European Genomic Data Infrastructure

Deliverable D1.10

Initial reports documenting the situation of and support provided to the NMGs

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Log of changes

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1. Executive Summary

The European Genomic Data Infrastructure (GDI) is a deployment and implementation project, co-funded by the Digital Europe programme. GDI's main objective is to realise the data infrastructure required by the 1+Million Genome Initiative (1+MG) to share high-quality genomic and health data across borders; the 1+MG Virtual Cohort. Countries participating have committed to establish an operational National Mirror Group (NMG) that promotes and supports the national implementation of 1+MG Initiative guide via the 1+MG Framework that brings together all the guidelines and recommendations as well as National resources that will support the implementation.

This deliverable presents the results of the first activities carried out within task 1.6. National Mirror Group (NMG) support of the GDI project. The activities would be classified as follows:

- Analysis of the NMG status in collaboration with ELIXIR. (Quarterly reports)
- Foster participation and capacity building actions. Following identification of gaps via the Quarterly Reports a workshop took place on June 25th "Towards the Implementation of National Genomic Plans in EU countries". Representatives from Belgium, Denmark, France and Italy gave updates on the implementation of their national genomic plans.

The data we worked with was collected from the Member States' answers of two of the non-technical steps of the Quarterly reports of GDI nodes operational readiness.

> 1.1.3. Have developed the 1+MG NMG or equivalent structure to contribute to the 1+MG Initiative.
> 1.1.4. Have developed a national genomic plan or similar that secures long-term funding that matches the target implementation level.

In addition, this deliverable includes a summary of the current national genomics plan of Belgium, Denmark, France and Italy.

Finally, common elements in the development process of the plan, and actors involved in the decision-making process were identified in order to help other countries develop their own National Genomics Plan.

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2. Contribution towards project outcomes

With this deliverable, the project has reached or the deliverable has contributed to the following project outcomes:

[Select 'Yes' (at least one) if the deliverable contributed to the key result, otherwise select 'No'. For more details of project outcomes, see here]

	Contributed
Outcome 1 Secure federated infrastructure and data governance needed to enable sustainable and secure cross border linkage of genomic data sets in compliance with the relevant and agreed legal, ethical, quality and interoperability requirements and standards based on the progress achieved by the 1+MG initiative.	Yes/No
Outcome 2 Platform performing distributed analysis of genetic/genomic data and any linked clinical/phenotypic information; it should be based on the principle of federated access to data sources, include a federated/multi party authorisation and authentication system, and enable application of appropriate secure multi-party and/or high-end computing, AI and simulation techniques and resources.	Yes/No
Outcome 3 Clear description of the roles and responsibilities related to personal data and privacy protection, for humans and computers, applicable during project lifetime and after its finalisation.	Yes/No

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Outcome 4 Business model including an uptake strategy explaining the motivation, patient incentives and conditions for all stakeholders at the different levels (national, European, global) to support the GDI towards its sustainability, including data controllers, patients, citizens, data users, service providers (e.g., IT and biotech companies), healthcare systems and public authorities at large.	Yes/No
Outcome 5 Sustained coordination mechanism for the GDI and for the GoE multi-country project launched in the context of the 1+MG initiative.	Yes/No
Outcome 6 Communication strategy – to be designed and implemented at the European and national levels.	Yes/No
Outcome 7 Capacity building measures necessary to ensure the establishment, sustainable operation, and successful uptake of the infrastructure.	Yes/No
Outcome 8 Financial support to the relevant stakeholders to enable extension, upgrade, creation and/or physical connection of further data sources beyond the project consortium or to implement the communication strategy and for capacity-building.	Yes/No

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3. Methods

3.1 Assessment of the NMG status

The establishment of an operational National Mirror Group (NMG) is essential for the countries to promote and support the national implementation of 1+MG Roadmap supported by implementations projects such as GDI. They are being set up and are used as efficient channels for activity alignment between national and European actions (generally promoted by 1+MG working groups), knowledge exchange and for national coordination of the implementation of the 1+MG Roadmap and the adoption of the 1+MG Framework.

Figure 1. 1+MG Governance counts with three layers for implementing 1+MG initiative: 1+MG Group, 1+MG Working Groups and 1+MG National Mirror Groups

The current scope and content of the GDI quarterly reports aim to monitor and to better support the GDI Nodes in their commitments and/or to facilitate reaching the overall project's initiatives. In these quarterly reports, project participants were asked to provide the monitoring information related to the deployment of the technical expertise and the self-evaluation of the GDI Node status. Because of their importance, there are some relevant steps from the GDI node operational readiness related to the NMGs in these quarterly reports:

- 1.1.3. Have developed the 1+MG NMG or equivalent structure to contribute to the 1+MG Initiative.
- 1.1.4. Have developed a national genomic plan or similar that secures long-term funding that matches the target implementation level.

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We analysed the answers of steps 1.1.3 and 1.1.4 in order to monitor the progression of the countries and identified capacity-building actions for the countries to set up the NMG and ensure long-term sustainability for the national deployment of the 1+MG. The quarterly reports analysed were M3, M6, M9, M12, M15, M18, and M21. For the global analysis, those countries in blank (i.e. with no positive, no negative, nor partial answer) were considered as a negative answer as ELIXIR had done in their GDI nodes operational readiness analysis.

3.2. Workshop "Towards the Implementation of National Genomic Plans in EU countries"

The 1+MG Roadmap 2023-2027[1] sets up "contribute to the definition and maintenance of a long-term national genomic plan that defines the roadmap for the national implementation of the 1+MG goals that highlight the benefits for the citizens" as one of the NMG objectives.

