Beyond One Million Genomes

D5.1

B1MG maturity level model and country-specific alignment within the model

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27/5/2022	1v0	Astrid Vicente (INSA)	Comments addressed.
27/05/2022	1v0	Nikki Coutts (ELIXIR Hub)	Version uploaded to the EC Portal

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1. Executive Summary

The Beyond One Million Genomes Maturity Level Model (B1MG MLM) was created as a tool for countries to self-assess the maturity level of implementation of genomics into their healthcare systems, according to a common matrix, and to define a path to optimization. As such, it aims to promote and facilitate the adoption of genomics in healthcare systems, close the best practice gaps across Europe, and make personalised medicine accessible to citizens and patients across Europe.

This report describes the design of the B1MG MLM and the content validation through a Delphi exercise. A draft version of the MLM was initially developed after careful review of recently published literature and input from experts from the 1+ Million Genomes Initiative[1] (1+MG) and the Beyond 1 Million Genomes Project[2] (B1MG). This initial framework included 8 domains, each comprising several subdomains for which indicators and respective levels of maturity were assigned. The maturity level per indicator was rated in a scale from 1 to 5, namely from a non-existent or *Ad hoc* level of implementation to a level of maturity characterised by a system adaptable to opportunity and change, and in support of international cooperation.

The content and structure of the designed framework was validated through a two round Delphi exercise to find consensus among a panel of 14 high level experts. The process validated the 8 proposed domains, namely:

I. Governance and strategy
II. Investment and economic mode
III. Ethics, legislation and policy
IV. Public awareness and acceptance
V. Workforce skills and organisation
VI. Clinical organisation, infrastructure and tools
VII. Clinical genomics guidelines and infrastructure
VIII. Data management, standards and infrastructure.

The 147 items initially proposed were validated after inclusion of comments and suggestions by the Delphi expert panel. The final version of the B1MG MLM can be found here[3].

To facilitate the use of the B1MG MLM an Assessment Tool Kit was developed, including a User's Guide and an Assessment Tool. A pilot with voluntary countries is currently ongoing, to assess feasibility in real life healthcare settings, stimulate discussion among stakeholders across European health systems, address transferability of best practices, and finally discuss the development of an action plan for progress towards optimization.

[1] https://digital-strategy.ec.europa.eu/en/policies/1-million-genomes
[2] https://b1mg-project.eu/
[3] https://b1mg-project.eu/resources/maturity-level-model

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2. Contribution towards project objectives

With this deliverable, the project has reached or the deliverable has contributed to the following objectives/key results:

[Select 'Yes' (at least one) if the deliverable contributed to the key result, otherwise select 'No'.]

	Key Result No and description	Contributed
Objective 1 Engage local, regional, national and European stakeholders to define the requirements for cross-border access to genomics and personalised medicine data	**1.** B1MG assembles key local, national, European and global actors in the field of Personalised Medicine within a B1MG Stakeholder Coordination Group (WP1) by M6.	No
	2. B1MG drives broad engagement around European access to personalised medicine data via the B1MG Stakeholder Coordination Portal (WP1) following the B1MG Communication Strategy (WP6) by M12.	No
	3. B1MG establishes awareness and dialogue with a broad set of societal actors via a continuously monitored and refined communications strategy (WP1, WP6) by M12, M18, M24 & M30.	No
	4. The open B1MG Summit (M18) engages and ensures that the views of all relevant stakeholders are captured in B1MG requirements and guidelines (WP1, WP6).	No
Objective 2 Translate requirements for data quality, standards, technical infrastructure, and ELSI into technical specifications and implementation guidelines that captures European best practice	**Legal & Ethical Key Results**	
	1. Establish relevant best practice in ethics of cross-border access to genome and phenotypic data (WP2) by M36	No
	2. Analysis of legal framework and development of common minimum standard (WP2) by M36.	No
	3. Cross-border Data Access and Use Governance Toolkit Framework (WP2) by M36.	No
	Technical Key Results	
	4. Quality metrics for sequencing (WP3) by M12.	No
	5. Best practices for Next Generation Sequencing (WP3) by M24.	No
	6. Phenotypic and clinical metadata framework (WP3) by M12, M24 & M36.	No
	7. Best practices in sharing and linking phenotypic and genetic data (WP3) by M12 & M24.	No
	8. Data analysis challenge (WP3) by M36.	No
	Infrastructure Key Results	
	9. Secure cross-border data access roadmap (WP4) by M12 & M36.	No
	10. Secure cross-border data access demonstrator (WP4) by M24.	No

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Objective 3 Drive adoption and support long-term operation by organisations at local, regional, national and European level by providing guidance on phased development (via the B1MG maturity level model), and a methodology for economic evaluation	**1.** The B1MG maturity level model (WP5) by M24.	Yes
	2. Roadmap and guidance tools for countries for effective implementation of Personalised Medicine (WP5) by M36.	Yes
	3. Economic evaluation models for Personalised Medicine and case studies (WP5) by M30.	No
	4. Guidance principles for national mirror groups and cross-border Personalised Medicine governance (WP6) by M30.	No
	5. Long-term sustainability design and funding routes for cross-border Personalised Medicine delivery (WP6) by M34.	No

3. Methods

Implementing genomic medicine in healthcare settings can bring us one step closer to making personalised medicine a reality. Accurate, timely diagnostics, personalised treatment protocols and preventative approaches based on genomic information have a major impact on patients and their families and can improve efficiency in health systems. For instance, genomic data analysis may provide better and faster diagnosis for many conditions and determine a more effective treatment based on a patient's pharmacogenomics profile, while accurate genomic profiling of individuals is enabling a shift of medical practice towards disease prevention.

However, it is clear that European countries are currently at varying stages of maturity for implementing genomics in healthcare. To close the maturity gaps across Europe (and globally) and to promote the more effective usage of genomic information for clinical practice, countries need to be able to understand their needs and challenges, and plan their path towards optimised implementation. Recognizing this need prompted the B1MG WP5 to develop a support tool for countries to self-assess their maturity, according to a common matrix that addresses the crucial issues for implementation of genomics in healthcare. The B1MG Maturity Level Model (B1MG MLM) was created to meet this challenge, promoting strategic planning for genomics in healthcare, as well as the dialogue and cooperation among countries.

To this end, the following activities and methodologies were carried out:

- Designing the B1MG MLM (Figure 1): based on a literature review, WP5 brainstorming, critical advice and input from B1MG WPs and 1+MG Initiative WGs experts knowledgeable in different fields, we developed a first version of the MLM framework (see Section 4.1).
- Validation of the B1MG MLM (Figure 1): to validate the content of the first B1MG MLM version, a group of international senior experts in the field of genomics medicine, healthcare systems, public policy and data standards and infrastructure was invited to participate in a Delphi exercise (see Section 4.2).

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- Developing a Tool Kit for application of the B1MG MLM: to support the process of applying the B1MG MLM in real world settings, we developed a Tool Kit including the MLM in a suitable online visualisation platform with Glossary, an Assessment Tool and a User's Guide. This Tool Kit is being tested in a pilot assessment by a group of volunteer pilot countries (see Section 4.3).

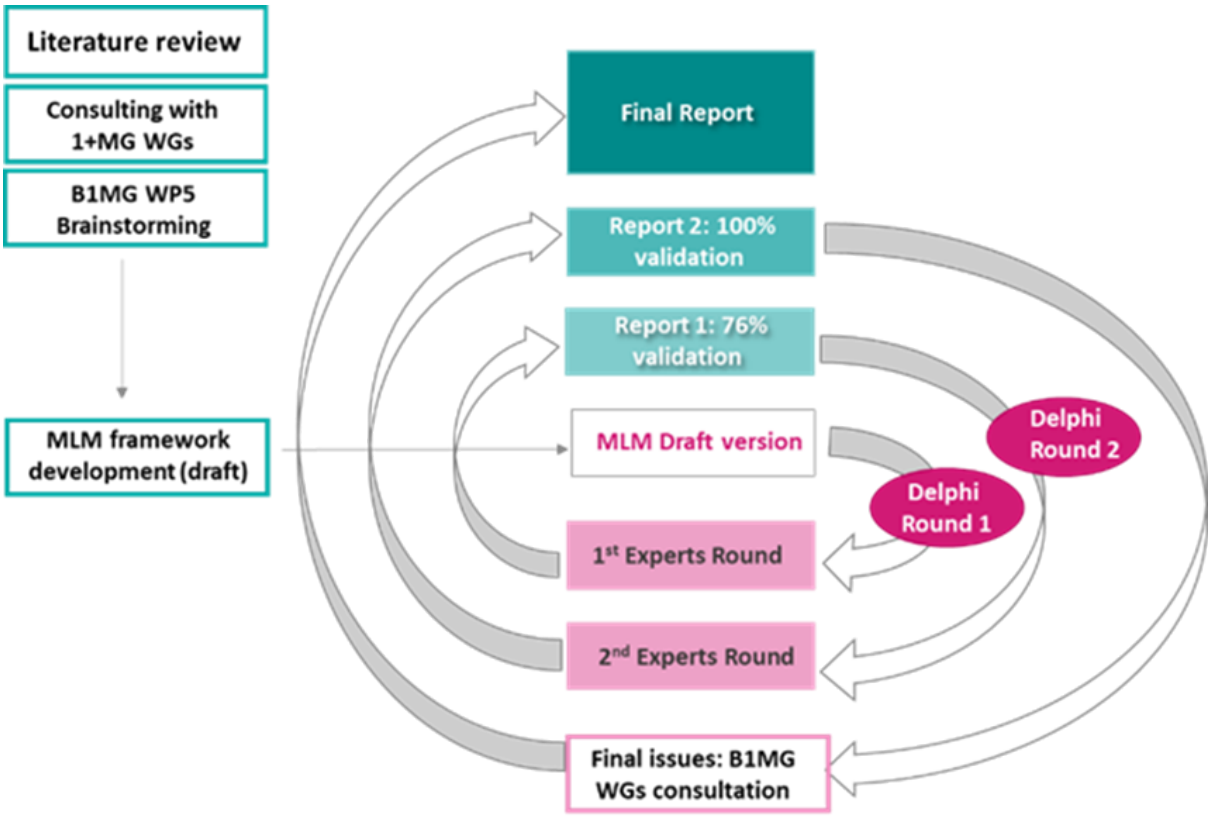

Figure 1. Overall development and validation of the B1MG MLM.

4. Description of work accomplished

4.1 Design of the B1MG MLM: Literature Review and expert input from 1+MG/B1MG

The first step to design the B1MG MLM was to perform a literature review. For this, a search was performed on Medline via PUBMED for papers with a publication date later than 2000 using the search terms: "maturity model" AND "health systems"; "maturity model" AND "hospital"; "maturity model" AND "governance" AND "indicators"; "maturity model" AND "public health"; "maturity model" AND "education"; "maturity model" AND "patient"; "maturity model" AND "genomics"; "maturity model" AND "genetics"; "maturity model" AND "big data"; "maturity model" AND

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"domains"; "maturity model" AND "dimension"; "maturity model" AND "data"; "maturity model" AND "survey"; "maturity model" AND "indicators"; "maturity model" AND "process"; "maturity model" AND "Delphi"; "maturity level" AND "healthcare"; "implementation" AND "genomic data" AND "healthcare systems". Titles and abstracts of the retrieved articles were analysed to identify the relevant ones. A search for studies reporting the use of Delphi on raising healthcare consensus was also done.

Based on this initial literature review, a first draft of the MLM framework was designed, which included 8 domains. At this stage, discussions with the 1+MG WGs/B1MG WPLs provided critical advice, particularly with WGs 2, 3, 4, 5, and 6, as they involve experts in different fields including ethics and legal issues, data infrastructure, data and genomic standards, public health and health economics. The initial draft maintained the 8 domains, but aspects were re-worked following WP5 brainstorming to include the WGs suggestions and advice. The domain on ethical and legal issues was entirely developed by WG2, while the domain addressing health economic models had crucial input from WG6 members.

4.2 Validation of the B1MG MLM content

To validate the initial draft proposal for the MLM framework, a group of experts was invited to enter the Delphi iterative process of reaching consensus. A group of international experts in the field of healthcare systems, public policy, data and genomics was identified by the B1MG team of international networks. Delphi experts were selected according to the following preferential criteria: 1) having senior leadership experience of national, European or international genomic medicine or personalised medicine-related initiatives (could be digital health or similar), and/or 2) having a medical background with expertise in public health, healthcare policy, genomic medicine and/or healthcare management, and/or 3) having experience in health policy for genomic medicine or personalised medicine.

Twenty-one experts were selected and invited to participate. Among the 16 experts who accepted the invitation, 14 completed the two rounds of the Delphi survey. The Delphi panel experts were invited by email to provide input on every item of the MLM framework, using a dedicated online platform.

In the first Round, the survey was divided into 10 sections. The first section was dedicated to gathering informed consent and expert's demographic information. In the second section, experts were asked about the relevance of the eight domains proposed as main blocks of the MLM framework structure. Further to their opinion about the relevance of each domain, experts were also able to add, remove or rephrase items as well as provide comments. The remaining 8 sections were each one dedicated to a domain, in a total of 147 items. For each domain, experts were interrogated about the suggested subdomains, indicators and respective maturity levels. For each indicator there was always a set of 5 maturity levels associated. Experts were asked to score the adequacy of the subdomains and indicators proposed according to a 5-point Likert scale ('strongly agree', 'agree', 'neither agree nor disagree', 'disagree', 'strongly disagree'). For every 'disagree' or 'strongly disagree' response, a free-text response box was available for participants to elaborate or further explain. An option of 'unable to answer' was also included. Any 'unable to answer' response was considered as a missing value.

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As depicted in Figure 1, the items that did not reach the agreement level used as the consensus criteria to validate an item were included in the Round 2 survey.

