancer, by including fresh tissue and improved results, and

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accommodate pharmacogenomics into personalised care.
- The UK is working towards a federated ecosystems as sensitive human data is used increasingly and regulations protecting this data are introduced, in a way that will allow for healthcare without borders.

Patient & Public Engagement

- For the UK's success story, the process surrounding consent was given a vital importance, parents and patients are willing to share their data (access for analysis) and they should be able to.
- Making patients part of every step in the process was vital to build trust and transparency, both crucial for the success of the UK's genomic strategy.

Implementation

- To implement a dynamic and reliable healthcare system based on genomic and clinical data, the partnership between research and healthcare is vital: creating a learning healthcare system ensures sustainability.
- Healthcare professionals in the UK were involved in the implementation strategy from the start. The UK's story shows that it is important to empower healthcare professionals through training and credit for their work and competencies.
- Trust in science from the medical profession is crucial, as they are at the centre of communication between the system and the patients.

Health Economics

- Although further development of the economic model is needed, several indicators (such as hospital costs, found in administrative data) can already be used to highlight the importance of genomic sequencing.
- It is important to ensure equity of access across countries and Europe.

2.2. Estonia: Genomics towards prevention

2.2.1. Introduction

The CEV to Estonia, on 19-20 May 2021, was organised under the theme 'Genomics Towards Prevention'. Throughout the visit, participants had an opportunity to hear about some major topics of the Estonia Genomic Medicine, namely about personalised prevention for common and complex diseases, pharmacogenomics, population Biobanks and population awareness. Outputs from this visit were used to produce a Policy Brief. The visit had contributions from the host country and from other European countries reporting on their stage of implementation of genomic medicine, namely Hungary, Latvia, and Spain (Table 2). More information on this

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CEV can be found in Minutes[23], Recordings[24] and Slides[25].

2.2.2. Personalised Medicine: how Estonia is doing

Genomic medicine in Estonia dates back 20 years to when the Estonian Biobank[26] was established (1999) and the Human Genome Research Act (HGRA)[27] was approved (2000). Estonia realized the potential of digital health already in the 90s, when there was a strong political will to invest in IT and genetics.

Factors impacting a person's health are wide and go beyond the clinical care, as pointed out by Kalle Killar, Deputy Secretary-General on E-Services Development and Innovation, Ministry of Social Affairs[28]. Thus, the importance of focusing on prevention and on gathering data on people's behaviour in order to provide the best health service to Estonian citizens. The current National Health Strategy (2021-2030) aims to assure accessible and quality health services integrated with social services in a way that it reduces inequity and ensures patients' rights. When personalised medicine is concerned, Estonia is very well positioned due to a very professional and established national Biobank, top professionals, willing patients, and ministry involvement providing the right legal and governance framework.

Despite the success of these last 20 years, Estonia still faces some challenges. Implementing the National Health Strategy is not always easy, as each institution has a different agenda for the outcomes. Moreover, developing the national health portal[29], involving the primary care and being able to provide the proper guidance are still needed. Also, personalised medicine needs a proper and sustainable financing framework, which Estonia hopes to set still this year. In particular, the Estonian Biobank needs more investment to ensure reaching as many citizens as possible. For this matter, it would be important to also focus on prioritizing EU investment in personalised medicine.

During the last 20 years, project e-Estonia[30] has made the country more digital with one electronic (mobile & SMART) ID card for all Estonian residents. The electronic ID card has access to all services with every government service, such as legislation, voting, education, justice, banking, taxes, policing, and naturally, healthcare, becoming digitally linked across one platform, the X-Road[31]. With the established internet X-Road, data stays where it is supposed to be, and is not centrally gathered. All the transactions are logged to assure citizens that they can see who has accessed their data and for what purposes. This system will be used for providing data

[23] https://docs.google.com/document/d/1fskfK9MJlOg1pX_tZSt9FXFiApSe15uhpYF-GYvIJng/edit?usp=sharing
[24] https://www.youtube.com/playlist?list=PLweO8RYcVPDMTY_Xi0nLSOtD67jeydJJ7
[25] https://drive.google.com/drive/folders/1_kBt9ltL1W_zBx9bL3L_5MrjwO6udNBE
[26] https://genomics.ut.ee/en
[27] https://www.riigiteataja.ee/en/eli/531102013003/consolide
[28] https://www.youtube.com/watch?v=M4UsEElb-ec
[29] https://www.digilugu.ee/login?locale=en
[30] https://e-estonia.com/
[31] https://e-estonia.com/solutions/interoperability-services/x-road/

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to use in personalised medicine. Another important aspect of Estonia's implementation of personalised medicine is the creation of the Patient Portal (Health Portal) through which both the state and the private sector may provide their products and services and the citizen has access to their own health data. Also, it will help citizens to recognize the genomic data potential to help them change their health habits. Estonia also introduced the Electronic Health Record (HER) system, digital prescriptions, e-consultations, and a drug interaction decision support system.

At the core of the Estonian implementation of personalised prevention and care is the IT structure. Annika Veimer, Director of Estonian National Institute for Health Development, explained that this infrastructure will allow data providers (Medical Laboratories and Biobank), data processors (which involves medical devices as software) and users of results (healthcare providers and patients) to access data[32]. Data flow, access and analysis go through the Estonian Central eHealth System. This IT infrastructure has already entered a testing phase in 2020. This year (2021) GPs training on how to use the infrastructure and to counsel patients on their genetic risk will start. Despite the successful achievements, Estonian implementation of personalised medicine is still facing some challenges, namely the constant need of adjustment based on new information and knowledge and the definition of tasks and partners is quite difficult due to constant information updating.

Databases of the implemented internet X-Roads are linked making it easier to plug in new services to the system, which are linked to the other services and parties. Once the data are in the medical use storage, required analysis, such as risk scores, is done in a safe and secure compute environment, generating a report (machines & human readable) that will be further processed by the doctors who can then provide recommendations accordingly. No information on genetic data analysis reaches a patient without prior analysis by the doctor. The major challenge in integrating computers within silico laboratory work is to ensure that the compute environment is CE-marked (software as medical devices), as explained by Jaak Vilo, Professor of Bioinformatics, University of Tartu, and Head of Institute of Computer Science[33].

The two main services are the polygenic risk scores (for example for cancer) and the pharmacogenetic warnings. In the case of polygenic risk scores, the aim is to assess high risk individuals and come up with a prevention strategy and its cost-benefit evaluation. The pharmacogenetic warnings, benefit from the huge amount of genetic data stored in the national biorepository, are based on the fact that there are multiple single nucleotide polymorphisms (SNPs) across one gene which can inform about response to a certain drug based on the allele variants. The feasibility of the implemented IT structure is planned to be demonstrated until 2023.

[32] https://www.youtube.com/watch?v=tuDhqM43tGQ

[33] https://www.youtube.com/watch?v=2ev0QaRVreY

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Digital health requires constant upgrades of information, knowledge, and technologies. This cannot be achieved without close collaboration among several entities, namely the private sector. The newly launched National Digital Agenda 2030[34] in Estonia discusses how to involve the private sector and what is the right legal, technical, governance, financial, data sharing and infrastructure frameworks, among others, to do it in a way that maintains public trust and improves personalised medicine services and care.

The players in the private sector that might be interested to be on board for the discussion on how to use data for the benefit of personalised medicine include not only private healthcare providers, healthcare workers, diagnosis and pharmaceutical companies and investors, but also general technological industry. This is due to underlying technical solutions, such as cyber security, and other areas of professional stakeholders are also needed. The system must be built in such a way that it shouldn't break the patients' trust which has been a key factor in the success of the Estonian Biobank.

Silja Elunurm, Attorney at law, Advisor at Ministry of Social Affairs, stated the challenges in this area:
(i) keeping trust of data suppliers
(ii) personalised medicine governance framework
(iii) how to move from collecting data to everyday healthcare purposes to using it for innovation and value creation
(iv) how to create functional, resource efficient, and not duplicating cooperation models and infrastructure (health data in the state system vs genome data in the Estonian Biobank)
(v) the creation of pricing models to incentivise the interest in investing into data analytics and innovation
(vi) how to combine provision of private and public personalised medicine services to ensure prevention and care continuity, and sustainable financing[35].

2.2.3. Population Biobank

The HGRA allowed Estonia, and in particular the Biobank, to fulfil the goals of promoting the development of genetic research, collecting health and genetic information on the Estonian population, and using the results of genetic research to improve public health. With currently 20% of its population registered in the Biobank, Estonia is now very well positioned to deliver results from analysis of genetic and genomic data to its citizens. Estonians are enthusiastic about the prospects of using personal disease risk scores to change their habits and improve their health and wellbeing.

Andres Metspalu, Professor of Genomics and Biobanking at University of Tartu explained that all Biobank donors signed an informed consent before donating their blood samples or filling in questionnaires[36]. For genetic data to be useful for medical purposes, phenotypes are very important. By law, the Biobank has access to several databases to collect different types of

[34] https://www.mkm.ee/sites/default/files/digitalagenda2020_final_final.pdf

[35] https://www.youtube.com/watch?v=EkH3c49fhGc

[36] https://www.youtube.com/watch?v=ItZTokVOOZ0

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phenotypic data such as ICD-10 based diagnosis[37], prescribed drugs, billing information, disease trajectories. The Estonian Biobank has now an Omics approach that includes already many samples for which whole genome sequencing (WGS), whole exome sequencing (WES), metabolomics, mRNA sequencing, genome-wide methylation and expression arrays, telomere length, among others, have been determined.

Despite the important role of the Estonia Biobank in the successful implementation of genomics into personalised prevention in Estonia, it still faces important challenges at the moment, including: (i) the low budget allocated for prevention, likely due to lack of awareness for the economic value of prevention among executives, doctors and patients; (ii) the large work-load to keep the database of known risk variance updated; (iii) the very conservative medical science mindset, as it is always a challenge to adopt new technologies/ideas; and (iv) the ethical issues, regarding balancing the patients' rights (to know and not to know, to treat vs not to treat) and the need to treat everyone.

2.2.4. Personalised prevention: common and complex diseases

The success of Estonian personalised care based on genomics has been made possible due to a long-term and continuous effort to implement the roadmap established to effectively deliver all personalised medicine services by 2023. The roadmap focused on two main services that are mentioned previously: polygenic risk scores for common and complex diseases, and pharmacogenetic warnings.

The vision for genomics of common diseases is to reach personal prevention at a population scale. This will include: (i) sequencing the whole genome of the population to capture the maximum amount of genomic variation, and then use it for imputation; (ii) using SNP-arrays for the major part of the population and impute the arrays; and (iii) use the imputed SNP data for polygenic risk scores (PRS) and pharmacogenetics.

2.2.4.1. Cardiovascular diseases

Mortality due to cardiovascular diseases in Estonia is, despite decreasing in the last two decades, still high. The current cardiovascular disease risk score does not take into account the genetic risk dimension. As explained by Margus Viigimaa, Medical Doctor and professor of cardiovascular medicine, Tallinn University of Technology, based on Biobank data it is possible to associate higher genetic risk score for cardiovascular diseases to higher cardiovascular disease and myocardial infarct rates[38].

The EstPerMed (2018-2021)[39] clinical randomised study on cardiovascular diseases assessed the impact of proactive polygenic risk score-based prevention on risks associated with these diseases during a

[37] https://icd.who.int/browse10/2010/en

[38] https://www.youtube.com/watch?v=AoRHLRrfKcI

[39] https://www.etag.ee/wp-content/uploads/2021/07/Lõpparuanne.pdf

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12-month time span. For this project, general practitioners involved received specific training on genomic medicine. Results of this project show that the proactive prevention strategy for cardiovascular disease in individuals using high polygenic risk scores is feasible. It is also important that both general practitioners and study participants reported that knowledge of the genetic risk improved lifestyle and medication compliance. A cost-benefit analysis showed that, although cost increased by 14% compared to usual care due to the polygenic risk score measurements and the larger use of statins and blood pressure lowering medication, 14,600 euros is the cost saved per life.