In fact, according to the 1+MG Roadmap 2023-2027[1], the National Genomic Plans are expected to be aligned with the 1+MG goals by 2027 and provide enough resources to ensure the flow of data to the 1+MG Nodes, the maintenance of the national infrastructure and access to data.

One of the weaknesses identified in the quarterly reports was the lack of a National Genomic Plan aiming to provide long-term funding and capacity building actions to move into deployment first and operations later.[1]

In order to encourage activities and improve coordination among NMGs, the EC has restructured the WG1 of 1+MG for National Mirror Groups recently, now led by Marc Van Den Bulcke from Sciensano, Belgium.

For the current work plan (to deliver within 2023-2027), WG1 will work as a forum for NMG coordinators to share experience, knowledge and to[1]:

1) involve policy-making bodies (such as ministries) as well as technical and scientific individuals as experts in the NMG.

2) increase engagement between NMGs and national leaders and representatives in the 1+MG Group.

3) consolidate organisational aspects, such as Terms of Reference, documents management, and shared calendars.

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The possible measures to address these objectives can be found under section 8 "Next steps"[i].

Taking all things into account, we took the opportunity to launch the first meeting of WG1 by organising the workshop "Towards the Implementation of National Genomic Plans in EU countries".

From the countries that answered YES/PARTIALLY in the 1.1.4 step and had availability and interest in presenting at the workshop, four countries were selected: Belgium, Denmark, Italy and France. The agenda is included in ANNEXE I.

To focus the workshop, some bullet points were provided to the speakers in order to comprise aspects related to the inception to the approval of the NGP (National Genomic Plan) and what each country's genomic plan consists of.

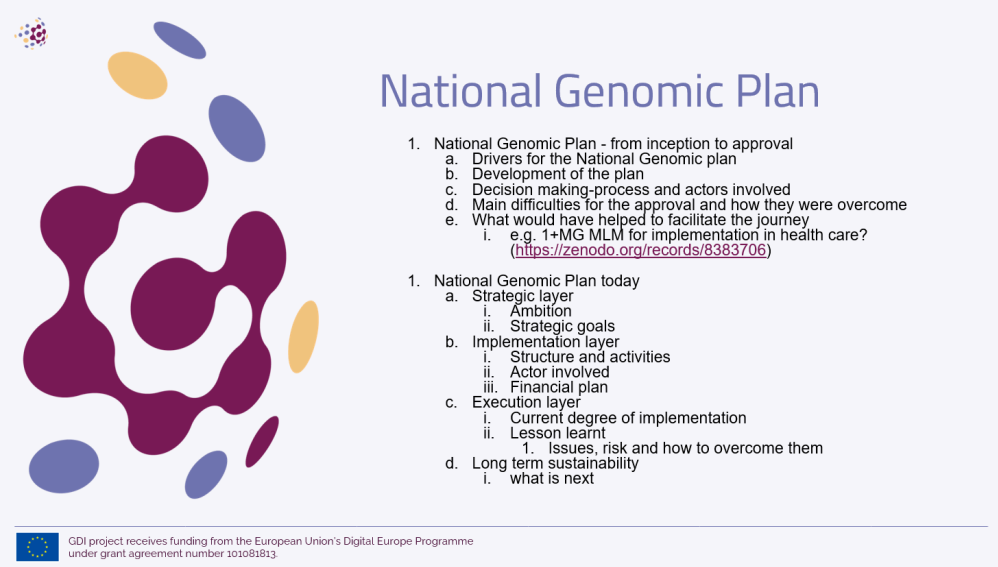

Figure 2. Presentations outline for the workshop "Towards the Implementation of National Genomic Plans in EU countries"

To increase the impact, we invited representatives of *WG1.National Mirror Group* and *WG7. Healthcare implementation of genomics* as target audience.

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i.https://docs.google.com/document/d/1qveUXwotCRX6MZ1KmkiA3dmQJvg1zqaR/edit#heading=h.qsh70q

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The meeting was recorded and edited to have a video presentation per country to be consulted. Lastly, the video presentations were published in the section "National Implementation" of the 1+MG Framework website.[ii]

4. Description of work accomplished

4.1. Assessment of the NMG status

With ELIXIR's collaboration, we used the data provided in the GDI nodes operational readiness, and analysed the answers in steps 1.1.3 and 1.1.4 in order to monitor the progression of the countries and identify capacity-building actions for the countries to set up the NMG and ensure long-term sustainability for the national deployment of the 1+MG. The quarterly reports analysed were M3, M6, M9, M12, M15, M18, and M21.

4.2. Workshop "Towards the Implementation of National Genomic Plans in EU countries

Following the identification of gaps via the Quarterly Reports, a workshop took place on June 25th "Towards the Implementation of National Genomic Plans in EU countries".

The aim of the workshop was to help countries lacking or in the process of preparing a National Genomic Plan (NGP) through the presentation of different NGPs or similar initiatives at different stages, from plans on initial phases to plans already in place among GDI member countries. In this workshop, the selected countries were Belgium, Denmark, France and Italy. Apart from explaining their respective NGPs, we scheduled slots for Q&A sessions where participants and speakers could exchange their views.

The recording of each presentation was edited and published in the 1+MG framework: 1+MG countries share success stories in GDI National Genomic Plans workshop[iii]

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ii. https://framework.onemilliongenomes.eu/national-genomic-plans

iii. onemilliongenomes.eu

Here below a summary per each country's presentation is elaborated.

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4.2.1 EC 1+Million Genomes Initiative in Belgium

As stated by the representative for the Belgian Mirror Group, Marc Van Den Bulcke, they have been very involved since the beginning of the 1+MG initiative; they have been working with mirror groups and they are currently working towards a goal focused on research and health.