For item validation and inclusion in the final B1MG MLM, or reformulation and reevaluation in the Delphi Round 2, decision criteria were established as follows:

1. Items with an agreement rate ≥86% (Strongly agree + Agree) were accepted in the final B1MG MLM. For reporting purposes these were labelled as "Validated";

2. Some items with an agreement rate ≥ 86% (Strongly agree + Agree) were slightly changed to accommodate very relevant comments from the expert panel, and accepted in the final B1MG MLM. For reporting purpose were labelled as "Validated with rewording";

3. Items with an agreement rate <86% (Strongly agree + Agree) and cumulatively with a disagreement rate ≥7% (Disagree + Strongly Disagree), were reformulated according to comments from the expert panel for validation in Round 2. These items were labelled "Reformulated";

4. Items with an agreement rate ≥79% (Strongly agree + Agree) and no disagreements (Disagree + Strongly Disagree), corresponding to a rate of Neither agree or disagree ≥21%, were accepted in the final B1MG MLM. For reporting purpose were labelled as "Validated";

5. Items with an agreement rate <86% (Strongly agree + Agree) without suggestions for improvement were deemed inconclusive and included for reevaluation in Round 2 with the original wording. For reporting purposes were labelled "Reevaluate".

For Round 2, each expert was asked to independently rank a total of 36 items ("Reformulated" and "Reevaluate"). Each expert also received a personalised report with his/her own scores in Round 1, as well as the group's collective response (percentage agreement/disagreement) to each statement, and the de-identified comments from all experts. This way, experts were given the chance to reconsider their responses in Round 2 in light of the group's responses in Round 1. For Round 2, there were only two answering possibilities: 'agree' and 'disagree'. For every 'disagree' response, a free-text response box was available to experts to elaborate or further explain. Items with an agreement rate ≥86% were validated and included in the final B1MG MLM.

Following Round 2, each expert received a personalised report by email with his/her own scores as well as the group's collective response (percentage agreement/disagreement) to each statement, and de-identified comments from all experts. For two domains, namely Domain II and Domain III, some experts still raised a few pertinent questions and concerns. After discussion with 1+MG/B1MG experts some minor changes were introduced. All experts received by email the final and validated through consensus MLM framework, and were asked to express and discuss any last opinions, concerns or doubts.

The Delphi survey was carried out using the Welphi® software. This online platform allowed the implementation of the survey, ensuring confidentiality and anonymity of experts throughout the Delphi exercise. Data were exported to Excel for further processing.

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4.3 Using the B1MG MLM – development of the process and a Tool Kit

A process and a Tool Kit were developed to facilitate the process of applying the B1MG MLM in real world settings. The general process includes 5 stages, namely:

1. Identification of stakeholders and assembly of the Assessment Team: a multidisciplinary group of experts from the ministries of health and other relevant national or regional agencies
2. Self-assessment: the Assessment Team completes the Assessment Tool, including rationale and supporting evidence, for all or selected domains according to expertise
3. Consensus building and completion of the Assessment Tool Consensus Tab, documenting rationale and supporting evidence
4. Analysis of assessment outcomes: identification of weaknesses and requirements for optimization
5. Developing an action plan: definition of current and desired maturity status, and path towards optimization according to the common matrix underlying the MLM

To support this process, we developed a Tool Kit including the MLM in a suitable online visualisation platform with Glossary, an Assessment Tool and a User's Guide.

A pilot is currently ongoing testing the Tool Kit and the general assessment process in 10 European countries. The main goals are to assess feasibility, stimulate discussion among stakeholders across European health systems, address transferability of Best Practices and address development of an action plan for progress towards optimization. Volunteer countries across Europe are participating in this challenge.

4.4 Problems and solutions

Delphi expert selection was carried out according to a number of criteria to ensure that the groups of experts were highly experienced in genomic medicine, leaders of national or international initiatives in genomic or personalised medicine and had a good understanding of healthcare systems. As such, most experts were medical doctors, and all were leaders in their fields and experts in at least one of the domains covered by the MLM. This meant a limited pool of 21 high level experts would fit this criteria, and were invited to participate. Of this group, 16 accepted the invitation, and 14 carried out the full assessment. We did not fully achieve the desired balanced geographical coverage sought, and had more northern and central European representation than eastern and southern. While we could not mitigate the less balanced geographical representation, the seniority, wide experience and deep knowledge on genomic medicine of this pool of experts was extremely reassuring that the validation exercise would be

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successful. We were also extremely pleased that all 14 experts who started completed the two rounds of the Delphi, which were challenging and very time consuming.

The Delphi exercise was slightly delayed due to three main factors:

1. We prioritised a high response rate from experts, and therefore extended deadlines to suit their schedules;

2. The Delphi exercise was carried out during summer, so had to accommodate summer vacation timings, which differ between European countries;

3. After the Delphi Round 2 all items were validated. However we still received a number of relevant comments and reached out again to WG experts for support on how to best accommodate these without changing the consensus.

These delays were compensated with a fast turnaround of analysis in between rounds and for the final version of the MLM.

5. Results

5.1 The B1MG MLM

The MLM framework is structured as a matrix of domains, subdomains and related indicators and maturity levels. The proposed 8 domains cover topics agreed as crucial for assessing the maturity stage of healthcare systems in implementing genomics in clinical practice, namely:

I. Governance and strategy
II. Investment and economic model
III. Ethics, legislation and policy
IV. Public awareness and acceptance
V. Workforce skills and organisation
VI. Clinical organisation, infrastructure and tools
VII. Clinical genomics guidelines and infrastructure
VIII. Data management, standards and infrastructure

The 8 domains comprise a total of 41 subdomains, 49 indicators and 49 sets of 5 maturity levels (one set for each indicator). The 5 maturity levels reflect a stepwise path towards higher genomic practice maturity, from *Ad hoc* practices to practices that are widely adopted, adaptable to new opportunities and novel developments and supportive of international cooperation (shown in Figure 2). Overall, the MLM is intended to provide a common matrix for countries to self-assess their current status and plan a staged progression towards optimization.

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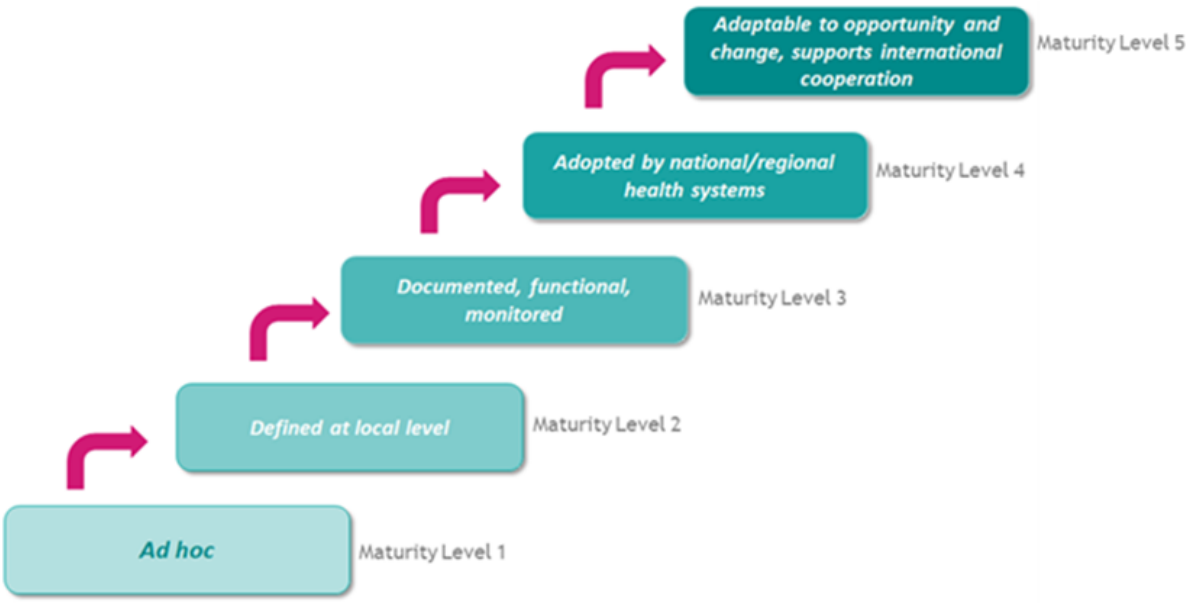

Figure 2. B1MG MLM maturity level framework - towards an increased maturity of genomics in healthcare systems.

5.2 Expert Delphi panel

The first version of the B1MG MLM was validated by a Delphi panel with senior experts, who completed both rounds of the Delphi exercise. Figure 3 provides a demographic and professional characterisation of the expert. Table 1 provides a characterization of the expert panel, while Figure 3 shows their geographical distribution. All experts originated from European countries except one, who provided an international perspective.

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Table 1: Characterization of the expert panel by sex, type of organization, position within the organization and main expertise areas.

Characteristic		No. (%)
Total		**14 (100%)**
Sex		
Total		**14 (100%)**
	Female	6 (43%)
	Male	8 (57%)
Type of organisation*		
Total		**13 (100%)**
	Ministry	1 (8%)
	Public Health organisations	2 (16%)
	Academia or Research centre	10 (77%)
Position within the organisation*		
Total		**10 (100%)**
	CEO	2 (20%)
	Director	4 (40%)
	Head of clinic/scientific council	2 (20%
	Advisor/Consultant	2 (20%)
Main Areas of expertise (more than 1)*		

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Total		**9 (100%)**
	Genetics/Genomics (clinical/research)	7 (78%)
	Medicine	3 (33%)
	Public Policies/Administration	2 (22%)
	Public Health	2 (22%)
Country		
Total		**11 (100%)**

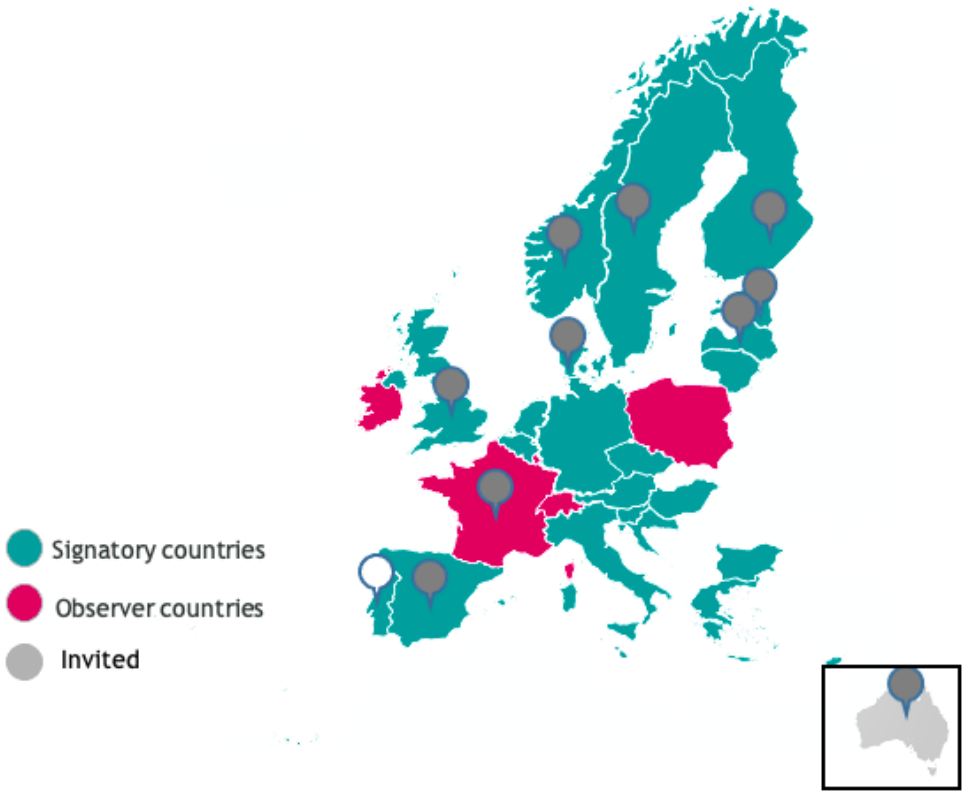

Figure 3. Geographical distribution of the Delphi expert panel.

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5.3 Delphi exercise for validation of the B1MG MLM framework

The first version of the B1MG MLM framework submitted to Round 1 for validation through Delphi panel consensus included 8 domains. These covered topics crucial for assessing the maturity stage of healthcare systems in implementing genomics into regular care. For each domain, subdomains were identified, and the level of maturity associated to each subdomain was assessed by ascribing a maturity level, between 1 and 5, to appropriate indicators. The original wording for each item included in the first version of the MLM framework is shown in Annex 1 (Tables 1-8).

Overall, the validation of the B1MG MLM using the Delphi method took around four months (Figure 4). During the two rounds, priority was given to having a 100% response rate from the Delphi expert panel over meeting pre-established deadlines. Both rounds were closed only after all 14 experts responded to the Delphi survey.

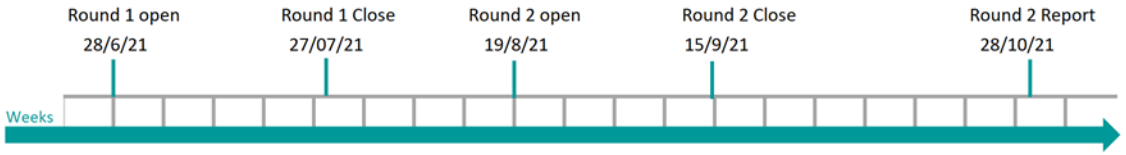

Figure 4. Timeline of the Delphi validation of the B1MG MLM.

The Delphi Round 1 allowed the validation, through expert panel consensus, of 76% of the 147 items that constitute the initial MLM version (Table 2). All remaining items were validated in Round 2.

The rates of approval and rewording differed between the 8 domains (Table 1), with Domain II "Investment and economic model" requiring the most extensive rephrasing. Two domains, namely Domain V "Workforce skills and organisation" and Domain VII "Clinical genomics guidelines and infrastructure", were fully accepted and validated in Round 1. After round 2, two domains suffered a minor rearrangement (merging of subdomains), namely "Investment and economic model" and "Ethics, legislation and policy", following expert suggestions.

Annex 1, Tables 1 to 8 show the descriptive statistics per item (Domains and respective Subdomains, Indicators and Maturity Levels), including rating by percentage (%) of experts, level of decision per item, experts comments per item, and rewording proposal in the 2 rounds. Tables 9 and 10 compile all other general expert comments of Round 1 and Round 2, respectively. Overall, all initial 147 items, distributed by the initially proposed 8 domains, were validated in the two Delphi rounds and included in the final MLM framework, 76% in the initial wording, and 24% with rewording to include the suggestions made by the Delphi expert panel.