The prevention strategy depicted from this project is now under study for implementation into the Estonian healthcare system. In Estonia, the general practitioner is main doctor and the key element in the personal prevention strategy implementation. If there is a moderate risk of cardiovascular disease the general practitioner will monitor the patient closely, yet, if the patient has a higher risk, they will be referred to a cardiologist who will measure several cardiovascular associated functions.

2.2.4.2. Breast cancer

Mortality rates associated with breast cancer in Europe have been decreasing mostly due to better screening methods. However, there is still a 20% difference in cancer survival among European countries, likely due to different screening programmes (Cancer burden statistics and trends across Europe | ECIS (europa.eu[40])).

As explained by Hannes Jürgens, Medical Doctor and lecturer of oncology and haematology, Tartu University Hospital, breast cancer risk factors are divided into those that can be controlled and those that cannot, with the first having a smaller impact. Some factors represent stronger risk of getting breast cancer, genetics being one of those, which explains the need of including genetic data in breast cancer prevention and early detection[41].

Tartu University created a new score using 3 meta-analysis databases, and validating it with Estonian Biobank data, to find the best polygenic risk scores for Estonian women. For those who have a high risk of getting breast cancer, secondary prevention measures (early detection), such as screening programmes, have shown to make a difference in mortality. For example, screening magnetic resonance imaging (MRI) has proven useful for high risk patients. Concerning primary prevention, a healthier lifestyle has the potential to decrease breast cancer risk by 25%. Currently, in Estonia, there is an age-based screening programme of biennial mammography, for 50–69-year-old women, with a participation rate of around 50-55%, which allows the detection of 25% of all breast cancers. There is room for improvement in screening and it has been proposed to move from age based to genetic risk-based screening for that

[40] https://ecis.jrc.ec.europa.eu/
[41] https://www.youtube.com/watch?v=mWqP3Sb-gSQ

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purpose. To evaluate this possibility, there is an ongoing large phase 3 trial in Europe recruiting patients with results expected in the next few years.

Also, under the EstPerMed Consortium, one Pilot study was initiated, dedicated to breast cancer prevention using genetics. This is a feasibility study to demonstrate the usability and acceptance of using risk scores, and includes two cohorts, namely hereditary mutation carriers and high-risk polygenic risk score carriers among healthy individuals. In the polygenic risk score cohort, 10 types of cancers were found, 70% of cases were out of screening age programme and breast cancers were more prevalent. In the monogenic mutation cohort, 4 types of cancers were found, and 75% of cases were out of the age screening programme. Based on these results, a model for personalised breast cancer screening was proposed, which includes genetics screening; screening starts 10 years earlier (40 years), counselling women on health behaviour risks (both genetics and non-genetics), including a prevention plan and ultimately a treatment plan. This way, it is possible to reduce breast cancer mortality by half and is cost-effective. In conclusion, introducing early genetic screening would reduce the risk of getting breast cancer. Based on these findings, the consortium will propose a framework for further implementation.

2.2.4.3. Pharmacogenomics

The effectiveness and safety of pharmacological treatments is far from optimal. According to Lili Milani, Vice Director, Professor of Epi- and Pharmacogenomics, University of Tartu when genomics is accounted for from the beginning in a new drug development phase, clinical trials success is increased by at least two times. Also, it is known that no dose fits all patients, drug response variation associated with several body functions, mainly in the liver, brain and kidney, genetic variants in all of these pathways able to affect drug efficacy[42].

The advantages of using pharmacogenetics are known and reported in many studies. DNA analysis can explain/predict the response of a patient to drug therapy, avoiding adverse events and non-response. Fifteen years ago, it was proposed that genotype-based dose medication should be implemented. Estonia is trying to implement pharmacogenomics into healthcare using a broad approach, having data available pre-emptively, with calculation for many different genes and drugs, so that the moment the doctor is prescribing a drug the data is already available.

Implementation of pharmacogenomics into healthcare is not an easy task. There are several hurdles, namely the cost of genetic testing, time waiting for the results, regulations, accessibility, and IT infrastructure. Estonia is trying to address these at many levels, in close collaboration with computer scientists, ministries, national health institutes and other partners and taking recommendations from the Clinical Pharmacogenetics Implementation

[42] https://www.youtube.com/watch?v=ILidPfkLHXI

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Consortium (CPIC)[43]. Taking advantage of the national Biobank, Estonia started translating this genotype data into clinical pharmacogenetics recommendations and tools for implementing pharmacogenetics into clinical care (Reisberg et al, 2019)[44]. Also, results have been returned to biobank participants through a pharmacogenetics report.

2.2.5. Population awareness: engagement and communication of results

To achieve this successful level of personalised prevention in Estonia, public voice is paramount. Currently, 75% of the population supports the use of genetics for clinical purposes. This acceptance level took time to build and is a consequence of wide-ranging public communication campaigns over the last 20 years through TV shows, newspapers, social media, and even a story in a soap opera episode.

But trust is also built from contact of patients with the healthcare professionals, with effective and careful communication of results and counselling, which is crucial. Also, an ethical and legal framework that supports the patients and citizens' rights and ownership of their data is key. The current HGRA in Estonia is very supportive and allows participants/donors to access their own data, giving them the right not to know their genetic data and the right to counselling upon accessing their data. Discrimination based on genetic data is strictly prohibited.

Concerning the psychosocial aspects of returning genetic risk results to patients, as explained by Neeme Tõnisson, medical doctor, geneticist and Associate Professor of Clinical Genetics, University of Tartu, studies in Estonia have shown that patients are largely able to cope well and value the results. The majority of participants consider the genetic risk information useful and can manage their psychosocial risks, and, with careful planning, counselling and appropriate guidelines a large-scale population biobank can indeed support implementation of precision prevention and personalised healthcare[45].

Similar results were found in another set of projects related to returning results and counselling. Liis Leitsalu, researcher of genomics and genetic risk communication, University of Tartu, shared results, and experiences on several return of results (ROR) projects involving the Estonian Biobank. These may be divided into three types, based on how the information flows:

- Biobank to Participant: Biobank offered to return results to participants
- Clinic to Participant: results were returned in the healthcare setting
- Participant to Biobank: with the largest participation, participants

[43] https://cpicpgx.org/

[44] Reisberg S, Krebs K, Lepamets M, et al. Translating genotype data of 44,000 biobank participants into clinical pharmacogenetic recommendations: challenges and solutions. Genet Med. 2019 Jun;21(6):1345–1354. doi: 10.1038/s41436-018-0337-5.

[45] https://www.youtube.com/watch?v=jRi47EbUFx4

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expressed interest in receiving results from the Biobank.

Each project type used different approaches to ROR[46].

In the case of Biobank to Participant projects, main considerations are:

- duty to warn and the right to (not) know
- results offered are clinically significant and actionable
- findings are relatively rare, which means that the number of participants is low (under 100)
- classic genetic counselling is offered by genetic counsellors from the Biobank.

In the healthcare setting projects, the main considerations are the same, but genetic counselling is provided by specialists, including general practitioners, oncologists, or cardiologists. The results returned were polygenic risk scores, which means a higher number of participants engaged (around 1000 per project). In the Participant to Biobank projects, results were broader, considerations were participant's interest and reciprocity, the number of participants was higher (nearly 3000 over two years) and counselling was offered by trained counsellors from the Biobank. Results from participants' feedback in this project show that participants tend to feel calm, relaxed and content with the results and that ROR with genetic counselling has a positive effect.

[46] https://www.youtube.com/watch?v=Sff0G6IrDKU

In all these projects, counselling has been done face-to-face, which although valued by the participants was also considered a bottleneck by them due to time constraints. Therefore, other options must be considered, and a model, dividing the type of communication based on the type of results offered was proposed, with the following approaches: traditional counselling when emotional and familial implications are found; targeted discussion when personalised risk management or treatment is considered; and brief communication when encouraging healthy behaviour (Ormond et al, 2019)[47]. Other approaches to risk communication include using digital tools to complement face-to-face communication, such as cascade screening (to increase the response rate of relatives), and long-term treatment plans to help with adherence.

2.2.6. Key discussion points from participants and speakers

During the Estonia CEV, participants were able to ask Estonian representatives and lecturers about the country's path in implementing genomic/precision medicine into clinical care, challenges, and recommendations. During these discussions, several issues were debated, with emphasis on the following:

[47] Ormond KE, Hallquist MLG, Buchanan AH, et al. Developing a conceptual, reproducible, rubric-based approach to consent and result disclosure for genetic testing by clinicians with minimal genetics background. Genet Med. 2019 Mar;21(3):727-735. doi: 10.1038/s41436-018-0093-6.

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Host Country: Estonia	
The age at which genetic information is included is currently 18 in Estonia, and there is public debate if data collected should start from early ages, i.e., children. On this issue, one topic of discussion is the use of, for example, data on new-borns from one country by a country that rules out this group of the population. This is not possible in Estonia at the moment, as both the GDPR and societal regulations must be met. Police have no access, by law, to Biobank data. Costs of storing and managing genetic data in the Biobank, and its use, are currently being discussed regarding how to cover those. Good and constant communication among all stakeholders, involved in the process of implementing genomics into clinical practice, is vital. Patients have access to all their data, including results on PRS and PGx reports, and they also manage others' access to their data. Moreover, doctors can assist patients in the interpretation and understanding of their own results.	The system and infrastructure is prepared to update PGx predictions as research or more data is gathered. To put patients at the centre, the health system must change its treatment paradigm, moving from the current "silo" approach to a more holistic one, to be able to analyse different disease risks in the same patient. Debate on combining monogenic (mutation) and polygenic findings on genetic risk models is still ongoing, regarding how to do it and its benefits. It is important to inform and educate the public, and involve, and train, the healthcare community, including on IT tools, namely GPs and medical societies, from the start. Regarding return of results, patients should be given the choice to not know, and be able to change their mind. Nevertheless, information on results is not enough; patients would also like to know that there is continuity and a proper care plan. Also important is to clearly inform patients about the limitations of genetic based predictions.

2.2.7. Main conclusions and takeaways

The success of Estonian personalised care based on genomics has been made possible due to a long-term and continuous effort to effectively deliver personalised clinical services and care (**Figure 4**).

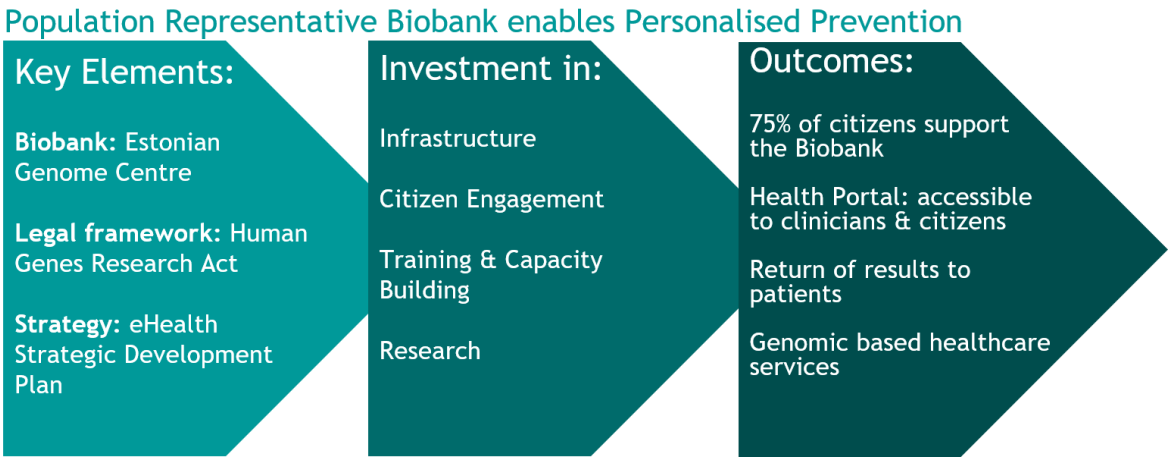

Figure 4. Main features of the Estonia strategy to implement genomics into healthcare.