Representatives of the Flemish and the French regions as well as from the Health department, which is Marc Van Den Bulcke himself, formed the mirror group. Key opinion leaders and experts from universities, rare diseases, cancer, population health institutes, governmental bodies, and charities who were interested in genomics formed the Belgian mirror groups and had meetings for one-and-a-half to two years on a regular basis. Unfortunately, these mirror groups have lost a little bit of their importance mainly due to extensive attention to the k(European Board of Cardiovascular Perfusion) EBCP and national incentives were taking over.

As a first step in the implementation process, Sciensano first tried in 2013 to link genomic information to the Belgian National Health Interview Survey (NHIS), which had been ongoing for the past 25 years. This was done under the BelPHG-21 project, which entailed a feasibility study to assess or estimate the genetic variability at the Belgian population level. The Belgian NHIS was done on the health of the general population on a representative sample of more than 10,000 participants with more than 700 variables on the general health of each person. Through this pilot program, some people from those interviews were contacted again, and with their information, an array mapping was created where the distribution of single nucleotide polymorphisms (SNPs) from saliva samples in different regions were analysed, thus establishing the first genetic variability map of the Belgian population. Its main objective was to test if they were going to be allowed to proceed with the project, and whether the privacy and ethics committees would agree on the procedure. The results on the project were published in 2018 and it concluded that "The Belgian genetic structure mirrors its geographic location in Europe with regional differences and clear signs of recent migration."[iv]

Building from that experience, five years later, in collaboration with Sciensano, they performed a Health Examination Survey wherein they collected blood and some general measurements of physical health from around 1200 people. Currently, they look forward to transfer the first 100 whole genome sequenced (WG-sequenced) to the Genome of Europe (GoE) and eventually extend it to 1000 representative samples of the Belgium population. They are studying how to build up the number into this representative cohort even more to complete the full 14,000 people expected in GoE.

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iv. https://humgenomics.biomedcentral.com/articles/10.1186/s40246-018-0136-8

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The next step for the implementation they are studying is to link the WG sequencing data from blood samples collected during the Health Examination Survey in 2018 with data from the Cancer Registry and the national Statistical Office. The idea is to look at the predisposition of cancer and try to corroborate some predictive models and see if those models fit or correlate with what they have in the small data set from the pilot program.

Also, as Genome of Europe was created, several groups interested in the creation of a Human Genomics Biobank, got together and introduced a project to the research funders in Flanders to get started with the sequencing. The project consists of using the data obtained from the samples, which are located at different Biobanks, to complete the GoE. This way, GoE would directly link the initiatives with the EDIC, and would provide an access point to GDI to this dataset.

Currently, their main focus point is making GoE completely operational.

Though some awareness has been raised among politicians to create a genomic medicine plan, a fair amount of evidence is needed before launching any kind of initiative, and if it's the federal government the one in charge of it, then it has to be health driven.

Luckily, in the can.heal project, an assessment model was prepared where it could be tested if a particular intervention such as the WGS could be implemented in the current healthcare system.

While they don't have sufficient funding yet, the EDIC has already received federal-level endorsement, positioning it as the key driver in the development of a genomic medicine plan over the coming months and years. They predict a Belgian Medical Plan will be available soon or at least a clear path towards a medical plan will be devised.

4.2.2 Implementation of Whole Genome Sequencing (WGS) in National Healthcare in Denmark

In order to understand the Danish NGP, Lene Cividanes began by explaining how Denmark has a long history of data collection since the 1960's as everything is put into registries since the day anyone in Denmark is born. This data has been available for research for the last 50 years and has created a high trust in the government for the data collection.

The inception of the plan began in 2015 with the realisation of the need for personalised medicine. This led to the publication of the "National strategies and NGC 2017-2023" which stated the wish for the implementation of WGS in healthcare settings. The initiative received a major donation from the private Novo Nordisk Foundation who were to fund a big part of the implementation of WGS in National Healthcare in Denmark.

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For the implementation to take place, a new law was created on the establishment of the Danish National Genome Centre and for the general reporting of data. According to it, every time a comprehensive genetic test is done in healthcare in Denmark, the data has to be sent to the National Genome Centre and stored in the National Genome Database.

As part of the implementation, a detailed roadmap was elaborated and the entire infrastructure was built around it. The infrastructure included:

- the construction of a supercomputer
- the creation of a genome database
- the basic systems and resources required to send the data back and forward between the National Genome Database and the hospitals
- the preparation of an inclusive governance around the whole infrastructure since the National Genome Centre base is based at a national level while hospitals work at regional level

Once the infrastructure was built, and in order to provide the same opportunities to every patient across Denmark, the variables to determine clinical pre-indications dictating which patients can be referred to the WGS were established.

Healthcare system-wise, they stated some difficulties as it follows a decentralised system organised across 3 levels. The Ministry of Health (MoH) works on a national level and hospitals function at regional level. The DNGC is a top-down initiative connecting the national and regional level by transferring the decision reached at political level, to an agreement at national level which is then operationalised at the regional level as an inclusive governance with representatives from all relevant stakeholder and specialist areas.

As part of the implementation of the plan, the WGS is taking place in two clinical laboratories according to the patients' geographical location. However, this posed challenges for collaboration, as the five regions in Denmark faced difficulties in getting data processing agreements in place. As a result, transferring samples and data between clinicians across regions proved to be somewhat complicated.

Another challenge in the implementation of the DNGP is a shortage of interpreters and clinicians with the specialised knowledge required, as clinic workflows have been evolving rapidly. This, combined with an increased number of samples and limited resources for interpretation, has temporarily led to longer response times.