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Table 2. Quantitative analysis of Round 1 results, namely number and percentage of validated and rephrased items in Round 1 and items included in Round 2.

Domains	items	Approved in Round 1	% Approved	Rephrased after Round 1	% Rephrased	Included in Round 2	% reevaluation
I	10	9	**90**	3	**30**	1	**10**
II	16	4	**25**	10	**63**	12	**75**
III	34	24	**71**	9	**26**	10	**29**
IV	10	5	**50**	3	**30**	5	**50**
V	18	18	**100**	0	**0**	0	**0**
VI	16	11	**69**	7	**44**	5	**31**
VII	19	19	**100**	0	**0**	0	**0**
VIII	24	21	**88**	2	**8**	3	**13**
Total	147	111	**76**	34	**23**	36	**24**

5.4 The B1MG MLM Tool Kit and assessment procedure

The Tool Kit includes:

- The full B1MG MLM framework in an online platform, namely GitHub. The online platform allows easy access to the model, with a simple but very clear visualisation of all domains, subdomains, indicators and maturity levels. The MLM includes a linked Glossary for clarification of definitions and concepts.
- The Assessment Tool is an excel file designed to:
    - Collect and record data, namely the:
        - Assessment Team members, with affiliation, contact, and Domains assessed according to expertise
        - The maturity level assessment per indicator by each Assessment Team member
        - Rationale and supporting evidence for maturity level choice for each indicator
    - Register the consensus for each Domain - 1 per country or region
    - Register the rationale and supporting evidence for the consensus maturity level assessment per indicator
- An informative User's Guide describing the development of the B1MG MLM, the assessment process, the consensus building phase, the analysis phase and the development of an action plan for optimization.

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The outcomes of the assessment process (Figure 4) provide the current status of maturity regarding practices in genomic medicine, systematically identifying areas of strengths and weaknesses according to a structured framework. This information can be used to set goals, define areas of priority investment and establish an action plan. The B1MG MLM process and tool can be:

- An instrument for self-assessment of current status, but also a framework for progression
- The indicators and maturity levels provide reference points to define the desired maturity status, and the processes, structures and capacities needed to reach higher maturity
- A support tool to be used considering other issues to define the maturity goals, eg healthcare system context, objectives and resources
- Once an action plan is implemented, the indicators can be used to monitor progress along the path for maturity
- The Assessment Team and other stakeholders with relevant expertise may be engaged to help implement the action plan.

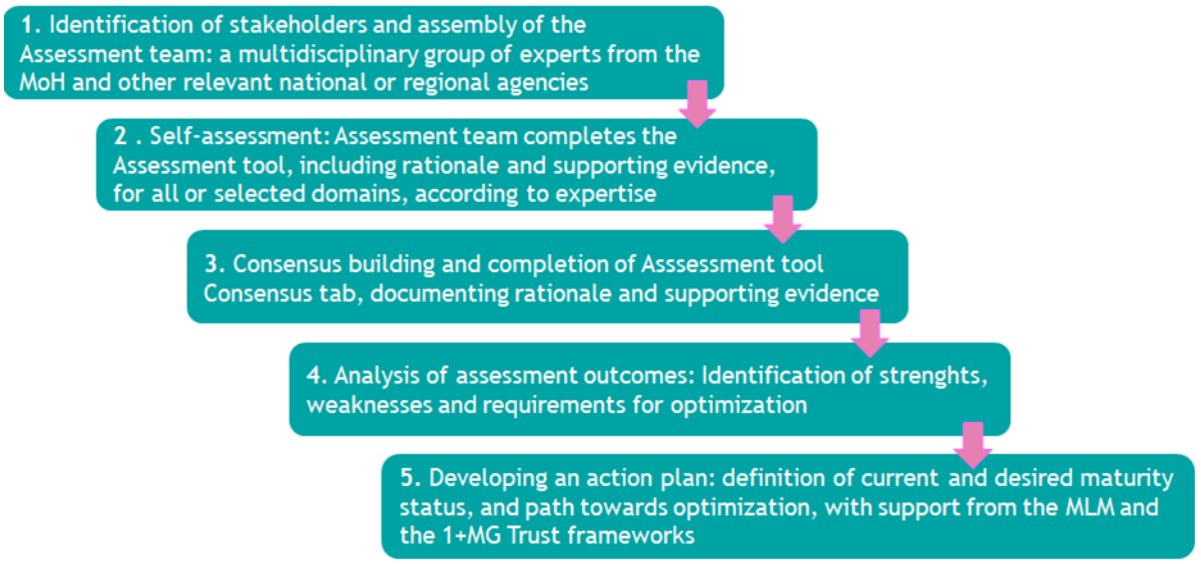

Figure 4. Description of the general process for using the MLM.

The assessment procedure and Tool Kit are currently being piloted in volunteer countries. To gather these countries' impressions regarding the B1MG MLM usability and challenges, we developed a pilot survey. We expect the answers to this survey will help improve the self-assessment process and the Tool Kit.

The B1MG MLM was presented to several audiences, namely:

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- Astrid Vicente for WP5, “B1MG Maturity Level Model”, the Global Health Implementation Forum (GHIF), “End-to-End Standards Implementations Session", 24th September 2020;
- Astrid Vicente, The B1MG MLM - an update. 1+MG Special Group meeting, October 19th, 2021
- Astrid Vicente for WP5, "Delivering Personalised Medicine cross-borders: Implementation in Healthcare systems and Societal Impact", the Stakeholder Meeting, 21st October 2020;
- Astrid Vicente for WP5, “B1MG Maturity Level Model”, the Global Health Implementation Forum (GHIF), 17th November 2021;
- Astrid Vicente for WP5, "How ready are European healthcare systems regarding the use of genomics in medicine? The Beyond 1 Million Genomes (B1MG) Maturity Level Model ", Workshop "Integrating the use of genomic data in personalised healthcare: implications across the board" at the European Public Health (EPH) Conference, 11th November 2021;

A manuscript describing the design and content-validation of the B1MG MLM is in preparation.

6. Discussion

In the area of healthcare, maturity models are necessarily cross-disciplinary in nature, and this is clearly reflected in the B1MG MLM. The 8 domains covered in the model are essential for the implementation of genomics in healthcare routine: Governance and strategy, Investment and economic model, Ethics, legislation and policy, Public awareness and acceptance, Workforce skills and organisation, Clinical organisation, infrastructure and tools, Clinical genomics guidelines and infrastructure and Data management, standards and infrastructure.

Altogether, the results of the Delphi exercise, namely that there were no rejected domains in the initial proposal of the model; evidence that a good preparation and deep reflection and debate previous to the Delphi survey, including the extensive literature review; the WP5 team brainstorming and the 1+MG expert inputs; were essential to the success of the exercise.

Two domains, namely Domain V, regarding “Workforce skills and organisation”, and Domain VII, regarding “Clinical genomics guidelines and infrastructure”, were fully accepted and validated in Round 1. These results evidence the progress and consensus in these two areas, likely to be the most developed, or at least the most discussed, among European countries.

Among the eight domains of the B1MG_MLM framework, Domain II, “Investment and economic model”, had lower agreement rates from experts in the first round of the Delphi process and was the least consensual. After round 2, although consensus was reached, we still addressed some comments from the experts that we considered relevant. For this, we consulted again the 1+MG WG6 Health economics and outcomes research, and made minor rewording to accommodate these last comments. The area of economic evaluation of genomic medicine and economic impact evaluation is still underdeveloped, and major efforts need to be made to define appropriate models that consider not only cost-effectiveness but also the benefit for patients and their families, and citizens at large. Another domain that required more effort to reach consensus was Domain III, “Ethics, legislation and policy”. Again, this reflects the controversies and intense discussions, at the national and international levels, on data access, security and privacy. Both these areas are crucial to ensure equity of access to all citizens.

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7. Conclusions

The B1MG MLM is a unique tool enabling the identification of strengths and areas that need more attention and investment for the implementation of genomics in healthcare. The MLM has been developed and validated as a common matrix that will contribute to closing the maturity level gaps across Europe. A complementary procedure and Tool Kit to facilitate its use in healthcare systems maturity assessments was developed and is currently being tested in volunteer pilot countries.

The final goal of the overall effort is to develop stronger and more effective healthcare systems for personalised medicine globally. The overall vision is to benefit all citizens and patients with equity of access to personalised medicine.

8. Next steps

A manuscript describing the B1MG MLM design and content validation is in preparation for publication.

A pilot is now running in 10 volunteer countries (Belgium, Denmark, Finland, Italy, Lithuania, Luxembourg, Portugal, Slovenia, Spain and Germany) to test the MLM in real world settings. Results of this pilot, focusing on the process and the Tool Kit (not on the national maturity levels) will be presented and discussed in a workshop planned to take place at INSA (Lisbon) in October 2022. This workshop will provide recommendations for the use of the B1MG MLM and for the development of action plans. The outcomes will be widely disseminated, and the B1MG MLM and Tool Kit will be made freely available globally.

As evidenced by results presented in this report, the area of Health Economic models still needs more research and data to better understand the economic impact and develop solid models for health care. It is thus very relevant that WP5 organises a workshop on this topic, taking place in May in Lisbon, Portugal. The results from this workshop will provide recommendations for what steps need to be taken, including more research, to develop appropriate health economic models for genomics in healthcare.

9. Impact

The validated B1MG MLM framework generated great interest among the 1+MG country representatives, National Mirror Groups and Working Groups, as well as from genomics experts globally. This interest recognizes the need for a structured tool to assess the challenges of each country or region in the implementation of genomic medicine in health systems and to plan how these can be overcome towards optimization. The B1MG MLM provides this tool.

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10. Annex 1

Table 1: Descriptive results for Domain I and respective sub-sections

Round 1						Round 2			
Item	Rating by % of experts			Comments	Decision after Round 1	Rewording Proposal	Agree %	Comments	Decision after Round 2
	Not Relevant	Relevant							
Domain I: Governance and Strategy	0%	100%		-	**Validated**	-	-	-	N/A
Item	Rating by % of experts			Comments	Decision after Round 1	Rewording Proposal	Agree %	Comments	Decision after Round 2
	Disagreement	Neutral	Agreement						
Subdomain 1: Governance	0%	0%	100%	-	**Validated**	-	-	-	N/A
Indicator 1: Country/region has a dedicated governance body for genomics in healthcare	14%	0%	86%	•1) We can see a solution that there are several or integrated governance bodies.; 2) The scale is very demanding as regards the rather strict definition.	**Validated with rewording**	Country/region has a dedicated governance for genomics in healthcare	-	-	N/A

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				Suggestion: ""Country/region has dedicated governance for genomics in healthcare". Scale 1 - No governance; 2 - Elements of governance exist but they are not fully functional; 3 - Governance for genomics has bee defined but elements (e.g. full legal mandate) are still missing. ; 4 - Governance is fully operating, led centrally, possibly in a dedicated agency or body.; 5 - as suggested.". •I think there is potential for confusion regarding the term governance-					

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				currently the framework states ... with legal mandate to establish and enforce legal, professional... .... conduct, conventions and practices related to genomic medicine. This is a very wide definition - in practice such organisations are likely not to have a legal mandate and effective governance can be provided through professional, financial and health system governance. Also any governance arrangements for genomic medicine will not be specifically for this area only but will form					

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				part of the governance arrangements for medicine. To suggest that genomic medicine requires a completely separate and different standard of legal governance from other areas of medicine would in my opinion not be appropriate.					
Item		Rating by % of experts		Comments	Decision after Round 1	Rewording Proposal	Agree %	Comments	Decision after Round 2
		Not adequate	Adequate						
MLs	1. Genomics in healthcare is not Validated in national/regional health plans 2. Inclusion of genomics in healthcare in relevant national/regional health	29%	71%	•There could be a level stating "under development" or "under discussion". •Move international cooperation to specific subdomains?. •Please see my earlier	Reformulated	1 - No dedicated governance for genomics in healthcare 2 - Elements of governance exist but they are not fully functional 3 - Scope of governance	93%	I think there needs to be an explanation of what is meant by governance. It is not in the glossary. It has different meaning in different countries.	Validated

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	plans is under discussion 3. Genomics in healthcare is Validated in relevant national/regional health plans 4. Genomics in healthcare is implemented as part of national/regional health and other relevant plans (e.g. education or research) 5. Genomics in healthcare is implemented in health and other relevant plans, and is periodically evaluated for optimization, taking into account			comment on governance body- greater clarity required. Otherwise maturity levels are fine.		for genomics has been defined but elements are still under development 4 - There is a governance body that is fully operating, led centrally, and activities are monitored based on a work plan. 5- Governance body is institutionalised, recognized as the lead for genomics in healthcare, and is open to novel developments and supportive of international cooperation.		Do you mean healthcare services, funders, regulators, political, health professional groups or all or any of these. All 5 points can relate to one or more of these different types of governance arrangements.	