The main features contributing to the success of this implementation are:

Biobank and Genome Centre

- Estonia has a well-established biobank with over 20% of the

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population registered and are now able to start delivering a service to the medical services.
- They can store and screen large amounts of samples and data.
- They are used for both research and healthcare.
- Storage of different types of genomic data, including WGS, allows genome-wide association studies (GWAS) and clinical use.
- Rules to access data and samples are clear, transparent and under strict regulation.

IT infrastructure and data

- Estonian citizens have an electronic ID card which enables them to link to all services.
- The nation-wide platform, X-road, is being used as the technical infrastructure that links information systems and ensures secure electronic exchange of clinical and other data.
- Health portal is interoperable with different databases, including ICD-10, prescription, billing, disease trajectories.

Awareness, engagement, and training

- Public: 75% of Estonian citizens support and expect the use of genomic data in healthcare. This level of support and trust was achieved due to several wide range public communication campaigns during the last two decades.
- Healthcare professionals: different healthcare professionals have been engaged in pilot genomic medicine projects, rising awareness for the advantages of genomic medicine in healthcare.
- Training of relevant human resources, including bioinformatics.

Healthcare services

- Use genetic information to estimate disease risk and drug/treatment efficacy and do it as a universal service.
- Polygenic risk scores improved risk prediction in breast cancer and cardiovascular diseases.
- Use of genetic information to estimate disease risk for some chronic and common diseases.
- Pharmacogenomics: to decrease clinical drugs' side-effects and increase their efficacy in each patient, digital prescription includes pharmacogenomic-based recommendations.
- Provide return of results of genetic risk to patients and counselling, both valued by patients. Counselling provides either by specialists or genetic counsellors.

2.3. Finland: Regulating the unknown

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2.3.1. Introduction

The CEV to Finland taken place on 16-17 June 2021, was organized under the theme 'Regulating the Unknown'. Throughout the visit, participants had an opportunity to learn about some major topics of the Finland Genomic Medicine namely Health sector growth strategy for research and innovation, creation of the regulatory framework, technical infrastructure, and collaboration with the industry. Outputs from this visit were used to produce a Policy Brief. Due to COVID-19 travel restrictions, this CEV was held virtually.

The visit had contributions from the host country and from other European countries reporting on their stage of implementation of genomic medicine, namely Bulgaria, Belgium, Denmark, Lithuania, Luxembourg, Portugal, and Sweden (Table 2). More information on this CEV can be found in its Minutes[48], Recordings[49] and Slides[50].

2.3.2. Health Sector Growth Strategy for Research and Innovation

The Health Sector Growth Strategy published in 2014, involves several ministries, namely the Ministry of Education and Culture, the Ministry of Economy and Employment, and the Ministry of Social Affairs and Health, working together with Academia Finland and Business Finland, the innovation funding agency of Finland. As highlighted by Anni Kaukoranta, Development Manager, Ministry of Economic Affairs and Employment, inter-ministerial collaboration is the key for implementing the strategy, along with investment in public-private partnerships, and strong and steady political support since the publication of the strategy[51]. The overall aim of the strategy is to innovate the healthcare sector's environment, achieve economic growth and create opportunities for better healthcare. The current Roadmap (2020-2023) aims to ensure sustainable growth and well-being with three interlinked areas of measures for developing health sector research and innovation, namely operating environment, expertise and partnerships and cooperation. The Finnish government is an enabler, investing in personalised medicine, research, innovation, education, data management and the creation of new clusters of excellence, including the National Genome Centre, Neurocentre Finland[52] and the Drug Development Centre[53]. The main purpose of the public R&D and innovation funding is to encourage enterprise's bold renewal and international growth. As the operational arm of the ministry regarding the health sector growth strategy, Business Finland is currently running the Personalised Health Finland programme, from 2018 to 2022 and works closely with research institutions and companies.

- ☐ Finland has an uneven population distribution and a decentralised healthcare system. Overcoming these obstacles and those posed by geography was included in the 2014

[48] https://docs.google.com/document/d/1tUqD-phovzzAJczUqcW41lQ0RPJiPD4IC9qTxk0bz9s/edit?usp=sharing
[49] https://www.youtube.com/playlist?list=PLweO8RYcVPDM5ydSVQuQO7WBpkZm8dycy
[50] https://drive.google.com/drive/folders/18gBumspAL5vIDBd56hOqe5qbj8ypG4k-
[51] https://www.youtube.com/watch?v=mFYSg6d9ypU
[52] https://stm.fi/en/personalized-medicine/national-cancer-center
[53] https://stm.fi/en/personalized-medicine/drug-development-centre

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strategy. Liisa-Maria Voipio-Pulkki, Director General, Ministry of Social Affairs and Health illustrated how Finland dealt with these challenges[54] with the example of the National Genome Centre. This centre, created by government decree, joins the 20 Hospitals districts and 5 medical universities, forming 5 regional cancer centres in a joint coordinating unit. This is now one of the pillars of the health sector in Finland. Another important point to start implementing the strategy is research. For this purpose, Neurocenter Finland was created, with several Universities, following the motto that collaboration makes research stronger. The Finnish Healthcare system has several pillars. One of them has been the creation and support of the national infrastructures related to data, creation, processing, utilisation and regulation of sensitive personal information, with genomic data being only the tip of the iceberg. Finland has the National Patient Data Service, KANTA[55], which works as an ecosystem that brings together different systems as a single repository, it is open to both professionals and citizens, and includes digital records and prescriptions. The genome database is the latest addition to KANTA. This ICT infrastructure is valued by citizens and is one of the reasons why Finland ranks as a top country in healthcare information technology. How to handle and regulate sensitive personal data is at the centre of the debate at the moment in Finland. Following an expert meeting in Brussels in 2019, the policy brief "Regulating the unknown" produced by the European Observatory on Health Systems and Policies was published in 2021. In the policy brief, public trust is identified a must in the process of regulating and handling sensitive personal data. It is crucial to protect data, communicate openly with the public, involve the public in creating the rules and regulations and demonstrate clearly how data use can benefit citizens' health.

2.3.3. Building relevant legislation

As established in the Genome Strategy (2015)[56], the National Genome Centre will be the public authority to manage the national-population genome database and promote the responsible and equal use of genomic data, though individuals are to maintain control of the use of their own data. Sini Tervo, lawyer and legal adviser from the Ministry of Social Affairs and Health is involved in writing the Genome Act, the legislation for establishing the National Genome Centre and the use of genomic data, and explained that there

[54] https://www.youtube.com/watch?v=CSIqr0W8L88

[55] https://www.kanta.fi/en/professionals/patient-data-repository

[56] https://issuu.com/sitrafund/docs/finland_genomestrategy

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have been two public consultations (2018 and 2019) on the draft law[57]. Most of the discussion was focused on the establishment of the National Genome Database. This raised many questions, and to avoid delaying the implementation of the National Genome Centre, the legislation was divided into two phases. In the first one (consultation in 2021), the Act will be on the governing of the Genome Centre and legislation related to the consent on performing a genetic analysis. The second phase (consultation in 2022) will be an Amendment Act on genome database and use of genomic data. After this it will be possible to use data for research and healthcare purposes. An expert group on genomic medicine has been established to help drafting the Genome Act.

Finland has a Social and Health Data Permit Authority, Findata[58], which bases its activity on the Act on Secondary Use of Health and Social Data[59]. Although connected to the Finnish Institute for Health and Welfare, Findata is an independent authority. Johanna Seppänen, Director of Findata, explained the cornerstones of secondary use of social and health data[60], Finland data registers covering practically 100% of the national population, with some registers, such as diagnosed cancers, dating back 70 years, an opt-out principle for secondary use, a personal identity code, which is key to linking personal information from various registers, and trust from the Finnish people on the authorities to keep their data safe and secure.

The legal framework for secondary use of data has to be able to improve and accommodate additions for new uses of the data. The secondary use of data covers several databases, namely the KANTA (mentioned above), the national registers (covering 100% of the Finnish population), the Biobanks (with new legislation being prepared) and the National Genome Database, mentioned previously by Sini Tervo. In this context, Findata has been acting as a one-stop digital shop since 2020 for the secondary use of health and social data, granting data permits, anonymisation services, collecting and linking data and providing an IT-secure environment for data permit applications, information requests and remote access to data.

2.3.4. Technical Infrastructure

The structures mentioned previously need to be supported by a technical infrastructure. The 1+MG initiative WG5 is working to provide the blueprint for this structure to support cross border data exchange, services, and interoperability. As explained by Tommi Nyrönen, Head of Node, ELIXIR Finland, a scoping paper for infrastructure[61] was delivered early this year and by the end of 2021 an end-to-end demonstration of the functionality of the infrastructure using rare diseases' data is expected to be published and will include a

[57] https://www.youtube.com/watch?v=74w9XZcsWvk
[58] https://findata.fi/en/
[59] https://stm.fi/documents/1271139/1365571/The+Act+on+the+Secondary+Use+of+Health+and+Social+Data/a2bca08c-d067-3e54-45d1-18096de0ed76/The+Act+on+the+Secondary+Use+of+Health+and+Social+Data.pdf
[60] https://www.youtube.com/watch?v=oPaZIgn3lTk
[61] https://docs.google.com/document/d/1L5imuKcL0wZNOQ1vOmPAXpR8SG42EL4iq1HZlH87Yv0/edit?usp=sharing

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data protection impact assessment through the entire workflow[62]. The infrastructure architecture cannot be set up dissociated from the ethical and legal issues and governance framework and therefore a permanent dialogue is required with these areas. The functionalities of this architecture involve data discoverability, data reception, storage and interfaces, data access management mechanisms that support data authorities, like Findata, and data processing, i.e., computing.

Although the data hubs are to be set up by each country, it is desirable to have a single national connection point and to ensure infrastructure interoperability for their engagement with the European 1+MG initiative. In Finland, these functionalities are being built at the National Genome Centre. For the cross-border use of genomic data for clinical and research purposes, it is important to have government-level collaboration to ensure interoperability to manage national sensitive data for European collaboration. So far in Finland this has not been a problem.

The Finnish Biobanks[63], presented by Olli Carpén, Scientific Director of the Helsinki Biobank, started in 2013 after the Finnish Biobank Act[64] entered into force. It is a key element of the data infrastructure in Finland[65]. The biobanks in Finland are coordinated under an umbrella cooperative organisation, the FINBB[66], owned by six largest hospital districts and universities in Finland, and the Finnish Institute for Health and Welfare (THL). The Biobank operates under the premise that it must be integrated in the Healthcare system, so that biobank data can be accessed and combined with other biological and phenotypic data and this way make personalised medicine possible. For this, a wide consent from the donors/patients is important, as well as the integration of consent into the healthcare routine, along with sample collection, and the right given to every patient to be a research patient. All University Hospitals have created data lakes that create and integrate data from different sources and types for use, including secondary use under the Secondary use legislation mentioned previously. As with Findata, the FINBB also operates under the one-stop-shop of Fingenious, which allows potential users to search for samples and associated data at a single-entry point and combined samples from different Biobanks. It is important that the biobank samples/data are used and that any findings in research projects will be returned to biobank. The Finnish Biobank thus collaborates actively with other institutions/research projects, like FinnGen, iCAN, the National Cancer Centre, and the Neurocenter Finland.