An important upcoming challenge is the transition from mainly private to public regional funds. Therefore, they would like to produce some evidence for the economic impact of WGS to make sure they can actually get these budget allocations made at political level.

Despite these challenges, a preliminary evaluation of WGS implementation shows generally positive results. Access to WGS is becoming more consistent and systematic, allowing patients to receive faster and more accurate diagnoses than before. There is also an increased

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knowledge of genetics across medical specialties and closer collaborations seems to be taking place among experts.

Up to today, the main focus of Denmark's National strategy for personalised medicine has been on diagnostics and implementation of the strategy in the healthcare system. For the next strategy, they hope to focus more on prevention.

They also aim to develop cost-effective models by determining which data should be stored and which can be more affordably generated again, and then running the necessary pipelines accordingly. Denmark is also working dedicated on connecting genome data with other health data registries.

Regarding Europe, they are expectant on the connections established with the EHDS and hope for a stronger European collaboration through GDI and the 1+MG initiative.

4.2.3 The 2025 French Genomic Medicine Initiative (PFMG2025)

The representative for France, Frédérique Nowak, indicated that in April 2015 the Prime Minister commissioned the French National Alliance for Life Sciences and Health, Aviesan, to examine the prerequisites to implement whole genome sequencing in clinical practice. From that point, four general working groups were established to identify focal areas and gather the necessary information for an interim report, which would then enable the creation of four more specific, cross-cutting working groups:

- National facility for secure data storage and intensive calculation
- Genomic healthcare pathway laboratories , pathways, and clinical studies
- Pilot projects and a reference centre for innovation, assessment, and transfer
- Industrial sector

With those set, a vast national structuring project under Aviesan coordination was created. It included:

- Experts in genetic diagnostics, ethics, legal affairs, economics and patients' representatives
- Research and health agencies representatives
- Policy makers : Ministries of Health , Research and Economics
- French HTA agency (Haute Autorité de Santé HAS) , French National Health Insurance Fund for Employees (CNAMTS)
- Private companies representatives (Biotech, IT, pharmaceutical industry)

In 2016, this structure allowed the official release of France Medicine Genomic 2025 Initiative (PFMG2025), in just under a year. The initiative hopes to integrate genomic medicine into the patient's care pathway and allow equal access to clinical whole genome sequencing while

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developing a genomic medicine sector. The implementation process has been divided into 3 major steps:

1. Set up the tools for a genomic healthcare pathway
2. Ensure these developments in a safe technical and ethical framework
3. Implement monitoring and management tools.

The implementation of the PFMG2025 relies on pre-existing national frameworks, as there is already a network of specialised laboratories, centres of reference, and a database to collect the information for rare disease and cancer. Also, they have already narrowed down the variables to define clinical pre-indications dictating which patients can be referred to the PFMG2025 Initiative.

As part of the implementation of the plan, the WGS will be taking place in two clinical laboratories, SEQOIA and AURAGEN, according to the patients' geographical location. Also, in order to use the data obtained in healthcare, clinical and research settings with the required security of data storage and intensive calculation, the Center Data Analyzer (CAD) has been established, however it is still not operational. Considering the need of patient information and consent, a multidisciplinary group has been working on a draft which varies according to the preindication (for tumour genetics and germline genetics), as well as the level of understanding of the patient (depending on the age of the patient, and the level of fluency in French i.e. translated into several languages).

In order to favour the progression between care and research, a dynamic open science system was established, where though the data is open, its security as well as the defined scientific and ethical criteria is ensured.

The sequencing activity for the pre-indications already mentioned started in 2020 as the creation and implementation of a structure took longer than expected. Since then, the n° of medical prescriptions have increased, currently reaching up to 30.000 prescriptions. Contrary to their expectation, the prescription for cancer patients was low as from those 30.000 prescriptions, 82% were for rare diseases, 17% for cancer, and 1% for cancer genetic predisposition.

Even though, as previously indicated, CAD is not operational yet, there seems to be some progress between healthcare and research as 12 research projects have already been validated for access, and PFMG2025 has successfully integrated genome sequencing into the French healthcare system for rare diseases and cancers.

Regarding difficulties over the implementation of the PFMG2025, Frédérique mentioned the complexity of the genomic medical pathway, data sharing and provision of operational data access for research purposes as well as a need for improvement in access to innovative treatments. They also found some issues with clinical biological interpretation and turnaround

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time mostly for rare diseases. Regarding the WGS, it was stated how unexpected it was to see a low number of sequencing prescriptions for cancer patients compared to rare diseases patients.

For next steps, they want to implement the "2030 or 2035 French Genomic medicine initiative" but they are still waiting on policy makers to commit and make the political decision required.

4.2.4 Italy National Genomic Plan

According to the Italian speaker, Domenico Coviello, they had a clear moment of inception of the plan as with the Public Health Genomics (PHGEN) meeting in 2008 in the United Kingdom, where an awareness over the vast possibilities of genetic sequencing was detected. Therefore, in 2009 the creation of a national plan was set in motion, through a network for genomics in public health, which was then completed in 2018 with the first national plan: "Plan for the innovation of the Health System based on omics sciences".