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	novel developments at the international level.								
Item		Rating by % of experts			Comments	Current Decision	Rewording proposal	Agree %	Comments	Decision after Round 2
		Disagreement	Neutral	Agreement						
Subdomain 2: Priority		0%	7%	93%	-	Validated	-	-	-	N/A
Indicator 1: Genomics in healthcare is established as a priority at national/regional level		0%	7%	93%	-	Validated	-	-	-	N/A
Item		Rating by % of experts			Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
		Not adequate		Adequate						
MLs	1. Genomics in healthcare is not included in national/regional health plans 2. Inclusion of genomics in healthcare in relevant national/regional health	0%		100%	-	Validated	-	-	-	N/A

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	plans is under discussion 3. Genomics in healthcare is included in relevant national/regional health plans 4. Genomics in healthcare is implemented as part of national/regional health and other relevant plans (e.g. education or research) 5. Genomics in healthcare is implemented in health and other relevant plans, and is periodically evaluated for optimization, taking into account								

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	novel developments at the international level.								
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Disagreement	**Neutral**	**Agreement**						
Subdomain 3: Strategy		0%	0%	100%	-	**Validated**	-	-	-	N/A
Indicator 1: There is a national/regional strategy for genomics in healthcare with a costed implementation plan.		7%	0%	93%	•There is a national/regional strategy for genomics in healthcare with an implementation plan *with identified resources*. reworded accordingly. The options to be.	**Validated**	-	-	-	N/A
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate		**Adequate**						
MLs	1. No genomics in healthcare strategy with costed implementation plan 2. A strategy for	14%		**86%**	•See my previous answer. •I believe the "costed implementation aspect" should be refunded to	**Validated with rewording**	1. No genomics in healthcare strategy with costed implementation plan 2. A strategy for genomics in healthcare	-	-	N/A

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	genomics in healthcare with costed implementation plan under discussion 3. A costed implementation plan for genomics in healthcare is developed and approved 4. The national/regional strategy for genomics in healthcare is under implementation 5. The national/regional strategy for genomics in healthcare is implemented with monitoring and long-term resources			costed and budgeted (or at least partially budgeted).		with costed implementation plan is under discussion 3. A costed implementation plan for genomics in healthcare is developed and approved 4. A national/regional strategy for genomics in healthcare is under implementation 5. A national/regional strategy for genomics in healthcare is implemented, with monitoring and long term resources and aligned with European and international strategies			

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Table 2: Descriptive results for Domain II and respective sub-sections

Round 1					Round 2			
Item	Rating by % of experts		Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
	Not Relevant	Relevant						
Domain II: Investment and economic model	7%	93%	•Too many items on cost-effectiveness: HTA, Cost-effectiveness model, and Societal (patient/citizen) benefits, all indicate the same aspects. Also framework and model are very close to each other. Finally, this should include tests and treatment. I would use only one indicator: "Framework for cost-effectiveness" - "There is a specified framework to model the societal benefits and costs of genomic tests and treatments, e.g. HTA".	Validated	-	-	-	N/A
Item	Rating by % of experts		Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2

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	Disagreement	Neutral	Agreement						
Subdomain 1: Investment	0%	7%	93%	-	**Validated**	-	-	-	N/A
Indicator 1: There is public funding for genomics in healthcare	21%	14%	64%	•The maturity levels imply an all or nothing approach. And also do not take into account government structures where there may be a shared costing between federal and state governments. This is the case in -. Some genetic testing (e.g. for childhood syndromes and intellectual disability) is covered by the federal government. Whereas other testing is at the discretion of the state or the hospital. SO depending on the condition - one could answer anything from 1-5.In addition - much testing is still in the realm of research (eg new	**Reformulated**	There is an investment plan at the national and/or regional levels for genomics in healthcare, with public or mixed public-private funding models	93%	Does the investment plan refer to investments only or also running actions? The first option is clearly limited and this should obviously cover also maintenance of the operations. Could this be clarified as "investment and funding plan"?	**Validated**

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				genes, VUS, the 50% of undiagnosed cases). •the most important is that there is sustainable funding rather than being only qualified as "public"... as this could be suppressed by the next government! Donation or foundation funding might also function well if sustainable and non profit. •public funding phrase implies a money flow model. I think this should be phrased as a healthcare system compatible funding. Basically, reimbursement models are fine.					
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**						
MLs	1. There is no	14%	86%	•There could be a level stating	Validated with	1. There is no established	-	-	N/A

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	established public funding for genomics in healthcare 2. Public funding for genomics in healthcare is allocated locally (e.g. at hospital level) 3. There is a national/regional investment plan for genomics in healthcare that is mostly dedicated to setting up infrastructure 4. There is a national/regional investment plan for the regular operational costs of genomics in healthcare			"under development" or "under discussion" •The fact that there is no public funding does not necessarily mean low maturity	**rewording**	investment plan at the national or regional levels for genomics in healthcare 2. An investment plan for genomics in healthcare at the national and/or regional levels is under development. 3. There is a national and/or regional investment plan for genomics in healthcare that is mostly dedicated to setting up infrastructure 4. There is a national and/or regional investment plan for the regular operational costs of genomics in healthcare (for specific tests e.g. for rare diseases diagnostics or specific			

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	(e.g. rare diseases diagnostics, cancer treatment) 5. There is a national/regional investment plan for genomics in healthcare that incorporates innovation according to opportunities and international developments					cancer treatments) 5. There is a national and/or regional investment plan for genomics in healthcare that incorporates innovation according to opportunities and international developments			
Item	**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
	Disagreement	**Neutral**	**Agreement**						
Subdomain 2: Access and reimbursement	0%	0%	100%	-	Validated	-	-	-	N/A
Indicator 1: Genomic tests have a reimbursement or no-cost access plan at national/regional level	14%	7%	79%	•As above - depends on the condition or set of conditions •No cost I find clunky wording.	Reformulated	There is a framework for reimbursement or no-cost access plans for genomic tests, at the national	100 %	-	Validated

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						and/or regional levels			
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**						
MLs	1. No central reimbursement or no-cost access plan for genomic tests 2.Reimbursement or no-cost access plans for genomic tests are developed and approved 3.Reimbursement or no-cost access plans for genomic tests are operationalized 4.Reimbursement or no-cost access plans for genomic tests are fully implement	23%	77%	•There could be a level stating "under development" or "under discussion" •No central reimbursement may again not mean low maturity, there may be a law/policy for disease specific/patient specific reimbursement, or even distributed models. This may even mean higher level of maturity •See previous comments	**Reformulated**	1. No framework for reimbursement or no-cost access plans for genomic tests 2. A framework for reimbursement or no-cost access plans for specific genomic tests is under development 3. A reimbursement framework or no-cost access plans for specific genomic tests are developed, approved and operationalized, with disease or patient-specific models 4. A reimbursement framework or no-cost access plans for specific	93%	If the maturation level 5 (Reimbursement or no-cost access plans for specific genomic tests are fully implemented, periodically evaluated and optimised, with plan for adoption of novel tools and technologies) implies that periodic evaluation and plan to adopt new tools also includes evaluation which disease entities and/or phenotypes (such as pharmacogenetics) should be covered by the plan, I AGREE, If not or if not clear, I think that aspect should be added	**Validated**

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	ed in national/regional healthcare systems 5.Reimbursement or no-cost access plans for genomic tests are fully implemented, periodically evaluated and optimised, with plan for adoption of novel tools and technologies					genomic tests are fully implemented in national and/or regional healthcare systems 5. A reimbursement framework or no-cost access plans for specific genomic tests are fully implemented, periodically evaluated and optimised, with plan for adoption of novel tools and technologies			
Item	**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
	Disagreement	**Neutral**	**Agreement**						
Subdomain 3: Health Technology Assessment (HTA) framework	7%	22%	71%	•See my comment on combining the three cost-effectiveness subdomains.	**Reevaluate**	-	93%	The three economic model subdomains can be combined using C-E assessment subdomain as the basis. Still struggling to understand the fundamental difference in between HTA and C-E frameworks and why societal benefits wouldn't be included	**Validated**

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								in them by definition. The other option is to have one subdomain "economic assessment" with three indicators. See my proposal under the C-E subdomain. Then in Domain II we would have three subdomains: - Investment and funding - Access and reimbursement - Economic evaluation	
Indicator 1: There is a specific HTA framework for genomic testing in healthcare	14%	22%	64%	•See my comment on combining the three cost-effectiveness subdomains. •it does not need to be specific (you might imagine other domains where the same framework applies) but it needs to be well adapted and easily applicable to genomics	Reformulated	There is a HTA framework to assess genomic tests in healthcare	93%	I don't think there is a HTA framework but NHS England are using Commissioning Through Evaluation via the Genomic Laboratory Hubs to bring new tests to evidence level.	Validated
Item	**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**	
	Not adequate	**Adequate**							

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MLs	1. No central HTA framework for genomic testing 2. HTA framework for genomic testing is developed and approved 3. HTA framework for genomic testing is operationalized 4. HTA framework for genomic testing is implemented in healthcare system 5. HTA framework is implemented, periodically evaluated and optimised, with plan for adoption of novel	29%	71%	•There could be a level stating "under development" or "under discussion" •need for follow up, development and update not considered •The options need to be adjusted if the three cost-effectiveness subdomains are combined as suggested. The best staring point is the options in the c-e subdomain, which might need to be slightly adjusted. •There seems to be an error in the survey. From the MLM framework for this subdomain - should read No central HTA framework for genomic testing HTA framework for genomic testing is developed and approved	Reformulated	1. No HTA framework for genomic testing 2. HTA framework for genomic testing is under development 3. HTA framework for genomic testing is developed and approved 4. HTA framework for genomic testing is implemented in healthcare system 5. HTA framework is implemented, periodically evaluated and optimised, with plan for adoption of novel tools and technologies	100 %	-	Validated

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	tools and technologies			HTA framework for genomic testing is operationalized HTA framework for genomic testing is implemented in healthcare system HTA framework is implemented, periodically evaluated and optimised, with plan for adoption of novel tools and technologies Which I do think is adequate.					

Item	Rating by % of experts			Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
	Disagreement	Neutral	Agreement						
Subdomain 4: Cost-effectiveness Model	22%	14%	64%	•See my comment on combining the three cost-effectiveness subdomains. •I understand that I should express here the situation of our health care system n •This sub domain in my opinion is not needed- the	Reformulated	Cost-effectiveness assessment framework	93%	See my comment on HTA to combine the three indicators.	Validated

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				cost-effectiveness model used by a particular health system will be defined by them in the context of how they assess/evaluate cost-effectiveness for healthcare interventions as part of their decision making. To imply that a specific c/e model needs to be in place to implement genomic medicine is incorrect in my opinion.					
Indicator 1: There is a cost-effectiveness model for use of genomic tests in healthcare	36%	7%	57%	•See my suggestion for the indicator formulation for a combined cost-effectiveness subdomains. •As above - this varies according to the condition. In - it is rigorous in single gene disorders. But less so in terms of testing for cancer. •why limit it to effectiveness; cost benefit could also work	**Reformulated**	There is a framework for cost-effectiveness assessment of genomic tests	93%	If three subdomains combined, then this could be reworded as follows: "There is a framework for economic assessment of genomics in healthcare, such as HTA or cost-effectiveness of tests and treatments and including benefit to the society".	**Validated**

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				instead of cost effectiveness; one of the two could be a good domain and indicator; but I am not an economist so disregard if not feasible! •See previous comment.					
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**						
MLs	1. No cost-effectiveness model 2. Cost-effectiveness model is developed and approved 3. Cost-effectiveness model is under implementation as pilots 4. Cost-effectiveness model is implemented in healthcare systems	36%	64%	•There could be a level stating "under development" or "under discussion" •There are many different scenarios when genomics can be used in healthcare. Some are the same as before (traditional clinical genetics) but many are completely new, i.e. genomics can now be integrated in the diagnostic workup for completely new disease groups across more or	Reformulated	1. There is no framework for cost-effectiveness assessment of genomic tests 2. A framework for cost-effectiveness assessment of genomic tests is under development 3. A framework for cost-effectiveness assessment of specific genomic tests in the healthcare context are under implementation as pilots	93%	There is still confusion in this subdomain. It is fine to ask whether a health system has a framework for cost-effectiveness assessment but the maturity levels are unhelpful. There is also the focus on cost-effectiveness assessment. It is unlikely to be possible nor desirable to undertake full cost-effectiveness evaluation for all genomic tests that are implemented. Health systems will need to prioritise which genomic tests will need this. I still believe this subdomain can be	Validated

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	nationally or regionally 5. Cost-effectiveness model is implemented, periodically evaluated and optimised, with plan for adoption of novel tools and technologies			less all of clinical medicine (personalised or precision medicine). More than one model will thus be needed. •The maturity levels may need to be slightly adjusted if the three cost-effectiveness subdomains are combined as suggested. •Again this is ""all-or-nothing"". It does not allow for there being cost-effectiveness models in place for some disease areas (eg monogenic rare diseases) vs others eg NIPT, Some cancers, pharmacogenomics" •Please see my previous comments - I think this subdomain is not required.		4. A framework for cost-effectiveness assessment of specific genomic tests is implemented in healthcare systems at the national and/or regional levels 5. A framework for cost-effectiveness assessment of genomic tests is implemented, periodically evaluated and optimised, with plan for adoption of novel tools and technologies		removed. There is a great overlap with the HTA subdomain.	
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**

	Disagreement	Neutral	Agreement						
Subdomain 5: Societal (patient/citizen) benefits	21%	0%	79%	•See my comment on combining the three cost-effectiveness subdomains. •Please see my comments on c/e model - so it applies to these as well as these are explicitly linked to C/E models	Reevaluate	-	93%	See my comment on HTA to combine the three indicators or put them under one subdomain.	Validated
Indicator 1: Societal benefits are integrated in economic modelling for genomics	21%	0%	79%	•See my comment on combining the three cost-effectiveness subdomains. •See previous comment.	Reformulated	Societal benefits are considered in economic modelling for genomic medicine	100 %	-	Validated
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**						
MLs	1. Societal benefits are not considered in economic models for genomics in healthcare 2. Societal benefits	23%	77%	•The options need to be adjusted if the three cost-effectiveness subdomains are combined as suggested. The best staring point is the options in the c-e subdomain, which might	Reevaluate	-	100 %	-	Validated

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	are quantified in economic models for genomics in healthcare 3. Societal benefits are integrated in economic models for specific genomic tests 4. Societal benefits are integrated in global genomics economic models for regional or national healthcare systems 5. Societal benefits are integrated in global genomics economic models for regional or national healthcare systems and optimised for novel			need to be slightly adjusted. •Need better definition of what is actually meant by the "integration of societal benefits into the economic model". Not clear to the non-expert in health economics. Perhaps expand the definition of societal benefits e.g. improved quality of life, benefit of "knowing", equity of access - all of which do not have a "direct" economic benefit." •Please see my previous comments					

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	tools and technologies								

N/A: Not Applicable.