FinnGen[67], presented by Aarno Palotie, Scientific Director, is a research project that aims to use genetic strategies to understand disease mechanisms. The goal is to enrol 500,000 sample donors (around 10% of the Finnish population), with samples becoming

[62] https://www.youtube.com/watch?v=jMMFMPhTKcE
[63] https://www.biopankki.fi/en/finnish-biobanks/
[64] https://finlex.fi/en/laki/kaannokset/2012/en20120688.pdf
[65] https://www.youtube.com/watch?v=Z1AtjHkkYSs
[66] https://finbb.fi/en/
[67] https://www.finngen.fi/en

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part of the Biobank and combine genetic data with national health register data[68]. This combined data is used for association analysis. The aim is to contribute to personalised medicine by providing individual genome data and researching and to understand the genetic contribution for diseases and drug response. FinnGen is a public-private project with several partners, including FINBB, academic institutions, public healthcare and 12 pharma companies. All diseases are included in the research. A project of this dimension requires data to be protected. The solution used to analyse data to prevent download and fulfil the regulatory requirements was to use Google Cloud in a sandbox environment. This allows approved users, including outside the EU, to access and analyse data.

iCAN[69] is a Digital Precision Cancer Medicine Flagship funded by Academy of Finland[70], hosted by Helsinki University. As explained by Tomi Mäkelä, Executive Officer, the aim is to link tumour molecular profiling with data from Finland's digital data, which will provide new discoveries to advance cancer medicine together with patients and partners[71]. Biobanks, national health registers and Findata are involved in this data input into the iCAN discovery platform, which operates within the hospital data lakes described earlier for the FinnGen project.

Another project involving the use of genetic data to produce new personalised therapy options with clinical trials showing promising results, was presented by Mika Kontro, Specialist, Helsinki University Hospital, Clinical Group Leader, FIMM[72,73]. This project focused on acute myeloid leukaemia (AML), the most frequent form of leukaemia in adults, and has allowed the identification of new biomarkers and uses for existing compounds in clinical use.

2.3.5. Industry collaboration

The current Finland Roadmap for the strategy recognises the industry as a valuable partner in both healthcare and research. As Sandra Liede, Lawyer, currently working for Healthtech Finland[74], a non-profit association, explained, industry partners cannot be taken out of the equation of genomic and personalised medicine since they are crucial for providing the technology, tools and equipment used for data production, analysis, collection and delivery, data producers and users, funders, service providers, and research partners.

In Finland, industry is actively collaborating with the healthcare system. FinnGen[75] is an example of the involvement and integration of the private sector in personalised medicine efforts. Although the industry agrees and supports the healthcare system approach to genomic medicine, it remains important that local solutions do not force the industry to fit too many different

[68] https://www.youtube.com/watch?v=LUy0q5HPBOs

[69] https://ican.fi/
[70] https://www.aka.fi/en/
[71] https://www.youtube.com/watch?v=ydGB0ZW3fa0

[72] https://www.helsinki.fi/en/hilife-helsinki-institute-life-science/units/fimm
[73] https://www.youtube.com/watch?v=BLXjwNe8yRk
[74] https://healthtech.teknologiateollisuus.fi/en
[75] https://www.finngen.fi/en

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systems as this will increase the economic burden for this sector. Also important for the industry is that legislation and regulations are set up for the long term. Setting up new regulations is time consuming and can slow down innovation and development. Therefore, it is important to involve the industry in the drafting phase of the legislation on genomic medicine.[76]

[76] https://www.youtube.com/watch?v=MC3xJv3qOqE

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2.3.6. Key discussion points from participants and speakers

During the two-day CEV to Finland, there was a large involvement of participants during discussion with speakers, both online and via chat. The discussion was mainly focused on practical approaches and solutions regarding specific issues related to the implementation of genomics into healthcare system in Finland, namely:

Host country: Finland	
Implementing PM is a "long run": it takes a lot of work and time, in addition to legislation, to decide goals and tasks. Decision on which areas to choose at first will depend, among others, on available knowledge and data, willingness to invest and remain at the forefront of cutting-edge subjects. Each disease may require different approaches. However, learnings from one can be applied to others, particularly if the use case chosen to be a proof of concept, or pilot, is well structured and based on sound research findings, as it may become a flag in the campaign for the use of genomics in clinical settings and creates momentum for collaboration of the different stakeholders. Pilot studies can be used to enhance collaboration between different stakeholders and provide evidence usable for public awareness campaigns. Recognising data security as a key issue, crucial to ensure that those accessing data are authorised after scrutiny, is paramount.	All comments and concerns from citizens to the Act under discussion are considered, but it is important to find balance and ensure an enabling regulation that does not overregulate. Possibility is given for researchers to freeze data sets used for publication, for reproducibility purposes. Data access requests are very complex and not easy to streamline. It is time consuming and requires input from specialists. To have an impact at the population level, Biobanks would likely include primary care patients. Regarding recruitment for large population genome sequencing, Biobank represented patients will be used, thus being unlikely to need to recruit new cases. Having patient organizations present in the WGs responsible for preparing legislation is vital to create trust and awareness. In parallel, public campaigns, surveys and websites also contribute to this goal. Having several countries simultaneously engaged in building people's trust would make it easier for all.

2.3.7. Main conclusions and takeaways

This Finnish CEV has shown that implementing genomic and personalised medicine into healthcare requires long term commitment and takes time. It can benefit from pre-existing Biobank, and related legislation, and government investment and organisational support on innovation and funding are crucial (**Figure 5**).

Finland is heavily invested in personalised medicine, with some key aspects contributing to its advancement, technically, legally and regarding public trust and engagement:

- Goal to attract investment in Finland on personalised medicine and build an ecosystem:
  - Establishing National Genomic Centres (use cases: Cancer and Neuroscience)
  - FinnGen as a good example of an ecosystem building block
- The Finnish Government is an enabler through provision of

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funding, capacity building, and education
- Health Sector Growth Strategy has been supported despite changing governments
    - Emphasis on creating national infrastructure for hosting & processing data in the health system, as well as digital services for patients
- Regulations on the primary and secondary use of personalised data are not easy - much debate, as these are key societal and political issues
- Public trust is a key element for successful implementation and acceptance.

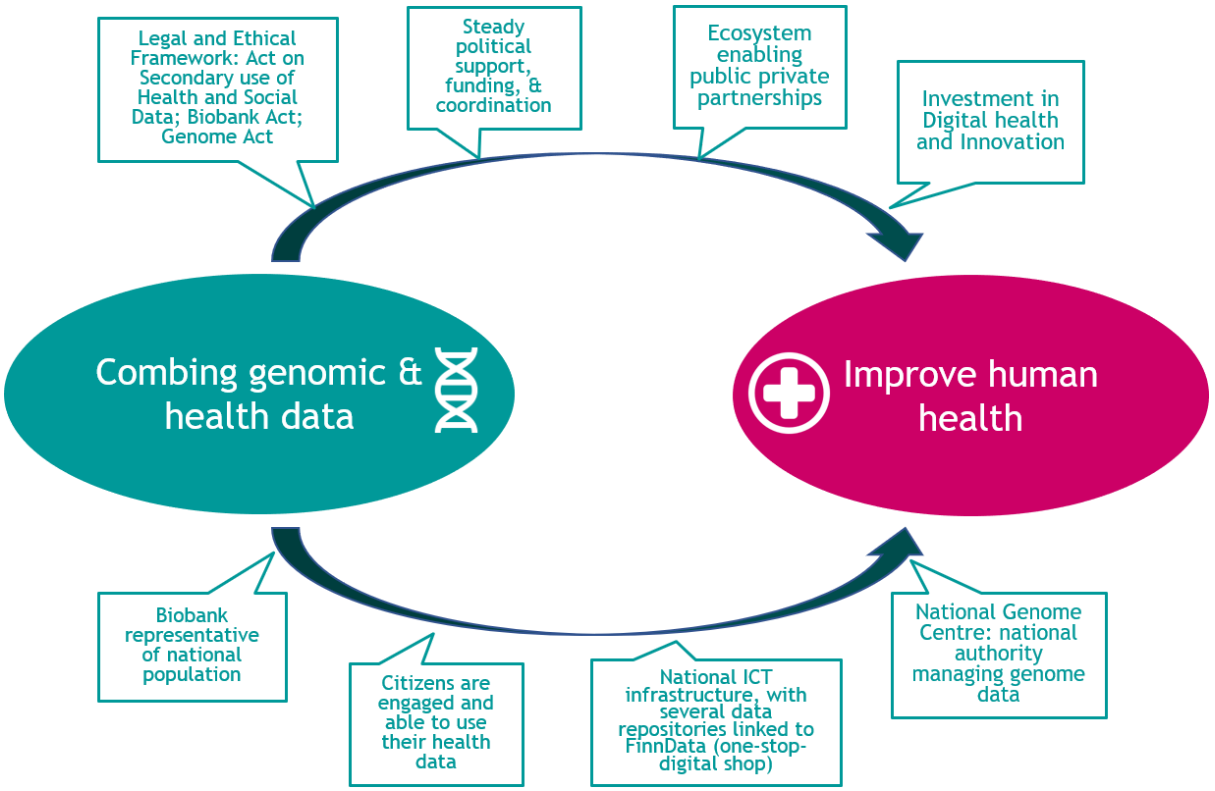

Figure 5. Main features of the Finnish strategy to implement genomics into healthcare services.

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3. Current status of Genomic Strategy in participating countries

During the three CEVs, several participating countries presented the status of their genomic initiatives, along with the most challenging issues and/or relevant recommendations. Some also reported on the needed support from the 1+MG initiative. A summary of these presentations is presented in **Table 1** and recordings can be found HERE[77].

Together with the three host countries of the CEVs (UK, Estonia, and Finland), the 13 countries presenting their genomic medicine status and strategies (Table 1) constitute 67% of the declaration signatory countries and may be viewed as a reliable representation of the current level of implementation of genomic medicine in Europe.

Table 1: Current status of the genomic strategy, key challenges and required support from the 1+MG initiative in participating countries.

Country	Current status	Key challenges	Support from 1+MG
Belgium	A Mirror Group has been created, along with the Governance structure, and several discussion groups are debating several issues, including ELSI issues, and clinical data and quality. The infrastructure to support genomic medicine will benefit from the already in place structure of the centralized Health data platform and from guidelines for NGS implemented for cancer data. (https://www.youtube.com/watch?v=3jCsiBDuhM0)	Bring together research and healthcare regarding WGS, with HTA analysis, roadbook preparation, pilot studies to test the structure and implement it.	Belgium would benefit from a common and centralized European commercial procurement approach as part of B1MG/1+MG to bring down sequencing costs; help in establishing the general framework (legal, ethics, QA/QC, models); common procedures for setting WGS in healthcare, including guidelines for analysis, interpretation, and reporting; technical advice for developing the infrastructure.
Bulgaria	Bulgaria has no National Genomics initiative or programme for personalized medicine, no secured funding for WGS yet and still no support from the Ministry of Health or the Ministry of Economy. However, Bulgaria has a national research infrastructure roadmap, supported by the ministry of Education and Science, with some initiatives in the area of Education on Genomic Medicine already taking place and with established plans to upgrade the IT infrastructure for Digital Health. Currently with Centres of Competence in the building phase, Bulgaria has one Centre of Excellence running and	Funding for the generation of the Bulgarian reference genome; political support and ministry engagement; infrastructure and capacity building; raising awareness amongst government and funding structures, citizens, and healthcare professionals; coordination of research, clinical and diagnostic activities and of relevant government and funding bodies.	Common standards and good practices; create political awareness and engagement; opportunity to share scientific and clinical results; improve communication and coordination between stakeholders; help on capacity building and education.