For the plan to work, an inter-institutional coordination group was needed which included:

- Ministry of Health (MoH)
- National Institute of Health
  - Biobanks coordination
  - Health Technology Assessment (HTA) coordination
- Italian Network for Public Health Genomics (GENISAP) – Professional expert
  - Public Health National Society
  - Human Genetics National Society
  - MoH Prevention Directorate
- Stakeholder Forum
  - Patients organisations
  - Industry
- Inter-Regional Coordination
  - 20 Italian regions

With the plan and the inter-institutional coordination group set, the decision-making process had to be prepared. They decided on following two types of processes, one for National laws and another one for National projects. The decision-making process for National laws is slower: a document is proposed by scientists and professionals and is reviewed, the national plan is approved by the MoH and real-life applications are discussed. Once all this is achieved, a second document "the implementation document" must be created and approved by the State Inter-regional commission which will lead to the creation of regional laws. They are at this point and hope to be finished by next year. On the other hand, the decision-making process for National projects starts with the project proposal of scientists/professionals which leads to the establishment of networks within national institutions and the approval of the projects by MoH or Ministry of Economics (MoE) or/and

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Ministry of Universities and Research (MoUR). The implementation of such projects often take place by Hub and Spoke schemes and finally their progress is verified each year by Ministry commissions and programs for national dissemination of results are prepared.

The implementation of the NGP is taking place through several projects:

1. Health Big-Data Project: its main goal is to set up an IT infrastructure (upgrading it in each Italian Research, Hospitalisation and Health Assistance Institute (Instituto di Ricovero e Cura a Carattere Scientifico: IRCCS), creating a network with the four already existing ones (cardiology, oncology neurology, and paediatric networks), and creating a centralised, integrated and federated IT platform) among all the Italian research institutes This would allow for "the generation/extraction, collection, storage, sharing and analyses of scientific and clinical data of patients of each of the 51 Research Hospitals of the project (IRCCS)".
2. Cloud National Infrastructure for Supercomputing: its main goal is to reinforce the physical connections through Italy. It follows a "data lake-centric architecture" where all the data is kept in the National Institute for Nuclear Physics but any researcher may access it as long as the data collected from each institution is readable.
3. Human Technopole: to create a Centre for Innovation and Technology (CITT) to promote research and technological innovation. They are also to identify national facilities with high technological impact in order to make them accessible to the scientific community as well as implement, maintain and open National Platforms.
4. Health Operational Plan: implemented with the publication of the first projects to be funded.
5. National Recovery and Resilience Plan: among several goals, there are two health-related, one is the digitalization of all the state activity including the accessibility to patient data and the other, is to put together and be able to use genomic health in a four-year plan.

Dominico laid out several difficulties concerning the implementation of the NGP. Among those were the fact that as Italy is divided unevenly into 20 regions, each of them present different size of population, area, and population density, each of them has the faculty to decide its own rules regarding health assistance leading to an inhomogeneous application of laws, and their IT infrastructure varies between hospitals. It was also highlighted the lack of coordination among PIs, as well as among politicians. In addition, they presented some concerns regarding European coordination among politicians of different member states and indicated a sense of lack of supported action to enforce national/European coordination.

Regarding Italy's maturity level, studied in 2022, for governance and strategy as well as public awareness and acceptance, the national plan was yet to be finished. Likewise, the investment and economic model were not yet well established. On the other hand, there are legislations and policies in place to favour the implementation of the NGP though a national ethics

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committee is still pending. They also detected a shortage of qualified personnel, which they intend to solve by offering specialised training programs.

4.2.5. Discussion and Q&A Session

After each country's presentation, a slot for discussion and questions was reserved. Some compelling comments were made which included the next ideas:

- A need to find key people to help launch the initiatives
- The need of more European collaboration on Personalised Medicine and how GDI should be involved
- The possibility of looking into different Partnerships – like Transforming Healthcare System - and other financial tools to get coordination grants

5. Results

5.1 Assessment of the NMG status

5.1.1. GDI node operational readiness step 1.1.3. Have developed the 1+MG NMG or equivalent structure to contribute to the 1+MG Initiative.

Almost all countries answered "YES" in M9 and M12 excluding The Netherlands and Ireland which stated "PARTIALLY". However, Ireland reached to set up their NMGs at M15 while The Netherlands still answered "Partially" at M21.

Quarterly reports at M15 were also sent to additional countries that were recently committed[2] with the 1+MG Initiative: Cyprus, Hungary, Malta and Romania. Hungary and Romania did not answer to any quarterly report (M15, M18, M21) so no information was collected from those countries. Malta seems to have set up their NMG in contrast to Cyprus that answer "NO" to this step from the Quarterly reports of GDI nodes operational readiness.

When globally analysed, there seems to be a positive progression in the implementation of a 1+MG NMG or equivalent structure to contribute to the 1+MG initiative, as there is an increase of 24% of positive answers and a decrease of 27% of negative answers. The percentage of partial implementation however does not show a great difference over time. This could probably be influenced by the late incorporation in M15 of Cyprus, Hungary, Malta, and Romania.

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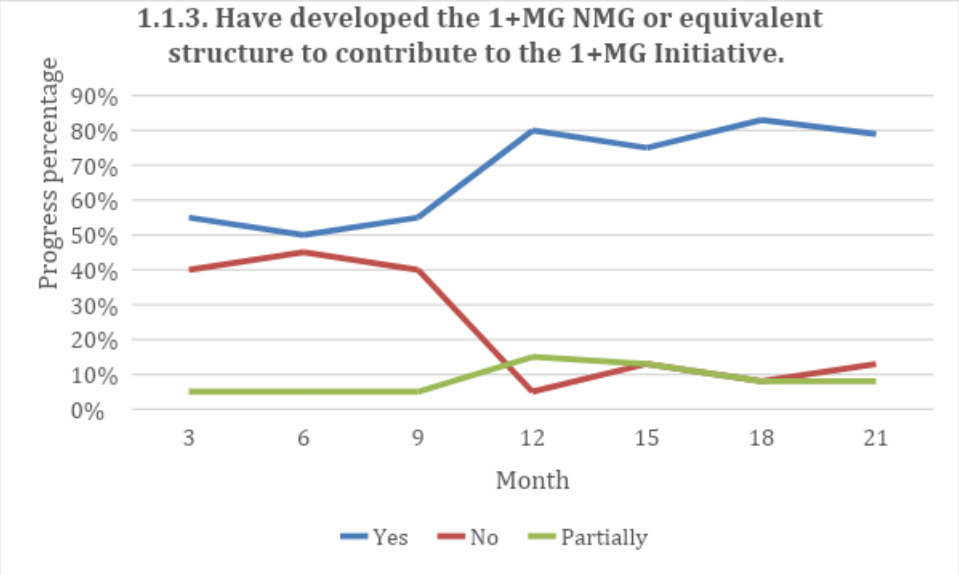