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Table 3: Descriptive results for Domain III and respective sub-sections

Round 1					Round 2			
Item	Rating by % of experts		Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
	Not Relevant	Relevant						
Domain III: Legislation and policy	7%	93%	•There are far too many subdomains in this section. Several could be combined. -Data protection and consent -Confidentiality and preventing misuse. Do we even need confidentiality as it is a common issue for all healthcare. - Data reuse and sharing - Research integrity and ethics. No proposals at this stage on possible wording.	Validated with rewording	**Domain III: Ethics, Legislation and policy**	-	-	N/A
Item	**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
	Disagreement	**Neutral**	**Agreement**						

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Subdomain 1: Data protection	7%	7%	86%	•To be combined to read: Data protection *and consent*	Validated	-	-	-	N/A
Indicator 1: There are norms to protect and ensure the lawful, fair and transparent processing of personal data	7%	7%	86%	•To be combined: There are norms to protect and ensure the lawful, fair and transparent processing of personal data *and obtaining the consent adapted to genomics*.	Validated	-	-	-	N/A

Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**						
MLs	1.Norms (e.g. legislation, policies, professional regulations, codes of conduct) do not exist 2.Norms are implemented but	7%	93%	•Need to have an option as to whether the existing norms are adequate and appropriate (eg the quality of the norm)	Validated	-	-	-	N/A

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	insufficient in scope 3.Norms are implemented but not yet consistently enforced 4.Norms are implemented and consistently enforced 5.Norms are implemented, enforced and fit-for-purpose								
Item	**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
	Disagreement	**Neutral**	**Agreement**						
Subdomain 2: Quality of patient care involving genetic/genomic testing	14%	0%	86%	•To be combined and read: Quality *and confidentiality* of patient care involving genetic/genomic testing	**Validated**	-	-	-	N/A
Indicator 1: There are norms ensuring the quality	21%	0%	79%	•When combined, to read: There are	**Reformulated***	There are norms ensuring the quality **of** genetic/	-	-	N/A

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genetic/genomic testing services (e.g. professional codes and self-regulatory bodies)					norms ensuring the quality *and confidentiality* of genetic/genomic testing services (e.g. professional codes and self-regulatory bodies) •just add "of" (quality of genomic testing)		genomic testing services (e.g. professional codes and self-regulatory bodies)			
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**	
		Not adequate	**Adequate**							
MLs	1.Norms (e.g. legislation, policies, professional regulations, codes of conduct) do not exist 2.Norms are implemented but insufficient in scope 3.Norms are	7%	93%	•I believe this is too specific	Validated	-	-	-	N/A	

	implemented but not yet consistently enforced 4.Norms are implemented and consistently enforced 5.Norms are implemented, enforced and fit-for-purpose								
Item	**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
	Disagreement	**Neutral**	**Agreement**						
Subdomain 3: Special rules for vulnerable groups (e.g. minors, adults with diminished capacity)	14%	7%	79%	•Counselling to be added: Special rules *and counselling* for vulnerable groups (e.g. minors, adults with diminished capacity) •Should you also think about diversity in terms of ethnicity/re	Reformulated	Special rules and counselling for vulnerable groups	100 %	-	Validated

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				cent ancestry as well?					
Indicator 1: There are special rules to ensure that vulnerable groups have access to genetic/genomic testing, with appropriate protections to avoid their exploitation	14%	7%	79%	•To read: There are special rules to ensure that vulnerable groups have access to genetic/genomic testing, with appropriate *counselling and* protections to avoid their exploitation •I would suppress "to avoid their exploitation" because it is too restrictive; may be if you want to specify reasons, "to fully respect their rights and especially avoid their exploitation"	Reformulated	There are special rules to ensure that vulnerable groups have access to genetic/genomic testing, with counselling and appropriate protections to fully respect their rights and avoid their exploitation	93%	-	Validated
Item	**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**	
	Not adequate	**Adequate**							

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MLs	1.Norms (e.g. legislation, policies, professional regulations, codes of conduct) do not exist 2.Norms are implemented but insufficient in scope 3.Norms are implemented but not yet consistently enforced 4.Norms are implemented and consistently enforced 5.Norms are implemented, enforced and fit-for-purpose.	23%	77%	•There could be a level stating "under development" or "under discussion" •I think these norms should not be specific to genetic data, but to health data and digital health interventions/therapeutics •I think protection of vulnerable groups should mandatory and equitably accessible	Reevaluate	-	100 %	-	Validated

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Item		Rating by % of experts			Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
		Disagreement	Neutral	Agreement						
Subdomain 4: Consent to genetic/genomic testing and genetic counselling		7%	7%	86%	•Combined with data protection	Validated	-	-	-	N/A
Indicator 1: There are norms to ensure appropriate consent is obtained and counselling is provided in relation to genetic/genomic testing		0%	7%	93%	-	Validated	-	-	-	N/A
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**							
MLs	1.Norms (e.g. legislation, policies, professional regulations, codes of conduct) do not exist 2.Norms are implemented but insufficie	23%	77%		•There could be a level stating "under development" or "under discussion" •Consent should be universal and offer opportunity for research to all •What is meant by	Reevaluate	-	100 %	-	Validated

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	nt in scope 3.Norms are impleme nted but not yet consisten tly enforced 4.Norms are impleme nted and consisten tly enforced 5.Norms are impleme nted, enforced and fit-for-pu rpose.			enforced in this context?					
Item	**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agre e %**	**Comments**	**Decision after Round 2**
	Disagree ment	**Neut ral**	**Agreem ent**						
Subdomain 5: Confidentiality, professional secrecy	7%	7%	86%	•Combined with Quality of care.	Validate d	-	-	-	N/A
Indicator 1: There are norms protecting the confidentiality of patient genetic/genomic test results, and clarifying where family members may have rights to	8%	8%	84%	•the formulation gives the impression that only family members are concerned; may be say "and	Reformul ated	There are norms protecting the confidentiality of patient genetic/genomic test results, and specifically clarifying where family members may have rights	100 %	-	Validated

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access these results					specifically clarifying where family members may have rights to access these results"		to access these results			
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**							
MLs	1.Norms (e.g. legislation, policies, professional regulations, codes of conduct) do not exist 2.Norms are implemented but insufficient in scope 3.Norms are implemented but not yet consistently enforced 4.Norms are	14%	86%		•There could be a level stating "under development" or "under discussion" •Confidentiality should be universally respected	Validated	-	-	-	N/A

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	implemented and consistently enforced 5.Norms are implemented, enforced and fit-for-purpose.								

Item	Rating by % of experts			Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
	Disagreement	Neutral	Agreement						
Subdomain 6: Preventing mis-use of genetic/genomic results	0%	7%	93%	-	Validated	-	-	-	N/A
Indicator 1: There are norms limiting genetic/genomic testing to legitimate purposes and preventing mis-use (e.g. no employer/insurer discrimination)	0%	7%	93%	-	Validated	-	-	-	N/A

Item		Rating by % of experts		Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
		Not adequate	Adequate						
MLs	1.Norms (e.g. legislation, policies, professional	23%	77%	•There could be a level stating "under development" or "under discussion"	Reevaluate	-	100 %	-	Validated

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	regulations, codes of conduct) do not exist 2.Norms are implemented but insufficient in scope 3.Norms are implemented but not yet consistently enforced 4.Norms are implemented and consistently enforced 5.Norms are implemented, enforced and fit-for-purpose.			--> generally this could be a level in most of the questions. •I believe these norms should not be addressed separately. The idea that insurers and employers as "the bad guys" is not always realistic, nor the best at time to foster societally use of what comes out of genetic information, particularly as well see and know that more and more other "omics" are equally relevant •Failure to universally address this may lead to reduced					

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				participant engagement					
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Disagreement	**Neutral**	**Agreement**						
Subdomain 7: Health data reuse and innovation		7%	7%	86%	•Combined with the next: Health data reuse, *sharing* and innovation	Validated	-	-	-	N/A
Indicator 1: There is a national strategy for promoting health research and innovation, and associated data protection rules allowing sharing and further processing of health/genetic data for research or treating other patients		7%	7%	86%	•the notion of transparency, public information about the use of data and may be leave open the use for training and education should be considered, unless it is clear that this is Validated in "treating other patients"?	Validated	-	-	-	N/A
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**							
MLs	1.Norms (e.g. legislation, policies,	7%	93%		•Again need to be more specific about the quality of	Validated	-	-	-	N/A

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	professional regulations, codes of conduct) do not exist 2.Norms are implemented but insufficient in scope 3.Norms are implemented but not yet consistently enforced 4.Norms are implemented and consistently enforced 5.Norms are implemented, enforced and fit-for-purpose.			the norms themselves. Are they appropriate by international standards - which is different to being "inadequate in scope". This will apply across the whole domain.					
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Disagreement	**Neutral**	**Agreement**						

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Subdomain 8: Data sharing	7%	0%	93%	•Validated in the previous.	**Validated**	-	-	-	N/A
Indicator 1: There are norms promoting genomic data sharing by researchers/healthcare providers	23%	0%	77%	•facilitating rather than promoting; and also the international dimension could be introduced somewhere, as data sharing can be organised locally/nationally but the facilitation of international data sharing is important •Needs further specification. There are norms promoting appropriate and legitimate genomic data sharing by researchers/healthcare providers". •Data sharing promotes/implies a	**Reformulated**	There are norms facilitating genomic data sharing by researchers and/or healthcare providers, at the national and international levels	100 %	-	**Validated**

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					model of data movement for some people. - secondary use of healthcare genomics for research is more open.					
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**							
MLs	1.Norms (e.g. legislation, policies, professional regulations, codes of conduct) do not exist 2.Norms are implemented but insufficient in scope 3.Norms are implemented but not yet consistently enforced 4.Norms	0%	100%		-	Validated	-	-	-	N/A

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	are implemented and consistently enforced 5.Norms are implemented, enforced and fit-for-purpose.								
Item	**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
	Disagreement	**Neutral**	**Agreement**						
Subdomain 9: Research Integrity	14%	7%	79%	To be combine and read: Research integrity *and ethics*	**Reevaluate**	-	100 %	-	**Validated**
Indicator 1: There are norms and processes ensuring the ethical and scientific integrity of genomic research	14%	7%	79%	•To read as combined: There are *ethical and scientific integrity* norms and processes *(and possibly bodies) adapted to… multi-centre genetic and* genomic research •I agree on the substance;	**Reformulated**	There are norms and processes ensuring the ethical practice and scientific integrity of genomic research	100 %	-	**Validated**

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					but the formulation would be better if you say "There are norms and processes ensuring the ethical practice and scientific integrity of genomic research" (add practice or exercise or equivalent as the ethical integrity of research sounds a bit strange)					
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**							
MLs	1.Norms (e.g. legislation, policies, professional regulations, codes of conduct) do not exist 2.Norms are	7%	93%		•Integrity should be universal	Validated	-	-	-	N/A

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	implemented but insufficient in scope 3.Norms are implemented but not yet consistently enforced 4.Norms are implemented and consistently enforced 5.Norms are implemented, enforced and fit-for-purpose.								

Item	Rating by % of experts			Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
	Disagreement	Neutral	Agreement						
Subdomain 10: Coordinated research ethics oversight	7%	7%	86%	•Combined with the previous	Validated	-	-	-	N/A
Indicator 1: There is a national research ethics committee or network to effectively and efficiently oversee the conduct of	0%	7%	93%	-	Validated with rewording	There is a national (or regional if appropriate) research ethics committee or network to effectively and	-	-	N/A

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multicentre genetic/genomic studies						efficiently oversee the conduct of multicentre genetic/genomic studies			
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**						
MLs	1.Norms (e.g. legislation, policies, professional regulations, codes of conduct) do not exist 2.Norms are implemented but insufficient in scope 3.Norms are implemented but not yet consistently enforced 4.Norms are implemented and consistently	29%	71%	•It is likely that there are national laws and regulations in place, but ethical committees may be local and not national/regional, and may not have common interpretation of regulations. There may not be one authority from who to apply ethical permits for national studies. Local vs national ethical committees should be Validated as options when	Reformulated	1. A framework for national or regional research ethics committee to oversee multicentre genetic/genomic studies does not exist 2. A framework for national or regional research ethics committee to oversee multicentre genetic/genomic studies is under development 3. A framework for national or regional research ethics committee to oversee multicentre genetic/genomic studies exists, but is not consistently enforced 4.A framework for national or	100 %	-	Validated

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	enforced 5.Norms are impleme nted, enforced and fit-for-pu rpose.			measuring maturity. •Although I don't necessarily agree on a ""dedicated"" centre for genetics/ge nomics studies - i think there such be a institution/b ody or network for multicentric biomedical research (including genomics), I think the existence of Norms and their level of implementat ion and fitness is not the best indicator for maturity of "the existence" of a national research ethics committee, or network.... RATHER its Capacity, its level of internal		regional research ethics committee to oversee multicentre genetic/genomic studies is implemented and consistently enforced 5. A framework for national or regional research ethics committee to oversee multicentre genetic/genomic studies is implemented, enforced and fit for purpose			

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				organisation and power for norm settling, conflict resolution and the SPEED of decision making and its participatory nature. •National ethics may need to be regional but this must be consistent •here I would use the word "framework" rather than "norms"					
Item	**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
	Disagreement	**Neutral**	**Agreement**						
Subdomain 11: Biobanking	0%	0%	100%	-	**Validated**	-	-	-	N/A
Indicator 1: There are norms addressing the accreditation, registration, supervision, secure storage, and responsible use of human biological samples	7%	0%	**93%**	•I would add "exchange" or "sharing" or specify it is Validated in the "responsible use, as the sharing chapter	**Validated with rewording**	There are norms addressing the accreditation, registration, supervision, secure storage, and responsible use (including exchange and sharing) of	-	-	N/A

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					before only address data		human biological samples			
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**							
MLs	1.Norms (e.g. legislation, policies, professional regulations, codes of conduct) do not exist 2.Norms are implemented but insufficient in scope 3.Norms are implemented but not yet consistently enforced 4.Norms are implemented and consistently enforced 5.Norms are	7%	**93%**		•This should be universal.	**Validated**	-	-	-	N/A

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	implemented, enforced and fit-for-purpose.								

*Despite classified as “Reformulated”, this item was not included in Round 2 as the only comment asked for the introduction of the word “of” missing in the previous phrasing; N/A: Not Applicable.