[77] https://www.youtube.com/playlist?list=PLweO8RYcVPDM9Bo_safKw9bQDWueEx6ZA

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	providing genetic diagnosis for rare diseases. This centre has recently (2020) upgraded its NGS core facility, enabling Bulgaria to perform WGS. Associated with this centre is the Bulgarian Biobank. This centre already has some clinical/research genomic data from WGS, WES and gene panels for some diseases. (https://www.youtube.com/watch?v=8-1BvnlEzUc)		
Denmark	Denmark has a national strategy for personalized medicine, with both regional and national political support. The Danish National Genome Centre (in construction), which mandate is established by health legislation in 2019, is an institution under the Minister of Health and centralizes administration issues related to personalized medicine. With the advantage of having a huge funding, along with a long tradition of health registries and Biobanks, Denmark can build the needed infrastructure, and is also benefiting from a strong public support on the use of data and genetics for health. As a pilot for the use of genomics in the healthcare system Denmark will start with WGS of rare disease patients, but other diseases are already planned to follow. Currently building up the national genome database. (https://www.youtube.com/watch?v=woCWT9ddETg)	To combine the needs from all stakeholders involved; re-evaluate and adapt the current legal framework to allow the use of genomics into the clinical practice; put data into use by the healthcare system; data handling and sharing in a secure way between different institutions.	How to handle cross-border data sharing, regarding legal and technical challenges, without moving the data; how to standardize sequencing and data presentation; work together to enlarge the support of citizens to be able to work across-borders.
Germany	Although some regional initiatives from the Healthcare System on Rare diseases and cancer exist, clinical and genomic data is still scattered on different databases and genome sequencing is not yet part of the healthcare provision. Pillar to the German Genome initiative is to build the data infrastructure, for which financing has been granted by the federal government. The German Human Genome-Phenome Archive (GHGA) can deliver the data archiving and analysis required for GenomeDE and also to integrate this data into the B1MG data space. Although initially concentrating on RD and Cancer, the perspective is to include other diseases for which phenotypic data already exists. The aim is to establish the GHGA as the infrastructure (distributed through a cloud-base structure) for human omics data, connecting German omics centres, and forming the federated German node within	-	-

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	the federated European Genome-Phenome Archive (EGA). (https://www.youtube.com/watch?v=xBihSnbYc6M)		
Hungary	Genomic medicine is mainly restricted to healthcare of rare diseases and cancers, education, and research activities. It is centralized and performed in 4 Medical schools and one National Institute, where the care by clinical geneticists is well organized. Also, all diagnosis and individualized therapeutic approaches (related to cancer and genetic diseases) are financed by the national health insurance fund (NEAK), including private diagnostics (done on individually requested basis). Hungary will emulate the UK experience with 3-4 national hubs supplemented with high-capacity sequencing platforms, bioinformaticians, and clinical and medical geneticists. (https://www.youtube.com/watch?v=teNs8CHrsqk)	Financing support is needed in order to face current needs and challenges related to education of health care providers, knowledge sharing with the general population and achieve short term goals related with data.	Support for development of best practices to develop and maintain registries, and for the financial models for covering expenses related to genetic testing and gene therapies.
Italy	Genome sequencing is not yet part of standard of care, but several initiatives have received funding, to strengthen the sequencing capacity and to increase awareness for genetics/genomics in healthcare. Guidelines are already established focusing on capacity building (namely citizen engagement and healthcare professionals' education) and health technology assessment of genetic/genomic testing and technologies. Training of healthcare professionals has already reached a substantial portion of this population, with Italy being involved in a European training program in cancer genomics. As a first step an active discussion on ELSI subjects is being held. Based on a survey, only a few genome datasets are accessible. The Italian genome initiative counts with the input and active involvement of several ministries. (https://www.youtube.com/watch?v=r5XJFr6zaCo)	-	Regarding data sharing, Italy needs standards for clinical and genomic data and for biobanking; an easy-to-use tool to connect institutional data with the national reference centre (FAIR model); software to connect the national node for interoperability.
Latvia	The Genome Database of Latvian Population (Biobank), one of the largest biobanks in Eastern Europe, has a good representation of various diseases, and contributed to development of the infrastructure. Latvia recently increased its genome	There is still a need for a clear roadmap and investments for infrastructure development; to improve legislation on data accessibility; insufficient human and technical resources in bioinformatics and data management.	Joining the 1+MG initiative itself has generated political support and momentum for genomic medicine in Latvia; need for clear information on activities and their impact transmitted to government authorities; shared technical solutions and standards; shared

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	sequencing and analysis capability. The creation of an ecosystem framework for biomedicine attracted a lot of interest from the private sector companies, including a collaboration agreement with the BGI/MGI company, and with national IT equipment producers and telecommunications companies helping to establish the genomic data network. The Latvian Covid-19 Data Portal serves as the prototype for data sharing in the 1+MG initiative. There are genomic projects on rare diseases, cancer, and common diseases, with 300 WGSs. The legal framework with the focus on secondary use of data is under development. (https://www.youtube.com/watch?v=rssGK6nRd84)		results from other countries' pilots and proof of concept results.
Lithuania	Genomic medicine in Lithuania is only at the very beginning, with services provided in 4 main hospitals and high throughput NGS service provided by the Vilnius University Life Sciences Centre. The national Biobank infrastructure is being built, and sample and genome collection has started. There are already data registries from the National Cancer registry and from E-Health records, and from WGS and WES for cancer and rare disease patients and from the population in general. (https://www.youtube.com/watch?v=guegogmuzAs)	Legislation related to data sharing and funding remain the main issues currently under discussion.	Advice and assistance related to coordination of activities, sharing experiences, guidelines, standardized protocols and legislation.
Luxembourg	There is no National genomic initiative yet, and although represented at the 1+MG initiative, Mirror Group has not been assigned yet. However, Luxembourg has a national centre of genetics, a national Biobank and a centre for systems biomedicine. WGS is starting to be implemented in the country, with programmes for cancer, RDs and CCDs planned or already financed, one with private funds.	COVID-19 led to lack of resources. There is also a lack of political support for WGS. Also needed is an ELSI framework and legislation around use of genetic data or secondary use of health data.	-
Norway	Norway has established a strategic plan for personalized medicine in Healthcare, a PM Board with stakeholders from different backgrounds, including Disease Societies, Medical Associations, Industry, National Healthcare system, and a competence network for PM to work on issues like standardization, competence, equal access, monitoring, and spanning across different areas like cancer, rare diseases and microbiology. It has one major hub which centralizes four	Development of the legal, ethical, organisational, and technical framework for the national genome centre and data registry; building the needed competences; capacity and funding to implement genomic medicine into the healthcare system; follow up on communication with the public.	ELSI framework for storing and sharing data; learn from experience from other countries; sharing tools and software; sharing genome data

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	regional nodes, each connected to clinics/hospitals. A trial (Drug-like) for precision cancer medicine is currently running and will serve as a pilot for precision medicine in Norway. Funding has been secured for establishing a Norwegian Genome Centre, planned for 2021. Norway is currently working on legal and ethical issues, with the legal basis for pseudonymised date for single genetic variants soon to be presented to the parliament. (https://www.youtube.com/watch?v=EFbhSeeVLcc)		
Portugal	Portugal is preparing the Portuguese Strategy for Genomic Medicine, PT_MedGen, but there are some national initiatives that will help implement genomic medicine in the country. Portugal already offers genetic services mostly for rare diseases and cancer, WES and gene panels, but WGS is still only used for research. There is a national network of Biobanks (Biobanco.PT) and a sequencing and analysis network infrastructure (GenomePT), currently set up for WGS, which works closely with research and the healthcare system. There is also a Portuguese node of Elixir, Biodata.pt. The contribution to the GoE will be used as a pilot project to test the Portuguese infrastructure for genomic medicine. (https://www.youtube.com/watch?v=-q2j4HU3pw0)	The 1+MG initiative already raised awareness from policy makers to genomic medicine but is still not enough and needs to come from different ministries; proper legislative framework; strategy for sustainability; information, education and literacy for policy makers, healthcare workers and citizens.	Guidelines and standards; ELSI best practises; alignment of programmes and policies at the EU level to allow transnational sharing of genomic and health data.
Spain	From the genetic point of view, Spain is a quite diverse country, but all autonomous regions are included in the IMPaCT Program (2021-2023), intended to set the infrastructure for the Spanish genomic medicine strategy. It is composed of three programs, IMPaCT Cohort, IMPaCT Data and IMPaCT Genomics, and transversal strategic actions related to ELSI aspects and internationalization. The IMPaCT Cohort will include 200000 individuals and is integrated into the National Health System. The IMPaCT Data program focuses on data (analysis, interpretation, infrastructure, management, etc.), prioritizing rare diseases as use cases. In the IMPaCT Genomics, still with no funding for infrastructure, will have rare diseases, cancer, and pharmacogenomics (severe adverse reactions to drugs and vaccines) as use cases.	-	-

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	(https://www.youtube.com/watch?v=v5FLtsqTpZU)		
Sweden	Genomic Medicine Sweden joins academia and the public health sector, and was formed in 2017 to work on precision medicine, with funding from the Swedish Innovation Agency Vinnova. It is clinically oriented and coordinates the 7 regional genomic medicine centres (GMC) in Sweden. Currently working on harmonizing procedures and guidelines, Sweden established a National IT infrastructure, with a National Genomics Platform, to which the 7 GMCs are linked to share data, and to be a national resource for research and innovation. Different diseases are already integrated in this system, and genomic medicine is already in clinical routine, including WGS, WES and gene panels. There are some issues regarding data sharing between regions, which the legal framework currently under discussion will clarify and solve. (https://www.youtube.com/watch?v=bJw25SuMhp4)	Issues regarding data sharing (with whom and how) are a challenge. For Denmark it is crucial to have a strong patient influence, partnerships with industry, training and skills development for healthcare professionals, a national platform for secured use of data and a national coordination and management, and increased access to national clinical studies.	Synchronized and harmonized view on privacy and processing of personal sensitive data, including joint principles for secondary use of data; create urgency around genomic and precision medicine involving policy makers and politicians.

Analysis of Table 1 clearly shows that the 13 participating countries are at different stages of implementation of genomic medicine into their respective healthcare systems and have different strategies and resources, both human and financial, and political support to achieve the goal. However, there are common challenges and needs regarding support from the 1+MG initiative.

Common key challenges faced by participating countries are practical in nature and related with:

- Bringing together research and healthcare for the benefit of implementing genomics into healthcare system routine.
- Dialogue and partnerships with industry.
- Legal framework related to ELSI issues, data handling and protection.
- Political support and engagement from different ministries.
- Raising awareness and communication with the public.
- Securing long-term funding.
- Models for HTA analysis.
- Technical issues regarding infrastructure for data storage, access, analysis, reporting.
- Guidelines for data handling and management.
- Increasing competences in genomics among professionals.

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From the 1+MG initiative, participating countries expect help and support:

- For generating political support and engagement from their governments.
- To provide proper economic models.
- By providing common standards and guidelines for data handling and sharing:
- Regarding technical tools and protocols for implementation of the technical infrastructure.
- To establish the proper legal and ethical framework.
- Training of healthcare professionals.

Despite all these challenges and needs, countries were unanimous in considering that participation in the 1+MG initiative has already provided the momentum to start, or further develop, discussion and organisation of national strategies for genomic medicine. Moreover, the CEVs were unanimously considered extremely important to share and learn from experiences and results from other partner countries.

4. Key messages and recommendations

Each host country materialised their respective genomic strategies by following different approaches. From each CEV important key messages for countries willing to engage their own genomic medicine programmes were extracted as shown in **Table 2**.

Table 2: Key messages from the host countries on the major topics addressed during the three CEVs.