Figure 3. Development level of 1+MG NMG or equivalent structure to contribute to the 1+MG Initiative.

5.1.2. GDI node operational readiness step 1.1.4.Have developed a national genomic plan or similar that secures long-term funding that matches the target implementation level.

Regarding National Genomic Plans, it seems that it is still a challenge for the countries as there is a limited number of countries that answered "YES" to this step from the Quarterly reports of GDI nodes operational readiness: France, Sweden and Ireland. France and Sweden responded "YES" from the beginning at M9 and Ireland stated "YES" at M15. As well as Ireland, Slovenia seems to advance their NGP changing the answer from "NO" to "PARTIALLY" at M15. There are no more changes among the rest of the countries over the quarterly report timeline.

At M21, only France, Sweden and Ireland have developed their NGP. Eleven of 24 countries state that they partially developed their NGP (Belgium, Denmark, Finland, Luxembourg, Germany, Italy, Spain, Slovenia, Norway, Latvia, Lithuania) and 7/24 countries did not develop any NGP (Czech Republic, Estonia, Portugal, The Netherlands, Bulgaria, Croatia, Cyprus). Hungary, Malta and Romania did not answer the corresponding slot for this step.

When globally analysed, though the progression of the development of a national genomic plan or similar strategy that would secure long-term funding matching the target implementation level is positive, it seems to be slow with only a 17% increase. The negative response decline is equally slow with a 23% of difference between M3 and M21. It is understandable as the creation, and implementation of a NGP is not precisely easy, as it greatly

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depends on political decisions, government policies, and country budgets. Fortunately, a partial development of the plan is increasing from 35% to 42% between M3 and M21, meaning the countries are definitely working hard to bring forward the needed NGP.

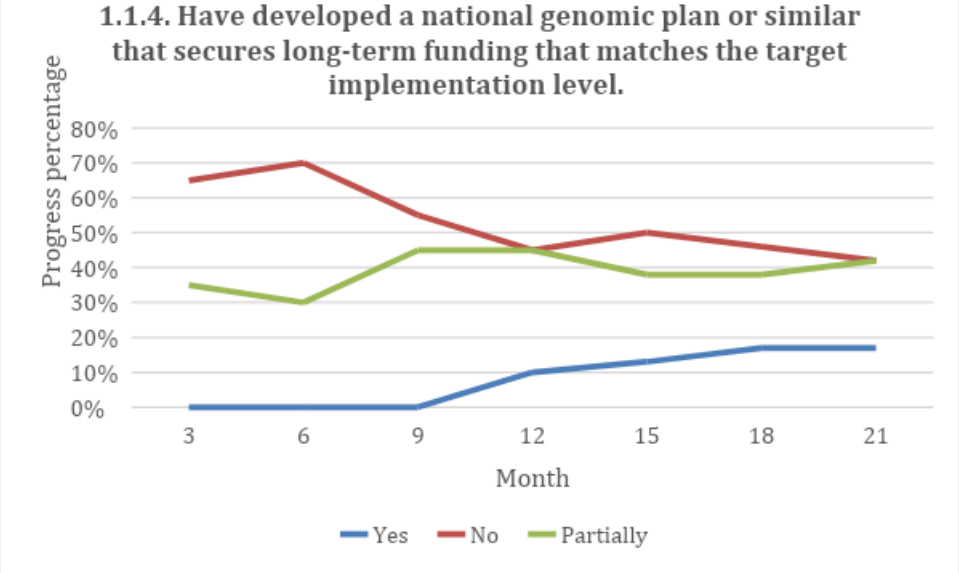

Figure 4. Development level of a national genomic plan or similar that secures long-term funding that matches the target implementation level.

5.2. Workshop "Towards the Implementation of National Genomic Plans in EU countries

A total of 40 people attended the meeting. Among them, 17 belonged to WG1 (currently 37 members) and 9 to WG7 (currently 33 members, some of them also nominated to WG1). The rest of the people that were not formally nominated as a representative of the WG, are part of the Coordination team or the EC. Regarding the attendance, the workshop was quite successful as a wide number of representatives from different countries were present (16 countries): Belgium, Czech Republic, Denmark, Finland, France, Germany, Ireland, Italy, Lithuania, Luxemburg, Malta, Norway, Poland, Portugal, Spain, Sweden and The Netherlands.

In a general overview of the countries taking part in the workshop, the following has been highlighted:

- The drivers for the National Genomic Plan were set either, through history as they already had a data collection registry, as it was the case in Denmark, or were prompted

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by European meetings (Public Health Genomics: PHGEN) which drew awareness over the vast possibilities of genetic sequencing, as it was the case in Italy.