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Table 4: Descriptive results for Domain IV and respective sub-sections

Round 1						Round 2			
Item	Rating by % of experts		Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2	
	Not Relevant	Relevant							
Domain IV: Public awareness and acceptance	0%	100%	-	Validated	-	-	-	N/A	
Item	**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
	Disagreement	**Neutral**	**Agreement**						
Subdomain 1: Awareness	14%	0%	86%	•Why is this needed more than for any other innovative area of medicine? Awareness yes, but general literacy programmes should be through formal education systems. This should not be confused with the necessary information requirements for the public to make decisions and access genomic medicine	Validated	-	-	-	N/A

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				services. Suggest this is rewritten to reflect this point.					
Indicator 1: There are literacy programmes or campaigns on genomic medicine	29%	0%	71%	•To increase the equality, there could be an indicator measuring how well educational programs reach of minority populations •This should focus on surveying the situation, campaigning would then be the third subdomain. Suggestion: There are surveys on literacy on genomic medicine among the population and professionals. •See previous comment.	**Reformulated**	There are literacy programmes or campaigns on genomic medicine with monitored impact on awareness	86%	-I am afraid I have not changed my mind on this sub domain - as previously stated. Why is this needed more than for any other innovative area of medicine? Awareness yes, but general literacy programmes should be through formal education systems. This should not be confused with the necessary information requirements for the public to make decisions and access genomic medicine services. Suggest this is rewritten	**Validated**

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									to reflect this point. I think it remains important to distinguish information for individuals to access and use services safely and in an informed manner including genomic applications and that of general population literacy programmes - at the moment it reads as the latter.	
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**	
		Not adequate	**Adequate**							
MLs	1. No 2. Literacy programmes or campaigns are available locally as a bottom up initiative, on particular topics 3. Strategy for literacy programmes or	21%	79%	•If reformulated, then ML 1. No.; ML 2. Literacy programs or campaigns are available locally as a bottom up initiative, on particular topics.; ML 3. Strategy for	Reformulated	1. No 2. Literacy programmes or campaigns are available locally as a bottom up initiative, on particular topics 3. Strategy for literacy programmes or campaigns	86%	-Maturity level 5 is not easy understand and should be rephrased. -See earlier comments.	Validated	

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	campaigns is defined and under implementation 4. Strategy for literacy programmes or campaigns is defined and widely implemented at national level, with dedicated funds 5. Strategy for literacy programmes or campaigns is widely implemented at national level, with regular update of topics to include innovation, and with dedicated funds			literacy programs or campaigns is defined and under implementation.; ML 4. Strategy for literacy programs or campaigns is defined and widely implemented at national level, with dedicated funds. 1. No; 2. A survey is being planned; 3. Basic information exists through a survey ; 4. Several ad-hoc surveys have been carried out; 5. There is a systematic programme for regular genomic literacy surveys. •See previous comments •I think this model wont fit some regions/place		targeting specific audiences is defined, based on genomic literacy surveys, and under implementation 4. Strategy for literacy programmes or campaigns targeting specific audiences is defined and widely implemented, with dedicated funds 5. Strategy for literacy programmes or campaigns is widely implemented, with regular evaluation and monitoring of impact on awareness, update of topics to include innovation, and with dedicated funds			

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				s - I don't think national is the right term rather different audiences perhaps, and I wonder if there should be a clinical outreach audience as well					
Item	**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
	Disagreement	**Neutral**	**Agreement**						
Subdomain 2: Acceptance	7%	0%	93%	•The subdomain and indicator is confusing. Acceptance is the wrong term to capture adequate awareness and being informed of what genomic medicine can provide in terms of clinical utility for an individual and a population. Please reconsider the subdomains and indicators.	**Validated**	-	-	-	N/A

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Indicator 1: Synergies with patient associations are well established		7%	7%	86%	•See previous comment	Validated	-	-	-	N/A
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**	
		Not adequate	**Adequate**							
MLs	1. No 2. Available locally as a bottom up initiative with specific associations 3. Strategy for engaging patient associations in genomic medicine issues is defined and under implementation 4. Strategy for engaging patient associations in genomic medicine issues is widely implemented at national level, with dedicated funds 5. Strategy for engaging patient associations in genomic medicine	21%	79%	•Is engagement and awareness limited to patient advocacy groups. Need consideration of other audiences. •See previous comments •Again, I worry about patient associations being a very "Anglo" thing - I am not sure this maps to every country well, and I don't want the cohesion of - say - Finland's approach to healthcare delivery and care be penalised by	Reevaluate	-	100 %	-	Validated	

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	issues is widely implemented at national level, with dedicated funds, regular monitoring and updates to include innovation			the way we frame this.					
Item	**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
	Disagreement	**Neutral**	**Agreement**						
Subdomain 3: Communication to the general public	14%	0%	86%	•it could be specified that the communication strategy integrates interactive tools as it seems to be only "information" and rather passive as it is formulated	Validated	-	-	-	N/A
Indicator 1: There is a communication strategy for genomic medicine	29%	14%	57%	•To increase the equality there could be an indicator how well the communication strategy reaches the minority populations, which may be less educated and have a different trust level	Reevaluate	-	100 %	-	Validated

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					•This should be broadened: There is a communicatio n strategy for genomic medicine implemented through literacy programmes or campaigns." •same the indicator could Validated tools for active involvement of the public					
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agr ee %**	**Comments**	**Decision after Round 2**	
		Not adequate	**Adequate**							
MLs	1. No 2. Available locally as a bottom up initiative with specific target audiences 3. Global strategy for communication to the public is under development 4. Strategy for communication is widely	21%	**79%**	•Slight modification: ML 3. A strategy for communicatio n to the public is under development. ; ML 4. A strategy for communicatio n is widely implemented at national level, with	**Reformul ated**	1. No 2. Available locally as a bottom up initiative with specific target audiences 3. A global strategy for communicati on with the public is under development	100 %	-	**Validated**	

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	implemented at national level, with dedicated funds 5. Strategy for communication is widely implemented at national level, with dedicated funds, regular monitoring and updates to Validated innovation			dedicated funds." •see my previous comment •Same comment, I worry about "national" here and I worry that the paths for communicatio n and responsible societal behaviour is quite varied.		4. A global strategy for communicati on with the public is widely implemented , with dedicated funds 5. A global strategy for communicati on with the public is widely implemented , with dedicated funds and regular monitoring, and includes tools for active involvement of the public in general, minorities and youth in particular			

N/A: Not Applicable.

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Table 5: Descriptive results for Domain V and respective sub-sections

Item		Rating by % of experts		Comments	Decision after Round 1
		Not Relevant	Relevant		
Domain V: Workforce skills and organization		0%	100%	-	Validated
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**
		Disagreement	**Neutral**	**Agreement**	
Subdomain 1: Education		14%	0%	86%	•Should this read: University education in medicine and health-related professions"	Validated
Indicator 1: Genomics is integrated in general university *curricula* for medical doctors		7%	0%	93%	•There isn't any mandatory subject matter in Genomics in the Faculties of Medicine in - with a few exceptions	Validated
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**
		Not adequate	**Adequate**		
MLs	1. No or *ad hoc* 2. Needs assessed, gaps identified, training options under development 3. Training available, under implementation 4. Training available and widely implemented 5. Training *curricula* regularly updated to incorporate novel technologies and tools	7%	93%	•Life-long education of medical doctors on genome medicine could be Validated in these options or made a separate indicator	Validated
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**

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		Disagreement	Neutral	Agreement		
Indicator 2: Genomics is integrated in general *curricula* for nurses		7%	0%	93%	•The same. No subject matters on the topic in -	Validated
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**
		Not adequate		**Adequate**		
MLs	1. No or *ad hoc* 2. Needs assessed, gaps identified, training options under development 3. Training available, under implementation 4. Training available and widely implemented 5. Training *curricula* regularly updated to incorporate novel technologies and tools	0%		100%	-	Validated
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**
		Disagreement	**Neutral**	**Agreement**		
Indicator 3: Genomics is integrated in general curricula for pharmacists		7%	0%	93%	•Not at all integrated as a subject matter even as optional	Validated
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**
		Not adequate		**Adequate**		
MLs	1. No or *ad hoc* 2. Needs assessed, gaps	0%		100%	-	Validated

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	identified, training options under development 3. Training available, under implementation 4. Training available and widely implemented 5. Training *curricula* regularly updated to incorporate novel technologies and tools				

Item	Rating by % of experts			Comments	Decision after Round 1
	Disagreement	Neutral	Agreemen		
Subdomain 2: Careers in genomic medicine	7%	0%	93%	-	Validated
Indicator 1: There are officially recognized professional titles and career paths for genomic medicine	7%	7%	86%	-	Validated

Item		Rating by % of experts		Comments	Decision after Round 1
		Not adequate	Adequate		
MLs	1. No workforce strategy or policy that recognizes genomic medicine professionals, and distribution of professionals is *ad hoc* 2. Strategy or policy for genomic medicine professionals is proposed and under review 3. Strategy or policy for genomic medicine professionals is approved and under implementation 4. Strategy or policy	0%	100%	-	Validated

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	for genomic medicine professionals is implemented, with full recognition and acceptance of career paths 5. Professional titles and career paths for genomic medicine professionals are flexible and regularly updated to incorporate needs from novel technologies and tools				

Item	Rating by % of experts			Comments	Decision after Round 1
	Disagreement	Neutral	Agreement		
Indicator 2: There are training programmes for genetic counselling	7%	7%	86%	• At least there are not official training courses, except some endorsed by the -	Validated

Item	Rating by % of experts		Comments	Decision after Round 1
	Not adequate	Adequate		

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MLs	1. No or *ad hoc* 2. Needs assessed, gaps identified, training options under development 3. Training graduates are available but not yet deployed 4. Training graduates are deployed, but essential personnel gaps remain 5. Sufficient numbers of training graduates are available to support evolving national/regional needs	7%	93%	•Training available but insufficient in scope would be an alternative indicator.	Validated

Item	Rating by % of experts			Comments	Decision after Round 1
	Disagreement	Neutral	Agreement		
Indicator 3: There are life-long or continuing education programmes in genomic medicine for different healthcare professionals	7%	0%	93%	•Nor regularly stablished. Only optional	Validated

Item		Rating by % of experts		Comments	Decision after Round 1
		Not adequate	Adequate		
MLs	1. No or *ad hoc* 2. Needs assessed, gaps identified, training options under development 3. Training available, under implementation 4. Training available and widely	0%	100%	-	Validated

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	implemented 5. Training *curricula* regularly updated to incorporate novel technologies and tools				
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**
		Disagreement	**Neutral**	**Agreement**	
Subdomain 3: Policy makers		14%	0%	86%	•I am a bit doubtful of the usefulness of this question. In any case, I would reformulate it to read (also reverse the order - managers mentioned first): Healthcare managers and health policy makers"	Validated
Indicator 1: There are programmes for policy makers and healthcare managers to raise awareness on genomic medicine and its implications for healthcare		7%	7%	86%	-	Validated
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**
		Not adequate	**Adequate**		
MLs	1. No or *ad hoc* 2. Needs assessed, gaps identified, program options under development 3. Programmes available, under implementation 4. Fully functional implementation of programmes at national level 5. Programmes are implemented and periodically evaluated for inclusion of novel tools and technologies	7%	93%	•Not sure training is the correct term? As it is a fast evolving field - it is about raising awareness and keeping these key groups informed of developments and applications in genomic medicine - this is about live appropriate information dissemination.	Validated

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Table 6: Descriptive results for Domain VI and respective sub-sections

Round 1						Round 2			
Item	Rating by % of experts		Comments	Decision After Round 1		Rewording proposal	Agree %	Comments	Decision after Round 2
	Not Relevant	Relevant							
Domain VI: Clinical organisation, infrastructure and tools	0%	100%	-	Validated		-	-	-	N/A
Item	**Rating by % of experts**			**Comments**	**Decision After Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
	Disagreement	**Neutral**	**Agreement**						
Subdomain 1: Information and Communications Technology (ICT) tools for clinical decision	14%	0%	86%	•I would focus here on *advanced* tools for genomics, and not include EHR or other normal healthcare tools. E.g. Use of advanced tools on genomics.	Validated	-	-	-	N/A
Indicator 1: There are ICT tools for clinical interpretation of genomic results implemented in public hospitals and clinics	21%	0%	79%	•Following from the subdomain, I would not Validated EHR (as in the tip) or other normal healthcare tools. E.g. Clinicians have access to and use of advanced (including AI-based) tools on genomics for clinical interpretation and decision-making.	Reformulated	There are ICT tools supporting clinical interpretation of genomic results, clinical decision-making and communication with the patient implemented in public hospitals and clinics	93%	The basic e-health tools should not be enough, suggestion: "There are ICT tools supporting SPECIFICALLY clinical interpretation of genomic results,..."	Validated

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				•I agree but would add the dimension that the tools are not only for interpretation but Validated elements for communicating/explaining the results to patients; just interpretation is too restrictive •Not in most of cases. Only very few exceptions					
Item	**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**	
	Not adequate	**Adequate**							

MLs	1. ICT tools not available 2. ICT tools available in selected hospitals, frequently associated with research projects 3. ICT tools under wider implementation in healthcare systems following a strategy for genomic medicine 4. ICT tools implemented where needed as part of national/regional health systems strategies for genomic medicine 5. ICT tools implemented and periodically evaluated and optimised for novel tools and updates	0%	100%	-	Validated	-	-	-	N/A
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**

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	Disagreement	Neutral	Agreement						
Subdomain 2: Multidisciplinary teams	7%	0%	93%	•Few exceptions in the country	Validated	-	-	-	N/A
Indicator 1: Clinical teams for genomic medicine are multidisciplinary and include ICT and biomedical experts	14%	0%	86%	•as you specify some elements of the interdisciplinarity (ICT and biomedical expert) I would also specify the presence of a psychology expert	Validated with rewording	Clinical teams for genomic medicine are multidisciplinary and include ICT, biomedical and psychology experts	-	-	N/A

Item		Rating by % of experts		Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
		Not adequate	Adequate						
MLs	1. Not available 2. Teams are assembled in some hospitals as a bottom up initiative, but not all areas are covered or necessary tools are available 3. Guidelines for assembling multidisciplinary teams exist, and	0%	100%	-	Validated	-	-	-	N/A

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	there are referral networks at regional/local level. 4. Guidelines for assembling multidisciplinary teams and referral networks are implemented at regional/national level, aligned with a strategy for genomics in healthcare and with dedicated funding 5. Multidisciplinary teams are the norm for implementation of national genomics in medicine strategy and the guidelines for their assembly and operation, and referral networks, are reviewed and optimised periodically								

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Item	Rating by % of experts			Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
	Disagreement	Neutral	Agreement						
Subdomain 3: Turnover/uptake of novel tools and technology	14%	7%	79%	•Could we simplify: Uptake of novel genomics technologies" •This subdomain - is too vague. There will always be a challenge in adopting the appropriate interventions in a timely manner across the whole of medicine. I think this subdomain should be about there being a process for considering and implementing new technologies and decision making tools and that this will Validated those for genomic medicine.	Reformulated	Uptake of novel tools and technologies for genomics	100 %	-	Validated
Indicator 1: Adoption of novel technologies and software tools to support clinical decisions is fit-for-purpose	7%	7%	86%	•See previous comment	Validated	-	-	-	N/A
Item	**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**