	United Kingdom	Estonia	Finland
Patient and citizen engagement	•***Citizens and patients need to be at the center of the initiative***, and their engagement and trust is essential from the outset: the system must be built on a transparent basis, and patients must be represented in the established governance framework, with a voice in every decision. •***Citizens and patients need to be offered the opportunity to consent the use of their data for research purposes.*** This will increase their interest and engagement, because they feel that they can contribute to a greater good. •***Clarifying*** that ***'sharing' of data*** means access to data for analysis not data "distribution"	•***Building citizen and patient trust*** for genomics medicine initiatives ***takes time and needs constant investment in bidirectional communication,*** rigorous information and public campaigns for raising awareness. •***Regarding return of results, patients should be given the choice to not know, and be able to change their mind.*** But information on results is not enough; ***patients would also like to know that there is continuity and a proper care plan.*** Also important is to clearly inform patients about the limitations of genetic based predictions. •***Engagement of patients*** into genetic healthcare services	•To maintain this trust, it is crucial ***to involve citizens and patients in the discussion of the legal framework*** supporting genomic medicine practices. •Having ***patient organizations present in the WGs responsible for preparing legislation*** was, and is, vital to create trust and awareness. In parallel, public campaigns, surveys and website also contributed to this goal. •Having ***several countries simultaneously engaged in building peoples trust would make it easier for all.***

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	is crucial to build trust. ●Regarding communication of results and updates to patients, it is important to know how willing they are to remain in contact. ***It is really important that every patient and family has a contact point.*** ●Regarding citizen engagement, ***surveys are a good way to involve citizens in the discussion and create awareness.*** Also, initiatives can be local, with an excellent example coming from the Onelondon (onelondon.online) initiative.	***benefits from a legal framework*** that ensures that ***health data is well regulated, with restricted transfer and strict laws in place, and that enables citizens to track access to their data.***	
Training and capacity building	●***Upskilled and engaged workforce is vital***: embedding Genomic Medicine into the healthcare system requires a specialized, collaborative, and trained workforce, with the possibility of training and improvement of proficiency and competences at any time and encompassing every step of the process and procedures in genomic medicine. ●For the effective and efficient implementation of a genomic medicine strategy ***it is important that a specialist workforce is built upon the existing workforce.*** Although new professions may be created, ***healthcare professionals must also be offered the possibility to upskill their competencies through relevant lifelong training.*** ●***Involving the healthcare community from the beginning avoids creating a new infrastructure and lowered initial resistance.*** This helped get political support. ●Shortage of clinical geneticists impairs the implementation of genomics in healthcare. It is thus important to ***identify skills needed in healthcare professionals and devise adequate training programs, thus ensuring that there is enough human power*** to run genomics in healthcare. ●Developed ***Education***	●To make genetic diagnosis, genetic risk scores and pharmacogenetic recommendations intelligible and accessible to patients, ***communication and genetic counselling in the healthcare system is crucial.*** ●Healthcare professionals directly communicate with patients, so ***their involvement in the strategy of genomic medicine implementation from the outset is fundamental.*** ●It is important to ***inform and educate the public, and involve, and train, the healthcare community, including on IT tools, namely GPs and medical societies, from the start.***	●***Involving all stakeholders in training and education programs for clinicians*** is important for the holistic vision of personalised clinical treatment.

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	resources might be shared with other EU countries. This possibility could be explored.		
Implementation into healthcare: infrastructure and regulation	●***Sustainable genomic medicine requires high-level political support and funding.*** ●Also helpful in getting ***political support*** was the involvement of the prime minister, ***driving pressure from top-down.*** ●***Standardization of procedures is critical to guarantee quality control, interoperability between services and cross-border data sharing***. ●The ***infrastructure should be able to accommodate new medical areas of interest*** (in cancer genomics, pharmacogenomics, RD diagnosis, etc) ***and adapt to technological and knowledge development***. ●Gathering phenotypic data from different sources is difficult and hinders its match with genetic/genomic data. It is important to ***channel investment to overcome these difficulties and integrate all data into HER of patients and allow clinicians to use them.*** In summary, it is important to work towards federated data. ●***COVID pandemic*** valued science, promoted technological innovation and readiness of healthcare systems, and promoted collaborations and dialogue, thus ***creating momentum that could be used for promoting actions conducting to effective implementation of genomics into healthcare.*** However, it is important to keep people's expectations real. ●***Sharing (data, knowledge, know-how) is crucial: dimension is key for solid findings and detection.***	●***Implementation of genetic medicine into the healthcare system requires high level political support and funding.*** ●A ***solid investment in secure digital technologies and services*** makes it easier and faster to incorporate genomic data into healthcare practises and services. ***Namely, Electronic Health Record (EHR) systems able to combine clinical information from multiple sources and in variable formats, linked to an automated decision support action,*** is fundamental for the efficient use of genomic information in clinical practice. ●***Genetic sampling of a representative part of the population enables more reliable GWAS and disease risk assessment*** and facilitates the inclusion of genetic analysis into healthcare personalised services for the entire population, these including polygenic risk scores for common and complex diseases and pharmacogenetic-based warnings and recommendations ●***The system and infrastructure must be prepared to update PGx predictions*** as research or more data is gathered. ●***In order to put patients at the centre, the health system must change its treatment paradigm, moving from the current "silo" approach to a more holistic one,*** to be able to analyse different disease risks in the same patient. ●***Access to health data and human biological samples*** must be under ***strict regulation***, within a ***solid ethical and legal framework***.	●***Implementing PM is a "long run":*** it takes a lot of work and time in addition to legislation to decide goals and tasks. ***Steady political commitment and sustainable funding, over time and involving inter-ministry cooperation***, are key to effectively supporting the implementation of genomics in healthcare systems, and to guarantee that patients are at the centre of the endeavour, and that health improvements are cost-effective. ●The ***infrastructure must be implemented in a way that allows linking genomic data to other information without breaking people's trust.*** This will benefit from ***population generalized digitalisation of health and genomic data***. ●***Centralised governance and management of genomic and health data accessibility*** facilitates the use of this information for clinical and research purposes, at regional, national, and international levels. ●In order to have an impact at the population level, ***Biobanks would likely have to include primary care patients.*** ●Each disease may require different approaches. However, learnings from one can be applied to others, particularly if the use case chosen to be a proof of concept, or pilot, is well structured and based on sound research findings, as it may become a flag in the campaign for the use of genomics in clinical settings and creates momentum for collaboration of the different stakeholders. ***Pilot studies can be used to enhance collaboration between different stakeholders and provide evidence usable for public awareness campaigns.*** ●***Well structured data is crucial for data sharing cross-borders.***

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			●In order to have a more ***homogenous Europe*** in terms of genomic medicine implementation into healthcare it is important that ***countries speed up their legislation, data protection and involve their scientific lawyers.*** ●***National Mirror Groups should cover all areas***. This will make it easier and faster to bring things together nationally, but also at the European level.
Building a sustainable ecosystem and industry engagement	●Need ***to ensure equity of access across countries.*** ● ***The partnership between research and the clinics is fundamental:*** it creates a learning health ecosystem and ***provides sustainability***. ●Further ***development of economic models for genomic medicine is needed***, and there is already interesting evidence for economic value: several indicators (such as hospital costs, found in administrative data) can be used to highlight the importance of genomic sequencing, before even acknowledging patient and family benefits. ●For GeLE goals success, ***partnership with NHS was crucial for sustainability and equity.*** ●Also, ***regarding economic evaluation*** of genomics in health, ***investing in working together*** (NHS, GeLE, industry) ***to investigate and make solid cases on cost-effectiveness*** of genomics is important to then ***make solid proposals to the proper ministries*** to integrate tests/treatments into the healthcare system and promote wide and equitable access to citizens. ●***Private industry is still not perceived by the public as trustworthy***. To overcome this, ***patients should be involved in conversations with industry*** and industry should clearly demonstrate its commitment to transparent and compliant access and usage of data. ●Regarding introduction and	●***Digital health requires constant upgrades of information, knowledge, and technologies.*** This ***cannot be achieved without involving the private sector*** in the healthcare service. ●***Good and constant communication among all stakeholders,*** with involvement, involved in the process of implementing genomics into clinical practice is vital.	● Although ***regulation must strongly avoid data misuse, it must also allow for innovation*** in the healthcare system. Therefore, ***involving all stakeholders (patients/citizens, policy makers, research, industry, the public healthcare system and the private health sector, and the technical infrastructure) in the discussion on the proper legal framework*** increases societal trust in the system and benefits society. ●***All stakeholders should be involved from the start in the design of the genomic strategy and the legal framework.*** ●Genomic Medicine requires ***constant updates of knowledge and technology. The private sector is an important stakeholder in this field, contributing with novel solutions at a faster pace.*** ●***Governments should be enablers and encouragers of the implementation of genome strategies in their countries.*** ●***Industry can come on board through its involvement in one of the first steps*** of PM implementation, i.e., through ***technical support of data integration into healthcare.***

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	implementation of new technologies within the NHS, advice is to ***have a unified directory and a framework for evaluating that so that changes, i.e., tests can be changed based on Health Economic evidence and more.*** However, this is not enough. It is ***important to use the "Infinity Loop" path to foster research and improve clinical care in a feed-back way.***		

To help countries in this endeavour, the three Country Exchange Visits to the UK, Estonia and Finland provided practical **recommendations** for each of the four above topics, as enumerated below.

On **patient and citizen engagement**, recommendations are:

- Establish information programs and wide-reaching communication campaigns to engage and inform citizens.
- Monitor patient trust and willingness to give samples and consent for the use of genomic-based diagnosis and treatments.
- Ensure representation of patients in the established governance framework.
- Incorporate patient representatives' compensation into budgets.
- Involve patient groups in all decisions and steps of implementing the genomic strategy from the outset of the programme, including discussion of the legal framework.

On **training and capacity building**, recommendations are:

- Tailor genomic education programmes for capacity building and training the existing healthcare workforce, including:
    - Online courses for professionals with limited or no genomics knowledge, with a final test and certificate
    - A competency framework with different levels for individuals and organisations to evaluate the need for increased knowledge/skills.

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- Invest in developing professionals, namely clinical geneticists and genetic counsellors, and new professions, such as medical informaticians.
- Define the roles of these and other professionals, such as general practitioners that specialise in clinical genetics and provide counsel related to genomic information.

On **implementation in healthcare, namely infrastructure and regulation**, recommendations are:

- Create an infrastructure with centralised governance and a robust ethical and legal framework for secure and transparent collection, analysis and use of data.
- Implement a standard genomic and health data management plan to facilitate sharing information for clinical and research at regional, national, and international levels.
- Ensure solid investment in secure digital technologies and services. For instance, implementing electronic health record systems that combine clinical information with automated decision support action to use genomic information in clinical practice.
- Seek inter-ministerial collaboration and inclusion of all stakeholders for implementing the strategy, gaining investment in public-private partnerships, and earning solid and steady political support.

On **building a sustainable ecosystem and industry engagement**, recommendations are:

- Involve all stakeholders in discussing the legal framework to allow for innovation while building trust and avoiding data misuse.
- Include industry stakeholders input in health economic evaluation.
- Create an umbrella structure that allows research, clinical and industry partners to share knowledge, support each other and ensure the coordination of research and clinical outcomes.
- Governments should embrace the role of enablers of the genome strategy by:
    - Encouraging the integration and management of innovation
    - Promoting dialogue among all stakeholders through partnerships
    - Funding initiatives that will support sustained growth and attract further funding
    - Creating the conditions for research results, digitalisation, and knowledge to be used for the benefit of citizens first, but also considering other stakeholders'

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needs.

5. Conclusions

With a participation attendance of around 80 participants from 24 countries on average, per visit, the purpose of the CEVs to engage signatory countries and stakeholders into debating practical issues related to implementation of genomic medicine into healthcare systems and allow for cross-border data sharing was fully achieved.

Overall topics addressed were related to (i) governance models, (ii) ELSI issues, (iii) infrastructure for data access and management,(iv)patient involvement and public trust, (v) training and recognition of healthcare professionals, (vi) finding reliable genomic risk assessment scores as clinical care services, (vii) funding, healthcare system collaboration with research and the private sector and (viii) the need to find adequate economic evaluation models to assess cost-benefit from genomic medicine services into healthcare system.

Although each of the three host countries implemented genomic medicine services into the Healthcare system by following different strategies, there are common elements (**Figure 6**) to the three approaches. This suggests that other countries which are planning or starting to implement a strategy for genomic medicine need to address these same issues in order to succeed. They may follow the examples from the host countries shared during the three CEVs.