- In all cases, the NGP started as a theoretical plan where the implementation of WGS was studied. Each followed a top-down approach, as government involvement was necessary not only to build the infrastructure required to implement the WGS, but also to establish the ethical and legal frameworks needed for its integration into personalised healthcare and research.
- In general, being a top-down initiative, the decision making process started at political level and/or within governmental structures. Then, it included the opinion of experts from public or private parties and patient organisations, and the decision taken was transferred at regional and local level.
- There are public as well as private funds at play depending on the country. In Denmark's case for example, the initiative was started with private funds and will be continued with public funds.
- The level of implementation varies between the countries as some of them are running early pilot programs, while others have a certain level of implementation with an infrastructure already in place or about to be operational. Some of them have already integrated genome sequencing into their healthcare system while others haven't.
- For countries with a clearer national plan in place, we will continue to observe how the transition to an operational plan will unfold, how financing will be secured, and how the national infrastructure for data collection will be implemented. It has also been mentioned the need for further commitment from policy makers at political level, a better coordination among State Members, and a stronger European collaboration.

Regarding the difficulties encountered by the countries, they vary according to the countries' political structure. They cover from decentralised healthcare systems, to countries divided into regions where each region would have its own legal regulations and data processing structure. In these cases, some countries have adopted the strategy of doing the WGS in two clinical laboratories according to the patient's geographical location. A common challenge seems to be data sharing between regions but hopefully, it could be solved once data processing agreements are in place. Another common challenge is the shortage of qualified personnel and a low level of implementation due to the complexity of the genomic medical pathway. One of the solutions regarding the shortage of qualified personnel or specialists suggested was to include the required knowledge as part of the curricula for clinicians and certain healthcare related researchers.

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6. Discussion

6.1 Assessment of the NMG status

There are some countries that haven't or have only partially built their NMG or similar structure according to the information from M21-GDI operational readiness questionnaire. These countries are Cyprus (just joined 1+MG initiative), The Netherlands and Bulgaria. The last two answered "Partially" to step 1.1.3. Additionally, Hungary and Romania which also just joined 1+MG did not answer the corresponding slot for this step. The NMGs are an essential structure for the countries to guarantee proper engagement and coordination with the 1+MG Initiative so the first step is to work on this structure. In order to boost the creation of their respective NMG, it seems necessary to contact with the representatives of Cyprus, Hungary and Romania and share the recommendations and the material elaborated in B1MG (D6.7 Guiding principles and best practices examples for mirror groups[v]), already published in the 1+MG Framework. Moreover, we should reach out to the representatives from The Netherlands and Bulgaria to analyse their situation and try to help them so they can finally create their NMG structure. Some countries that could raise a special interest to inspire others could be Malta, that, despite their recent inclusion, already has an NMG, and Ireland that went from partially to having a NMG and also a NGP in place (M12-15).

As shown in the step 1.1.4 of the assessment of the NMGs, there are still a little less than half of the countries with no NGP. Having this in mind, we would like to offer as much assistance as possible providing information from other countries as guidelines to help them achieve the required NGP. Regarding the countries with an NGP partially developed, which are also a little less than half of the countries, we understand they are working tirelessly to advance their plans, but may be encountering obstacles related to legal, budgetary, political, or other issues that we are unable to resolve. Nonetheless, we would like to organise capacity building actions, similar to the workshop that already took place, to improve the engagement level among the 1+MG initiative and all the NMGs in order to better align the efforts.

v. https://zenodo.org/records/10058201

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6.2. Workshop "Towards the Implementation of National Genomic Plans in EU countries"

According to step 1.1.4. of the last available report on GDI node operational readiness for the member countries (M21), besides France who already presented their NGP during the workshop, only Ireland and Sweden have developed a NGP or similar plan that secures long-term sustainability for the 1+MG initiative. Therefore, it would be useful to organise another workshop in which these countries could present their NGP. This idea was well received in the discussion of the first workshop and Germany was pointed out as another country of interest for the audience. For this next workshop, probably to be organised around the first quarter of 2025, we should consider opening the event to spread the information and not only invite WG1 and WG7 representatives as a target audience. However, a wider audience could limit the discussion among the country's representatives. As a complementary material to the video presentations already uploaded to the 1+MG Framework, country's factsheets giving information from their NGP could be useful to synthesise the information and display key aspects of each NGP. For that aim, countries would have to be involved and agree to the content.

7. Conclusions & Impact

The work done in this deliverable is completely aligned with the fourth track of the 1+MG Roadmap 2023-2027: National Engagement: National Mirror Groups. With the analysis of the GDI operational readiness questionnaire, we were able to identify those countries that have not still set up their NMG and plan capacity building actions to facilitate their implementation. In addition, the workshop "Towards the Implementation of National Genomic Plans in EU countries" marked the launch of the recently created WG1. National Mirror Groups of the 1+MG initiative, kicking off the WG1 and paving the way for successive activities of the group.

Moreover, the video presentations resulting from the workshop have fed the 1+MG Framework contributing to the current work plan of the first tract of the 1+MG Roadmap 2023-27. The video presentations have been uploaded to the National Implementation section where NMGs could make dissemination material and national solutions available supporting national deployment by making it accessible to their national stakeholders.

Finally, it should be remarked that the workshop brought up great interest from GDI countries (16 of the current 24 country members attended the meeting). Therefore, we expect that representatives of WG1/WG7 spread this available information to their Ministries and make an impact at the country's policy level, facilitating the setting up of a NGP.

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8. Next steps

Considering the importance of promoting national engagement, contributions and alignment, as it is one of the five tracks from the European 1+ Million Genomes Initiative Roadmap 2023-2027, we cannot overlook the need of NMGs being established in all 1+MG countries. It is a milestone that needs to be completed before the end of this Roadmap, so that all the country members of the Initiative are set in the same starting line for the next steps of the 1+ Million Genomes Initiative.