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		Not adequate	Adequate						
MLs	1. No or ad hoc 2. Novel technologies and tools are selected and implemented locally (e.g. hospital, laboratory) 3. There are plans and processes for adoption of novel technologies and tools to support clinical decision making, but not widely implemented at regional/national levels 4.Plans and processes for adoption of novel technologies and tools to support clinical decision making are centralised at the regional/national levels, and aligned with a national	14%	86%	•Funding should be Validated in the maturity level options •See previous comment	Validated	-	-	-	N/A

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	strategy for genomics in healthcare 5.Plans and processes for adoption of novel technologies and tools to support clinical decision making are centralised at the regional/national levels, and aligned with a national strategy for genomics in healthcare, and with international standards								

Item	Rating by % of experts			Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
	Disagreement	Neutral	Agreement						
Subdomain 4: Synergies with research	14%	7%	79%	•I agree generally but synergy is may be too demanding at the start; organised link with research might be more applicable without reaching at first a true synergy; may be add an indicator to specify if it is	Reevaluate	-	100 %	-	Validated

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				synergy yet or not yet! •I do not understand what is meant by this subdomain and indicator? Do you mean there is close collaboration between clinical services and academia?					
Indicator 1: There are processes established for the integration of the clinics with research outcomes		7%	7%	86%	•See previous comment.	Validated	-	-	-	N/A
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**	
		Not adequate	**Adequate**							
MLs	1. No or ad hoc 2. Implemented at a local level, depending on free will 3. Implemented at local and regional level according to a local strategy for integrating stakeholders and partnerships 4.	14%	86%	•See previous comment •I think using the phrase "free will" is a bit odd here.	Validated with rewording	1. No or ad hoc 2. Implemented at a local level, depending on individual initiative 3. Implemented at local and regional level according to a local strategy for integrating stakeholders and partnerships 4. Implemented	-	-	N/A	

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	Implemented at national level with well established partnerships, support from public funds and dedicated budget 5. Implemented at national and international level with well established partnerships, periodically evaluated, support from public funds and dedicated budget					at national level with well established partnerships, support from public funds and dedicated budget 5. Implemented at national and international level with well established partnerships, periodically evaluated, support from public funds and dedicated budget			

Item	Rating by % of experts			Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
	Disagreement	Neutral	Agreement						
Subdomain 5: Synergies with industry	14%	7%	**79%**	•same comment regarding the use of "synergy"; there may be other steps before reaching synergy •The term integration is perhaps incorrect in health systems - collaboration,	**Reformulated**	Partnership with industry	100 %	-	**Validated**

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				effective partnerships are alternative terms to consider?					
Indicator 1: There is integration of stakeholders and partnerships from the industry sector		14%	7%	79%	•I would add the "transparency" element here as it can strongly influence the adhesion of the public to collaboration with industry; may be in indicators? •See previous comment.	Reformulated	There are effective partnerships with stakeholders from the industry sector	93%	As the significance and role of the industrial partnerships differs between countries, a better indicator would be level of implementation of a national strategy or framework for industrial partnerships and stakeholders.	Validated
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**						
MLs	1. No or ad hoc 2. Implemented at a local level, depending on free will 3. Implemented at local and	14%	86%	•See previous comment •I think the use of the phrase "free will" is a bit odd	Validated with rewording	1. No or ad hoc 2. Implemented at a local level, depending on individual initiative 3. Implemented at local and	-	-	N/A

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	regional level according to a local strategy for integrating stakeholders and partnerships from the industry sector 4. Implemented at national level with well established partnerships, according to a national strategy for integration of industry stakeholders 5. Implemented with well established national and international partnerships, according to a national strategy for integration of industry stakeholders					regional level according to a local strategy for integrating stakeholders and partnerships from the industry sector 4. Implemented at national level with well established partnerships, according to a national strategy for integration of industry stakeholders 5. Implemented with well established national and international partnerships, according to a national strategy for integration of industry stakeholders			

N/A: Not Applicable.

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Table 7: Descriptive results for Domain VII and respective sub-sections

Item		Rating by % of experts		Comments	Decision after Round 1
		Not Relevant	Relevant		
Domain VII: Clinical genomics guidelines and infrastructure		7%	93%	•"Sequencing/ genotyping infrastructure" would better fit the previous domain. The name of the 7th domain could be simply Clinical Genomic Guidelines"". A related question is whether we need ""clinical"" in the names of the two domains. I understand that it seeks to drive thinking towards clinical implementation but this is still rather rare. Thus ""genomic organisation, infrastructure and tools"" and ""Genomic guidelines..."" could be better expressions.	Validated
Item		**Rating by % of experts**			**Decision after Round 1**
		Disagreement	**Neutral**	**Agreement**	
Subdomain 1: Sequencing/genotyping infrastructure		7%	7%	86%	•To be moved to the previous domain. The subdomain as such is ok.	Validated
Indicator 1: Genomic centres are established		7%	0%	93%	-	Validated
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**
		Not adequate	**Adequate**		
MLs	1. No 2. Genomic centres are local (e.g. hospital,	7%	93%	•Again, this presupposes that organisational centres is the right model. I would	Validated

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	laboratory) 3. Genomic centres infrastructure networks are under development, to include common working guidelines and shared policies 4. Genomic centres infrastructure networks are implemented at the regional/national levels, and operate under common guidelines and policies 5. Genomic centres infrastructure networks are implemented at the regional/national levels, and operate under common guidelines and policies and aligned with global standards			draw upon radiology as a discipline for this.	

Item	Rating by % of experts			Comments	Decision after Round 1
	Disagreement	Neutral	Agreement		
Subdomain 2: Sequencing guidelines	0%	7%	93%	-	Validated
Indicator 1: Guidelines for sequencing are defined	0%	7%	93%	-	Validated

Item		Rating by % of experts		Comments	Decision after Round 1
		Not adequate	Adequate		
MLs	1. No 2. Guidelines for sequencing data generation are available locally (e.g. hospital, laboratory, project)	0%	100%	-	Validated

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	3. Local level genomic sequence generation for clinical use is aligned with ISO lab accreditation/protocols 4. Genomic sequence generation is coordinated at regional/national level and aligned with ISO lab accreditation/protocols 5. Genomic sequence generation at regional/national level is governed in alignment with ISO accreditation/protocols, reviewed periodically, and in line with international standards				

Item	Rating by % of experts			Comments	Decision after Round 1
	Disagreement	Neutral	Agreement		
Subdomain 3: Primary bioinformatics analysis	0%	0%	100%	-	Validated
Indicator 1: Guidelines for genomic data analysis are defined	0%	0%	100%	-	Validated

Item		Rating by % of experts		Comments	Decision after Round 1
		Not adequate	Adequate		
MLs	1. No 2. Guidelines for genomic data analysis are available at local/organisation level 3. Guidelines for genomic data analysis are available at the	7%	93%	•Similar to ISO previously, I think you can make explicit reference to GA4GH standards here.	Validated

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	regional/national level 4. Standardised genomic analysis guidelines are implemented at national level and reviewed periodically 5. Standardised genomic analysis guidelines are implemented at national level, reviewed periodically and aligned with global standards				

Item	Rating by % of experts			Comments	Decision after Round 1
	Disagreement	Neutral	Agreement		
Subdomain 4: Structure of sequence-associated metadata	0%	7%	93%	-	Validated
Indicator 1: Guidelines for sequence metadata structure to support clinical interpretation are established	0%	7%	93%	-	Validated

Item		Rating by % of experts		Comments	Decision after Round 1
		Not adequate	Adequate		
MLs	1. No 2. Guidelines to structure metadata to meet clinical use cases are defined locally (e.g. hospital, laboratory) 3. Guidelines to structure metadata to meet clinical use cases are defined regionally/nationally 4. Standardised guidelines to structure metadata to meet clinical use cases are implemented at the	7%	93%	•Similar to previous answer, I think you can make explicit use of a phrase "such as GA4GH standards" here.	Validated

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	national level and are reviewed periodically 5.International guidelines to structure metadata to meet clinical use cases are followed, implemented at the national level and are reviewed periodically				
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**
		Disagreement	**Neutral**	**Agreement**	
Subdomain 5: Clinical interpretation		0%	0%	**100%**	-	**Validated**
Indicator 1: Guidelines for clinical interpretation of genomic results are defined		0%	0%	**100%**	-	**Validated**
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**
		Not adequate	**Adequate**		
MLs	1. No 2. Guidelines for clinical interpretation of genomic results are defined locally (e.g. hospital, laboratory) 3. Guidelines for clinical interpretation of genomic results are defined regionally/nationally (e.g. by national genetics societies) 4. Guidelines for clinical interpretation of genomic results from internationally recognised bodies (e.g.	7%	**93%**	•I agree generally but if you give examples of internationally recognised bodies you should not give only one example from USA (ACGM) but Validated several bodies from different regions in the world, including European ones	**Validated**

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	ACMG, ClinGen) are implemented nationally 5. Guidelines for clinical interpretation of genomic results from internationally recognised bodies are implemented nationally, and there interactions with these international bodies for guideline definition for specific diseases (e.g. ACMG, ClinGen)				
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**
		Disagreement	**Neutral**	**Agreement**	
Subdomain 6: Clinical reporting		0%	0%	**100%**	-	**Validated**
Indicator 1: Guidelines for clinical reporting of genomic results are defined		7%	0%	**93%**	•for this reporting phase it would be important to mention that establishing a link with relevant patient associations is Validated; may be in levels of maturity?	**Validated**
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**
		Not adequate	**Adequate**		
MLs	1. No 2. Consistent clinical reporting guidelines are developed at an organisation level 3. National best practices for clinical reporting are defined and monitored, but not consistently enforced 4. National best practices for clinical	7%	**93%**	•What is meant by the term enforced in this context. Suggest remove enforced in these and then fine.	**Validated**

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	reporting are enforced and monitored 5. Guidelines for clinical reporting are enforced at the national levels, in alignment with international standards and regularly reviewed based on changes in technological, regulatory and ethical considerations				

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Table 8: Descriptive results for Domain VIII and respective sub-sections

Round 1					Round 2			
Item	Rating by % of experts		Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
	Not Relevant	Relevant						
Domain VIII: Data management, standards and infrastructure	7%	93%	•The elements of the Domain VIII are obviously important to understand the maturity, however, I believe that this domain should be broader then data management standards and infrastructure, there are aspects of ehealth/digital health maturity more broad that as equally relevant. De way EHRs for example are organised, or how MS have, or not, the capacity to aggregate about an individual from different organisations, is, to me equally critical to the capacity to compare genomics data with outcomes, clinical profile, behaviours and	Validated	-	-	-	N/A

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			risk. So maybe a broader term - ehealth maturity at national and local level, or "data management" and "clinical information systems usage" standards and infra.... could be a better concept					

Item	Rating by % of experts			Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
	Disagreement	Neutral	Agreement						
Subdomain 1: Data security	7%	0%	93%	•There is a potential overlap with Domain III, first subdomain. This should focus on technical safety of the infrastructure rather that data protection policy.	Validated	-	-	-	N/A
Indicator 1: Infrastructure and policies for data security are established	0%	0%	100%	-	Validated	-	-	-	N/A

Item		Rating by % of experts		Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
		Not adequate	Adequate						
MLs	1. No 2. Security policies and infrastructure are defined at the organisation	14%	86%	•Data security is a big risk to public and patient trust so vital it is universal	Validated	-	-	-	N/A

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	level 3. Security policies and infrastructure are nationally defined but not sufficiently enforced 4. Security policies and infrastructure are established under national regulation and fully enforced 5. Security policies follow international best practices for data security and are regularly reviewed based on changes in technological, regulatory and ethical considerations			•What does the term enforced mean in this context? Do you mean implemented?					
Item	**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
	Disagreement	**Neutral**	**Agreement**						
Subdomain 2: Data discoverability (findable)	0%	7%	93%	-	Validated	-	-	-	N/A
Indicator 1: Guidelines for structuring metadata for datasets are established	14%	7%	79%	•There is a potential overlap with Domain VII, subdomain on metadata. This could focus whether there is a technical means	Reevaluate	-	86%	-The indicator should not only consider local level, but the aim should be national level	Validated

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					of indeed finding the data, eg. a query mechanism exists. •the fact of using stable and unique identifiers should be Validated and specify which kind of such identifier is used; may be in level of maturity?				(as indicated by the maturity levels). -This should focus on infrastructure, not on guidelines, suggestion: "Infrastructure and practices for finding the relevant data are established." The guideline overlaps with Domain VII, subdomain 4. - Note: If accepted, the MLs need to be readjusted.	
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**							
MLs	1. No 2. Guidelines for structuring metadata for datasets are established at the local level 3. Guidelines for structuring metadata for datasets established at the local level	7%	93%		•I think similar to some of the ISO and ACMG call outs, you should put (eg GA4GH and/or HL7 standards) explicitly here.	Validated	-	-	-	N/A

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	are documented and implemented, and their usage is tracked. 4. Guidelines for structuring metadata for datasets are established nationally 5. Guidelines for structuring metadata for datasets are established nationally, and there is national level interaction with the development and adoption of international standards for dataset metadata structure and labelling								

Item	Rating by % of experts			Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
	Disagreement	Neutral	Agreement						
Subdomain 3: Data access management (accessible)	7%	0%	93%	-	Validated	-	-	-	N/A

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Indicator 1: Data sharing policies and data flows are established		7%	7%	86%	-	Validated	(Swap position with next indicator)	-	-	N/A
Item		**Rating by % of experts**		**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**	
		Not adequate	**Adequate**							
MLs	1. No 2. Data access granting is fully manual, with individual agreements created with each request 3. Standardised local data sharing policies are established, with limited data flows managed electronically 4. Electronic systems are implemented to support data sharing policies and are adopted nationally 5. Application for data access is semi-automated and follows international standards and	0%	100%	-	Validated	-	-	-	N/A	