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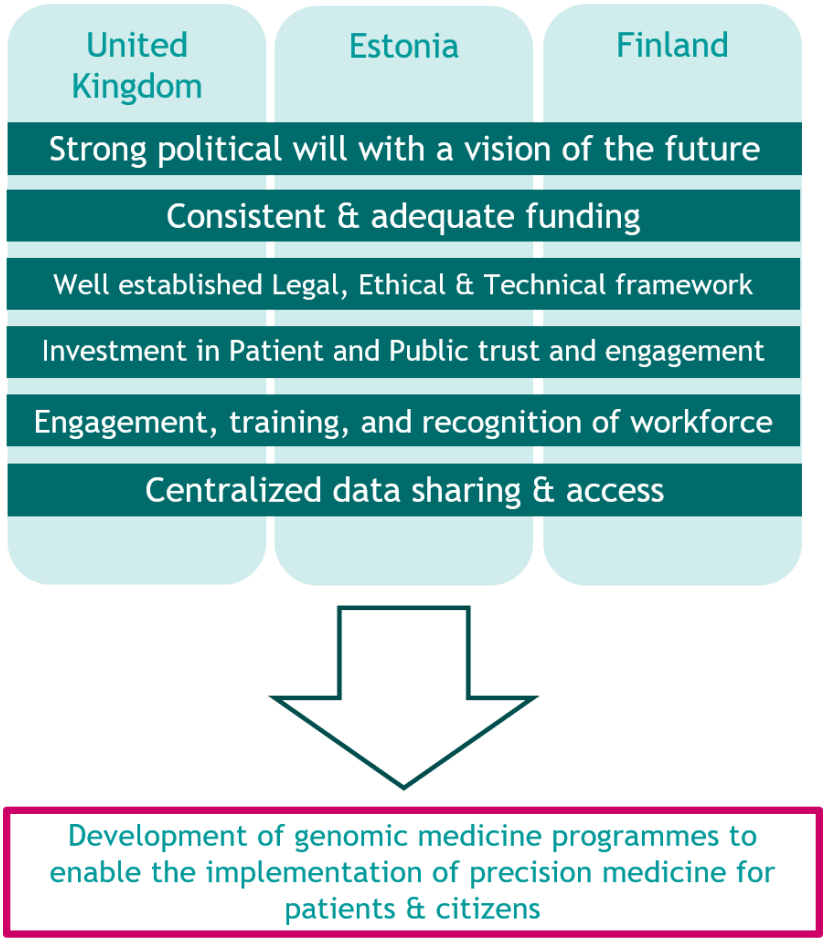

Figure 6. Common features to the genomic medicine strategies of the three host countries.

The CEVs to the UK, Estonia and Finland generated a fruitful discussion among participants and representatives of the host countries, with several issues highlighted as of key importance and requiring urgent attention, namely:

- Organisation and governance framework across countries is highly variable. This is a challenge for fulfilling the goal of the 1+MG Initiative Declaration. However, it is also an opportunity to, by rapidly providing signatory countries with regulations and standards, help nations to pace up.
- In line with this, countries across Europe need support, guidance and input from the 1+MG Initiative for matters related to coordination, common guidelines, best practices and standards.
- Political commitment, sustainable funding and establishment of a robust legal framework are main challenges to genomic medicine implementation in countries across Europe.

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- Priority is given to ELSI issues, standards and governance frameworks for countries starting to embed genomics into healthcare systems.

In order for genetic data to be useful in healthcare services for personalised medicine, either preventive or therapeutic, it needs not only to be combined with phenotypic data, but it also requires as much genomic information from as many individuals as possible. Every citizen from every country in the EU will benefit from cross-border genomic data sharing. But for this to become a reality, countries need to align strategies and address common issues that will allow the cross-border sharing of data (**Figure 7**).

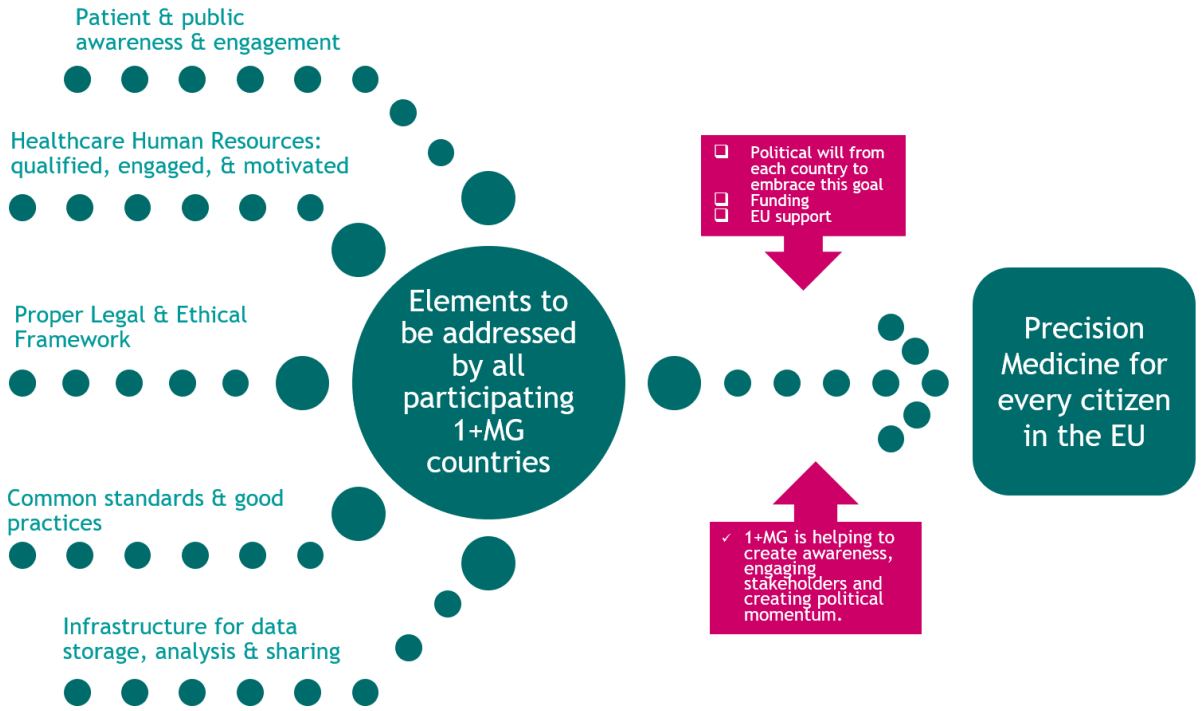

Figure 7. Topics that need to be addressed and shared by all 1+MG signatory countries in order for the EU to deliver PM to EU citizens.

Appendix

A1. Agenda: CEV to the UK

Date: March 23-24 (2021)

Time (CET)	Arrival & Registration (waiting room open for virtual participants)

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10:00	Day 1
10:00 am (20 mins)	Welcome Introduction to Country Visits - Dr Astrid Vicente, Instituto Nacional de Saúde Doutor Ricardo Jorge Introduction to Genomics England - Dr Mark Bale, Genomics England
10:20 - 11:45 am (85 mins)	Session 1 - Chair, Dr Serena Scollen, ELIXIR **Infrastructure (England) - Sir Mark Caulfield, Genomics England** (25 mins + 5 mins Q&A) **Devolved Nations Infrastructure and Collaboration** (15 mins each + 10 mins Q&A at the end) ***Scotland - Professor Zosia Miedzybrodska, University of Aberdeen*** ***Wales - Dr Clive Morgan, All Wales Medical Genomic Service*** ***Northern Ireland - Dr Shane McKee, Belfast Health and Social Care***
11:45 -12:00 (15 mins)	Coffee Break
12:00 - 13:05 (65 mins)	Session 2 - Chair, Dr Esther Rodriguez, ISCIII **Member State Presentations** - (10 mins each + 20 mins Q&A at the end) **(**Current state and relevant activities in (respective) countries • **Belgium - Dr Marc Van Den Buckle,** Sciensano • **Germany - Prof. Dr. Oliver Kohlbacher, F and Dr Sophia Schade,** German Genomics Initiative • **Italy - Prof Stefania Boccia,** on behalf of Italian Ministry of Health • **Norway - Dr Grethe Foss,** The Norwegian Directorate of Health
13:05 -13:15 (15 mins)	Questions for Panel Discussion - via mentimeter Code 18672543
	End of Day 1
10:00 CET	Day 2
10:00 - 11:30 (90 mins)	Session 3 - Chair, Dr Mark Bale (20 mins each followed by 10 mins Q&A each) **Implementation in the NHS - Ms. Alexandra Pickard, Genomics Unit - Special Commissioning, NHS England** **Patient Engagement - Ms. Jillian Hastings-Ward, Genomics England (Chair of Participant's Panel)**

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	Tools & Training - Dr Christine Patch, Clinical Lead for Genetic Counselling and Caldicott Guardian Genomics England
11:30 -11:45 (15 mins)	Coffee Break
11:45 - 13:10 (85 mins)	Session 4 - Chairs, Dr Serena Scollen and Dr Astrid Vicente Panel Discussion **Panelists:** **Dr Mark Bale**, Genomics England **Ms. Jillian Hastings-Ward**, Genomics England (Chair of Participant's Panel) **Professor Tim Hubbard**, HDR UK & Genomics England **Dr. Mark Kroese**, PHG Foundation **Professor Sarah Wordsworth**, University of Oxford
13:10 - 13:20 (10 mins)	Closing Remarks Szymon Bielecki, European Commission
	End of Day 2

A2. List of participants: CEV to the UK

Country exchange visit to the UK	
B1MG Team	
WP5: Delivering Personalised Medicine Cross-borders: Implementation in Healthcare systems and Societal Impact	**Astrid Vicente** (INSA) **Serena Scollen** (ELIXIR Hub) **Arshiya Merchant** (ELIXIR Hub) **Melissa Konopko** (ELIXIR Hub) **Xènia Pérez-Sitjà** (ELIXIR Hub) **Alexandra Costa** (INSA) **Maria Luís Cardoso** (INSA) **Mafalda Bourbon** (INSA) **Teresa Caldas Almeida** (INSA)
WP6: Coordination Office: Project Management, Communication, Governance & Sustainability	**Esther Rodriguez** (ISCIII)

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Host Country Participants	**Mark Bale** (Genomics England) **Mark Caulfield** (Genomics England) **Zosia Miedzybrodska** (University of Aberdeen) **Clive Morgan** (AWMGS) **Shane McKee** (Belfast Health and Social Care) **Alexandra Pickard** (NHS England) **Jillian Hastings-Ward** (Genomics England) **Christine Patch** (Genomics England) **Mark Kroese** (PHG Foundation) **Tim Hubbard** (HDR UK & Genomics England)
Country representatives	**Marc Van Den Buckle** (Belgium) **Oliver Kohlbacher** (Germany) **Sophia Schade** (Germany) **Stefania Boccia** (Italy) **Grethe Foss** (Norway)
European Commission	**Szymon Bielecki**

B1. Agenda: CEV to Estonia

Date: May 19- 20 (2021)

Time (CEST)	Arrival & Registration (waiting room open for virtual participants)
10:00 am	Day 1
10:00 am - 10:10 (10 mins)	Welcome - Astrid Vicente, Instituto Nacional de Saúde Doutor Ricardo Jorge Work Package 5 Lead Overview - Andrés Metspalu, Professor of Genomics and Biobanking, University of Tartu

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10:10 am - 12:10 pm (120 mins)	Session 1 Chairs: Andrés Metspalu & Serena Scollen *(20 mins presentation each + 10 mins Q&A)* **Governance of personalized medicine in Estonia – Kalle Killar,** Deputy Secretary-General on E-Services Development and Innovation, Ministry of Social Affairs **Implementation of personalized medicine in Estonia - Annika Veimer**, Director of Estonian National Institute for Health Development **IT architecture and bioinformatics behind the Estonian Personalised Medicine Programme - Jaak Vilo**, Professor of Bioinformatics, University of Tartu **Biobank - Andres Metspalu**, Professor of Genomics and Biobanking, University of Tartu
12:10 -12:25 pm (15 mins)	Coffee Break
12:25 - 1:45 pm (80 mins)	Session 2 **Chair: Esther Rodriguez** **Member State Presentations** *(10 mins each)* Current state and relevant activities in (respective) countries (limited to 8 countries) • **Hungary - Professor Attila Patócs,** National Institute of Oncology • **Latvia - Professor Janis Klovins,** Head of the Scientific Council Latvian Biomedical Research and Study Centre • **Spain - Professor Angel Carracedo**, University of Santiago de Compostela & Coordinator of the Genomic Medicine Group
1:45 - 2:00 pm (15 mins)	Collect questions for panel discussion via Mentimeter - Arshiya Merchant ***Please go to www.menti.com & put in the code: 47647776***
10:00 am CET	Day 2