As such, we have considered several actions as possible next steps to encourage further such establishment and consequently, promote the implementation of the Initiative.

As already mentioned throughout the deliverable, we are concerned that some of the countries have only a partial or with no development of the NMGs. Therefore, it might be interesting, during the first and second quarter of 2025, to prepare and ask the country members to fill-in some sort of survey, similar to a NMGS nodes maturity model, as to identify the countries with more difficulties in the NMGs creation, their gaps in the process and come up with ideas to help them in the NMGs establishment process. An initial draft of the survey can be found in ANNEXE II. As to avoid overlapping actions it is essential to be working in close collaboration with GDI.

Next, during the third and fourth quarter of 2025, a bilateral meeting with those identified countries would be in order, to help them explore the possible issues they could be facing and help them identify possible gaps they may be having in the NMGs setting up process. In such meetings, if possible, we would also like to provide them with leaflets, or guidelines with possible steps to follow to lead them towards a successful creation of their NMG. For the resources layout, some help might be needed from GDI.

Regarding the development of NGP, it is clear throughout the study that more than 80% of the countries are having issues as to M21. Having this into account, in order to help and learn from one another, we would like to prepare another workshop for the first quarter of 2025. We would like to include as presenters, countries with a NGP in place or in process of implementation such as Ireland, Sweden, Finland and Germany. This way, some of the countries with NGP development issues could find similarities with other countries, transfer and adapt those solutions to their own impasses as well as their own country policies and structural systems. In order for the country members to have easily available the highlights of each of the countries with a NGP already developed or in an advanced state of development, factsheets or dashboards might be useful.

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Also, in order to complement this, we believe some sort of country visit (virtual or in person) to those countries with a NGP already developed and implemented would be greatly beneficial. Considering the budgetary problems that could arise from in person country visits, one possibility could be the arrangement of such visits during a few hours of the already established annual GA meetings. If virtually, the visits could be set periodically every several months, so that more countries could be visited. This way, a better support system could be in place where resources in place as well as the ones required but still lacking could be identified, and the possibility to attain the level committed to by the countries would be more likely.

All the material generated could feed the section "National Implementation" of the 1+MG Framework contributing to the current work plan of the first tract of the 1+MG Roadmap 2023-27.

9. References

1. European 1+ Million Genomes initiative: 1+MG Roadmap 2023-2027 Scale up and sustainability.
2. European GDI - New countries join the European Genomic Data Infrastructure project https://gdi.onemilliongenomes.eu/news/new-countries-joining-gdi-project

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European Genomic Data Infrastructure

Annexe I

Workshop "Towards the Implementation of National Genomic Plans in EU countries"

11:30-14:00, 25 th June 2024

Agenda

How to develop and implement a National Genomic Plan?

Success stories (20min presentation + 10min Q&A):

- 11:30-12:00. 2025 French Genomic Medicine Initiative. Frédérique Nowak.
- 12:00-12:30. Italian National Genomic Plan. Domenico Coviello

—----------Break (15min) —----------

- 12:45-13:15. Belgian National Genomic Plan. Marc Van Den Bulcke
- 13:15-13:45. The Danish National Genome Center. Lene Cividanes

13:45-14:00. Wrap up and conclusions. Marc Van Den Bulcke

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Annexe II

Questions regarding the development and organisation of National Mirror Groups (NMGs) in the framework of the 1+MG initiative

Profile and contact information

*Mandatory answers

Country:*

WG1 Representative:*

Name	Affiliation	e-mail address

NOTE: A representative designated to represent a Member State in the WG1).

WG1 Special Group Representative:*

Name	Affiliation	e-mail address

NOTE: A representative designated to represent a Member State in the Special Group of 1+MG (via Working Group 1).

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NMG's Scientific Coordinator:*

Name	Affiliation	e-mail address

NOTE: The NMGs Scientific Coordinator is the person in charge of managing the nominations and validations of scientific experts to take part in the NMG of your country.

NMG's National Contact Point:*

Name	Affiliation	e-mail address

NOTE: The National Contact Point for an NMG is the person in charge of managing the internal communication within the NMG.

If there is a different or additional figure in your structure, please describe its role and profile*:

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1. What stage is the NMGs at? Please select one of the following options:*

	No tangible activities yet (No expert nominees for the NMGs yet)
	Planning/preparing (Not all NMGs exist but expert nominations have begun)
	Developing (Much of the nominated experts and governance structure is beginning to be implemented)
	Operational (All groups have their nominated experts and have an operational governance structure)

Please provide a short explanation to your answer: *

2. About NMG composition and functioning:

a. Composition of NMGs (please click here to fill out the attached Excel format and return it with this document).*

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b. Expert nomination process to join the NMGs:*

c. Communication format and frequency with and among NMGs (please describe how NMGs exchange information and/or meet and how often):*

d. Governance structure in the NMGs:* (please specify which ministry the NMGs depends on)

e. Do you organise activities at the national level with the NMG?*

	Yes
	No

f. What kind of activities?

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g. Are the activities of the NMG funded in your country?*

	Yes
	No

How?

i. Is the NMG in your country formalised?*

	Yes
	No

In which way?

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3. NMG links to the 1+MG Initiative

a. How active are NMG members in the initiative? (evaluate the activity level of the NMGs between 1 and 5, being 1 not active and 5 very active)*

1	2	3	4	5

b. Do you think there is sufficient links between the NMGs and the 1+MG Initiative?*

	Yes
	No

If not, please describe how they could be further involved/engaged.

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