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10:00 am - 11:40am (100 mins)	Session 3 **Chairs: Helen Lepa & Serena Scollen** *(15 mins each)* **Highlights of Day 1 - Serena Scollen,** ELIXIR, B1MG WP5 Co-Lead *(5 mins)* **Including genetic data in breast cancer prevention and early detection – Hannes Jürgens**, Medical Doctor and lecturer of oncology and haematology, Tartu University Hospital **Precision medicine in cardiovascular diseases prevention - Margus Viigimaa**, Medical Doctor and professor of cardiovascular medicine, Tallinn University of Technology **Pharmacogenomics - Lili Milani,** Vice Director, Professor of Epi- and Pharmacogenomics, University of Tartu **Return of genetic data to patients and biobank participants. A doctor's view - Neeme Tõnisson**, Medical Doctor, geneticist, associate professor of clinical genetics, University of Tartu **Genetic risk communication and counselling - Liis Leitsalu**, PhD, researcher of genomics and genetic risk communication, University of Tartu **Private sector in personalized medicine in Estonia, governments' view - Silja Elunurm,** Attorney at law, Advisor at Ministry of Social Affairs
11:40 - 11:55 pm (15 mins)	Coffee Break
11:55 -1:10 pm (75 mins)	Session 4 - Panel Discussion **Chairs: Astrid Vicente & Serena Scollen** **Panelists:** **Prof Margus Viigimaa,** **Prof Andres Metspalu,** **Prof Lili Milani,** **Prof Jaak Vilo,** **Silja Elunurm** **Prof Neeme Tõnisson** **Dr Liis Leitsalu** **Dr Hannes Jürgens**
1:10 - 1:20 pm 10 mins	Closing Remarks - Szymon Bielecki

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B2. List of participants: CEV to Estonia

Country exchange visit to Estonia	
B1MG Team	
WP5: Delivering Personalised Medicine Cross-borders: Implementation in Healthcare systems and Societal Impact	**Astrid Vicente** (INSA) **Serena Scollen** (ELIXIR Hub) **Arshiya Merchant** (ELIXIR Hub) **Melissa Konopko** (ELIXIR Hub) **Xènia Pérez-Sitjà** (ELIXIR Hub) **Helen Lepa** **Alexandra Costa** (INSA) **Maria Luís Cardoso** (INSA) **Mafalda Bourbon** (INSA) **Teresa Caldas Almeida** (INSA)
WP6: Coordination Office: Project Management, Communication, Governance & Sustainability	**Esther Rodriguez** (ISCIII)
Host Country Participants	**Andres Metspalu** (University of Tartu) **Kalle Killar** (Ministry of Social Affairs) **Annika Veimer** (National Institute for Health Development) **Jaak Vilo** (University of Tartu) **Hannes Jürgens** (Tartu University Hospital) **Margus Viigimaa** (Tallin University of Technology) **Lili Milani** (University of Tartu) **Neeme Tõnisson** (University of Tartu) **Liis Leitsalu** (University of Tartu) **Silja Elunurm** (Ministry of Social Affairs)
Country representatives	**Attila Patócs** (Hungary) **Janis Klovins** (Latvia) **Angel Carracedo** (Spain)
European Commission	**Szymon Bielecki**

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C1. Agenda: CEV to Finland

Date: June 16- 17 (2021)

Time (CEST)	Arrival & Registration (waiting room open for virtual participants)
9:30 am	Day 1
9:30- 9:50 am (20 mins)	Overview - Astrid Vicente, INSA, B1MG WP5 Lead **Welcome - Tuula Helander,** Director at Ministry of Social Affairs and Health
9:50 am - 10:40 am (50 mins)	Session 1 **Chairs: Tuula Helander & Serena Scollen** **Health Sector Growth Strategy for Research and Innovation** (15 mins each + 20 mins Q&A at end) • ***Sustainable growth and wellbeing: Health Sector Growth Strategy for Research and Innovation Activities* - Anni Kaukoranta,** Development Manager, Ministry of Economic Affairs and Employment • **Liisa-Maria Voipio-Pulkki**, Director General, Ministry of Social Affairs and Health
10:40 - 10:50am (10 mins)	Coffee Break
10:50 - 11:40 am (50 mins)	Session 1 **Chairs: Tuula Helander & Serena Scollen** **Building relevant legislation** (15 mins + 10 mins Q&A each) • **Sini Tervo**, Lawyer, (member of WG2) - the Genome Act; short overview of challenges & relevant solutions • **Johanna Seppänen**, Director, Findata - legislation; authorizations for companies/research groups to use data from various registries
11:40 - 11:55pm (10 mins)	Coffee Break

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11:55am - 1:15 pm (80 mins)	Session 2 10 mins each + 10 mins Q&A at the end **Chair: Esther Rodriguez, ISCIII** **Member State Presentations** Current state and relevant activities in (respective) countries: • **Luxembourg - Barbara Klink**, Head of National Center of Genetics • **Sweden - Mikaela Friedman**, External Relations Officer Genomic Medicine Sweden • **Bulgaria - Radka Kaneva**, BBMRI & Medical University of Sofia; **Zhasmina Koeva-Balabanova**, BAPPM • **Belgium - Marc Van Den Bulcke**, Sciensano • **Denmark - Bettina Lundgren**, CEO Danish National Genome Center • **Lithuania - Sonata Jarmalaite**, National Cancer Institute of Lithuania • **Portugal - Patricia Calado**, AICIB
1:15 - 1:30 pm (15 mins)	Questions for panel discussion via mentimeter - Arshiya Merchant
10:00 am CET	Day 2
10:00 am - 10:45pm (45 mins)	**Session 3** **Chairs: Tia-Maria Kirkonpelto & Serena Scollen** (15 mins each + 15 mins Q&A at the end) **Day 1 Recap - Serena Scollen** (5 mins) ***Towards European Genomic Data Space - How e-Infrastructures could support sensitive data governance and processing needed by the EU 1+ million genomes initiative*** **- Tommi Nyrönen,** Head of Node, ELIXIR Finland **Sandra Liede**, Lawyer, Healthtech Finland **Olli Carpén**, Scientific Director, Helsinki Biobank (Biobank Data - practical presentation)
10:45 - 11:00am (15 mins)	Coffee Break

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11:00 - 11:45 am (45 mins)	**Session 3** **Chairs: Tia-Maria Kirkonpelto & Serena Scollen** (15 mins each + 15 mins Q&A at the end) ***The FinnGen project: opportunity for discoveries and translation*** **- Aarno Palotie**, Scientific Director, FinnGen **Tomi Mäkelä**, Executive Officer, iCAN Digital Precision Cancer Medicine Flagship ***Personalised therapy for acute leukemia*** **- Mika Kontro**, Specialist, Helsinki University Hospital, Clinical Group Leader, FIMM3
11:45 - 12:00am (15 mins)	Coffee Break
12:00 - 1:15 pm (75 mins)	Session 4 Panel Discussion **Chairs: Tapani Piha & Serena Scollen** **Panelists:** **Joni Komulainen**, Ministerial Adviser, Ministry of Social Affairs and Health **Tommi Nyrönen**, Head of Node, ELIXIR Finlan **Sandra Liede**, Lawyer, Healthtech Finland **Mika Kontro**, Specialist, Helsinki University Hospital, Clinical Group Leader, FIMM **Tuula Helander**, Director, Ministry of Social Affairs and Health
1:15 - 1:30 pm (15 mins)	Closing Remarks - Ruben Kok

C2. List of participants: CEV to Finland

Country exchange visit to Finland	
B1MG Team	
WP1: Framework for Cooperation through Stakeholders Engagement, Awareness & Alignment	**Ruben Kok** (DTL-Projects)

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WP5: Delivering Personalised Medicine Cross-borders: Implementation in Healthcare systems and Societal Impact	**Astrid Vicente** (INSA) **Serena Scollen** (ELIXIR Hub) **Arshiya Merchant** (ELIXIR Hub) **Melissa Konopko** (ELIXIR Hub) **Xènia Pérez-Sitjà** (ELIXIR Hub) **Alexandra Costa** (INSA) **Maria Luís Cardoso** (INSA) **Mafalda Bourbon** (INSA) **Teresa Caldas Almeida** (INSA) **Maria de Fátima Lopes** (INSA)
WP6: Coordination Office: Project Management, Communication, Governance & Sustainability	**Esther Rodriguez** (ISCIII)
Host Country Participants	**Tapani Piha** (Sitra) **Tuula Helander** (Ministry of Social Affairs and Health) **Anni Kaukoranta** (Ministry of Economic Affairs and Employment) **Liisa-Maria Voipio-Pulkki** (Ministry of Social Affairs and Health) **Sini Tervo** (Ministry of Social Affairs and Health) **Johanna Seppänen** (Findata) **Tommi Nyrönen** (ELIXIR Finland) **Tia-Maria Kirkonpelto** (Ministry of Social Affairs and Health) **Sandra Liede** (Healthtech Finland) **Olli Carpén** (Helsinki Biobank) **Aarno Palotie** (FinnGen) **Tomi Mäkelä** (iCAN) **Mika Kontro** (FIMM) **Joni Komulainen** (Ministry of Social Affairs and Health)

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Country representatives	**Barbara Klink** (Luxembourg) **Mikaela Friedman** (Sweden) **Radka Kaneya** (Bulgaria) **Zhasmina Koeva-Balabanova** (Bulgaria) **Marc Van Den Bulcke** (Belgium) **Bettina Lundgren** (Denmark) **Sonata Jarmalaite** (Lithuania) **Patrícia Calado** (Portugal)

D. List of Abbreviations and Acronyms

AI: Artificial Intelligence
AML: Acute Myeloid Leukaemia
AWMGS: All Wales Medical Genomic Service
B1MG: Beyond One Million Genomes
CCD: Common and Complex Diseases
CE: Conformité Européenne
CEV: Country Exchange Visit
CPIC: Clinical Pharmacogenetics Implementation Consortium
DNA: Deoxyribonucleic Acid
ELSI: Ethical, Legal and Social Issues
EstPerMed: Estonia Personalised Medicine
EU: European Union
FAIR: Findable, Accessible, Interoperable and Reusable
FIMM: Finnish Institute of Molecular Medicine
FINBB: Finnish Biobanks
Findata: Finnish Social and Health Data Permit Authority
GA4GH: Global Alliance for Genomics and Health
GeCiP: Genomics England Clinical Interpretation Partnership
GeL: Genomics England
GenOCEANIC: Genomics Open Core Engine for Accelerating Northern Ireland Care
GEP: Genomics Education Programme
GMC: Genomic Medicine Centre
GMS: Genomic Medicine Service
GPW: Genomic Partnership Wales
GWA: Genome Wide Array
GWAS: Genome Wide Association Studies
HER: Electronic Health Records
HGRA: Human Genome Research Act

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HTA: Health Technology Assessment
ICD: International Classification of Diseases
iCAN: Digital Precision Medicine Finland
ICT: Information and Communications Technology
ICU: Intensive Care Unit
ISO: International Standards Organisation
IT: Information Technology
1+MG: 1+ Million Genome
MRI: Magnetic Resonance Imaging
mRNA: Messenger Ribonucleic Acid
NGRL: National Genomic Research Library
NHS: National Health System
PM: Personalised Medicine
PRS: Polygenic Risk Score
RD: Rare Diseases
R&D: Research and Development
ROR: Return Of Results
SNP: Single Nucleotide Polymorphism
UK: United Kingdom
WES: Whole Exome Sequencing
WGS: Whole Genome Sequencing
WP: Work package

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