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	there is national representation on the continued development of these standards								
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Disagreement	**Neutral**	**Agreement**						
Indicator 2: Data access governance framework is established		7%	14%	**79%**	• I agree but I would invert 1 and 2, putting first a governance framework and then a data sharing policy as data access governance framework is broader than just data sharing policy	**Reevaluate**	(Swap position with previous indicator)	100 %	-	**Validated**
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**							
MLs	1. No 2. Data access governance is established locally (eg by department or institution) 3. Scope of data access governance is defined nationally,	14%	86%		•Maturity level 5 - Data access governance structure is institutionalised, protected from interference or organisational changes, and open to novel developments is confusing for me, what is meant? How can data	**Validated with rewording**	1. No 2. Data access governance is established locally (eg by department or institution) 3. Scope of data	-	-	N/A

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	with stakeholder consultation 4. Data access governance is led centrally, fully functional, and implementation is monitored based on a national work plan 5. Data access governance structure is institutionalised, protected from interference or organisational changes, and open to novel developments			access governance structures be open to novel developments? Surely in some cases good data access governance structures are there to prevent novel developments from inappropriately accessing data? •Should it be national or regional? I often feel the best unit is the unit in which healthcare is organised (this is a bit of meta-issue applied to all uses of the word "national"). Think Catalonia/Andalucia, Scotland/England, Baden-Wuttenberg/Bavaria etc.		access governance is defined nationally or regionally, with stakeholder consultation 4. Data access governance is led centrally, fully functional, and implementation is monitored based on a national or regional work plan 5. Data access governance structure is institutionalised, protected from interference or organisational changes, and open to novel			

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						developments			
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Disagreement	**Neutral**	**Agreement**						
Subdomain 4: Reception and interfaces (interoperable)		0%	14%	86%	-	Validated	-	-	-	N/A
Indicator 1: Guidelines for record level data structure are established		7%	14%	79%	•Could indicator 1 and 2 be combined, or are they covered by Domain VII?	Reevaluate	-	93%	Still thinking that Indicator 1 (record level data structure) and 2 (dataset structure) could be combined.	Validated
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate	**Adequate**							
MLs	1. No 2.Guidelines for record structure for discovery are established at the local level 3. Guidelines for record structure for discovery are established at the local level and are documented, implemented and their usage is tracked	7%	93%		•What is meant by - Guidelines for record structure for discovery? Do you mean guidelines for the access of electronic health records for research purposes?	Validated	-	-	-	N/A

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	4. Guidelines for record structure for discovery are established nationally and are documented, implemented and their usage is tracked 5. Guidelines for record structure are established nationally and there are national level interactions for the development and adoption of international standards for dataset structure for discovery								

Item	Rating by % of experts			Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
	Disagreement	Neutral	Agreement						
Indicator 2: Guidelines for dataset structure are established	0%	21%	79%	-	Validated	-	-	-	N/A

Item		Rating by % of experts		Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
		Not adequate	Adequate						
MLs		7%	93%	•See previous comment.	Validated	-	-	-	N/A

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	1. No 2.Guidelines for dataset structure and access for discovery are established at the local level 3. Guidelines for dataset structure and access for discovery are established at the local level and are documented, implemented and their usage is tracked 4. Guidelines for record structure and access for discovery are established nationally and are documented, implemented and their usage is tracked 5. Guidelines for dataset structure and access for discovery are established nationally and there are national level interactions for the								

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	development and adoption of international standards								
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Disagreement	**Neutral**	**Agreement**						
Indicator 3: Data sharing infrastructure is established using a federated model		0%	21%	79%	-	Validated	-	-	-	N/A
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate		**Adequate**						
MLs	1. No 2. Data sharing infrastructure is set up locally (eg by department or institution)3. Data sharing infrastructure interoperates within the region. 4. Data sharing infrastructure interoperates with infrastructures from other regions. 5. Data sharing infrastructure interoperates with an international federation	14%		86%	•This indicator assumes that a federated model is better than another and this may not be always the case on a MS by MS level •Data at national scale is needed so either they need to be interoperable	Validated	-	-	-	N/A

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Item		Rating by % of experts			Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
		Disagreement	Neutral	Agreement						
Indicator 4: Services for data reception to support interoperability are established		0%	21%	79%	-	Validated	-	-	-	N/A
Item		**Rating by % of experts**			**Comments**	**Decision after Round 1**	**Rewording proposal**	**Agree %**	**Comments**	**Decision after Round 2**
		Not adequate		**Adequate**						
MLs	1. Genomic data services accept unstructured data without quality control measures 2. Genomic data services have quality control measures and formats implemented locally (eg by department or institution)3. Genomic data services quality control measures and formats are implemented locally but all data received align with international standards 4. Genomic data services	7%		93%	•Similar to other standards, one can call out "(eg, GA4GH or HL7 standards)	Validated	-	-	-	N/A

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	accept data only in formats agreed nationally/regionally and there is automatic quality control upon reception 5. All data received into genomic data services are automatically validated to ensure alignment with international standards								

Item	Rating by % of experts			Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
	Disagreement	Neutral	Agreement						
Subdomain 5: Processing and analysis (reusable)	0%	7%	93%	-	Validated	-	-	-	N/A
Indicator 1: A computational and data infrastructure for medical reuse and secondary data analysis is available	7%	7%	86%	•I agree with this indicator but the reusability for research could be mentioned as a second indicator and link with the previous section where research use was addressed, to assure coherence	Validated	-	-	-	N/A

Item	Rating by % of experts		Comments	Decision after Round 1	Rewording proposal	Agree %	Comments	Decision after Round 2
	Not adequate	Adequate						

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MLs	1. No 2. A computational and data infrastructure is available to support local analysis of data 3. A computational and data infrastructure is available to support trans-regional analysis of data 4. A computational and data infrastructure is in place to support national analysis of data 5. A computational and data infrastructure supports national analysis of data and is aligned with and supports cross-border data analysis	0%	100%	-	Validated	-	-	-	N/A

N/A: Not Applicable.

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Table 9: Delphi Panel Round 1 General Comments (exact transcription).

Items	Comments
Are there any other DOMAINS that have not been Validated in this MLM and you find are of great relevance for this model?	• I have already mentioned this in my previous comment. I believe broader ehealth maturity, particularly in what it respects to clinical information systems usage at both national (capacity to aggregate and summarise data on one individual across multiple organisations) and local levels. • No I don't think so • "I would add the word ""ethics"" in the title of the domain ""Legislation and policy". I would add a sub- domain on ""interactive tools with the public"" in the domain ""awareness and acceptance"" • Personally I think the Research level is too buried here - it is an important part, and has components like feedback
Do you have any other comments?	• In the interest of the usability of the MLM tool, we should rather shorten the list of questions than expand it. See my suggestions for the relevant domains for reducing the number of questions. • I would prefer to see legislation separated from policy. I believe in the data/genomics context, legal is very heavy load (complex, controversial etc etc) but policy, particularly enabling policy and policy on citizen participation, communicating the vision/goals of personalised medicine etc is and can be a very important activity, not to be "only associated" with law making • This seems comprehensive • It is not obvious from the titles of domains that the relation between research and clinical exercise of genomics are addressed. That would be important to be made visible from the start
Are there any other SUBDOMAINS and/or INDICATORS that have not been Validated in DOMAIN I and you find are of great relevance for this model? Please, specify.	• A successful initiative must involve all relevant actors such as universities and research environments. Further, in relation to “public awareness and acceptance” it might be relevant to not only communicate to the public through campaigns and literacy programs, but also communicate with the public through citizen advisory boards or the sort. • I believe a "network" and a Participatory Activity for citizens "around" the national/regional entity is a sign of maturity. It is not uncommon to find very centralised bodies closed from society, this is not a good thing for the topic of genomic related research. models and ways to organise large parts of the society are still to be developed and matured and good practices should be shared in the EU. • A fourth subdomain could be dedicated to the European level: is there a plan to connect regional/national infrastructures to European infrastructures A fifth subdomain could be dedicated to international databases: is there a plan to integrate generated data in international databases such as TCGA, ICGC for cancer data. • Re Governance - the Indicators and maturity levels do not easily take into account or reflect countries that have both federal governments AND state or province governments as part of their oversight of healthcare. State governments and federal governments may have different approaches in terms of funding (who pays for what) and oversight. This is an issue for example in - where there are both state and national initiatives.

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	• The fact of considering the centralised governance body and not a coordination of local/regional/institutional bodies may be a handicap; think of considering a coordination function as a possible governance mechanism.
Are there any other SUBDOMAINS and/or INDICATORS that have not been Validated in DOMAIN II and you find are of great relevance for this model? Please, specify.	• investments are often public-private partnerships, not solely public. • Plan to ensure that most relevant technological solutions are used (sequencing platforms, methods) and that services are optimally centralised vs offered regionally • I believe that public funding may not be the only way forward, and hence associating public funding to maturity may be incorrect. In some countries mix funding models may actually be a sign of higher maturity • Consider evaluating the role/place of, or synergy with, private companies/structures in operating infrastructures for regional/national plans? Model could be synergy with industry in domain VI • There is nothing about "access" as it relates to remote or regional communities. And who is able to order genomic testing (eg geneticist vs paediatrician for child with intellectual disability) • criteria of inclusion should be indicated; maybe this can be in the clinical domain, but needs to be mentioned in the economic model • I think a sub domain - Societal (patient/citizen) benefits - is still required but not narrowly linked to c/e model - perhaps - Societal benefits are quantified, considered and integrated in health system investment decision making regarding genomic medicine? • I think there should be funding for the bridge between Research and Healthcare as at least a "nice to have".
Are there any other SUBDOMAINS and/or INDICATORS that have not been Validated in DOMAIN III and you find are of great relevance for this model? Please, specify.	• Eleven subdomains is too many: I suggest reducing to 7 by combining overlapping domains and adapting the indicator. Even seven subdomains is more than in any other domain. • I believe in many aspects genomics data should NOT be treated differently from other health data. More regulation is not necessarily a sign of maturity. More practices, and preferably data sharing confidence building legal/regulatory frameworks that assume all ""restrictive aspects "" have been dealt with adequately but not necessarily ""in a special way"" with special laws." • Consider evaluating the legislation and policies regarding data sharing at the supranational level? • the international dimension I already mentioned should appear as it is important for patients ; it should be specified if it is feasible or not and the norms for it
Are there any other SUBDOMAINS and/or INDICATORS that have not been Validated in DOMAIN IV and you find are of great relevance for this model? Please, specify.	• Again: it might be relevant to not only communicate to the public through campaigns and literacy programs, but also communicate with the public through citizen advisory boards or the sort. • I believe the campaigns should not be specific to genomic medicine. but personalised medicine and particularly biomedical research that Validates genomic/genetic aspects. But always framed in a bigger picture • In this domain - there is no breakdown as to whether the communication strategies are adequate and high quality - vs whether or not they exist

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	• I consider that specific campaigns and communication towards the young public (schools, adolescents) should be specified and Validated as such • See previous comments- I suggest changes needed
Are there any other SUBDOMAINS and/or INDICATORS that have not been Validated in DOMAIN V and you find are of great relevance for this model? Please, specify.	• Other relevant educational programs: bioinformatics, molecular biologists , bioanalytics, lab technicians. • Continuous education of medical doctors (even more importantly than other medical professionals), even though the young doctors would get the necessary education in med school, there are still large group of doctors making the decisions who potentially don't have adequate knowledge on genome medicine • Consider education programs dedicated to patients and families? • Need to also target existing clinicians - rather than just undergraduate programs • In addition to MD, nurses and pharmacists I would add a line with "other health care professionals" as it is important that also physiotherapeutes and "sage-femmes" and others like dentists, orthoptists and orthophonists have at least some notions, given the broad scope of genetic diseases • Not clear why the education subdomain is restricted to medicine, nursing and pharmacy? Should there be an additional indicator - Genomics is integrated in general curricula for all healthcare professionals? What about public health professionals?
Are there any other SUBDOMAINS and/or INDICATORS that have not been Validated in DOMAIN VI and you find are of great relevance for this model? Please, specify.	• database architecture/storage. • Note that I would Validate in this section the subdomain "Sequencing/ genotyping infrastructure" as a part of the clinical infrastructure. • May be indicators mentioning the international aspect, as strategy with industry sector may be local or Validated international partnerships • See comments
Are there any other SUBDOMAINS and/or INDICATORS that have not been Validated in DOMAIN VII and you find are of great relevance for this model? Please, specify.	• database architecture/storage • Note. The title of the domain can then simply read: "Clinical genomics guidelines" • When analysis of raw data is performed in a centralised manner, is this data shared with local investigators for double check? • The pipelines should be standardised throughout and ISO accredited
Are there any other SUBDOMAINS and/or INDICATORS that have not been Validated in DOMAIN VIII and you find are of great relevance for this model? Please, specify.	• The main issue in this domain is the potential overlap with previous domains. This could probably be addressed by reformulating some of the questions and indicators. Subdomain 4 (reception...) might be better with only 2 indicators. • I think subdomain 4 should be worked in broader level then genomics context, it should be included in a national interoperability strategy level • the return of results aspect is not mentioned anywhere and is an important issue; it should be mentioned explicitly somewhere
Final Comments	

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Now that you have gained a detailed view of the MLM framework, are there any other comments on the proposed Domains or other aspects of the MLM that you would like to make?	• I have made some restructuring proposals along the way. • I think the Model as a whole covers well the national/org level, It could perhaps benefit from a domain on cross-border tools and cooperation mechanisms. also in light of future usage of the EHDS to foster research • It is not a domain, but the difference between international standards and global standards used sometimes is not clear and would require either harmonisation for one of those terms only or precise definition of both underlying differences • I think it is important to define what is in scope when using the term genomic medicine- the use of genomics in the practice of medicine or specifically specialists in clinical genetics/genomics. Also in addition to ISO standards the use of EQA schemes should be mentioned. • I think one major meta thing is how to handle the national vs regional aspect. I think the key organising principle is that this maturity model should be appropriate to however a healthcare system is organised. In federal countries where healthcare is federated - Germany (Länder), Spain (autonomous regions), Italy (health care regions), UK (Scotland vs England, complications on Wales) etc the maturity model is to the highest level with full autonomy on healthcare. Otherwise looks good and although much of this is ""obvious"" nevertheless one needs to have a checklist and a scheme to show regions/countries on."
If you have proposed a new Domain, please use this box to add your ideas regarding the respective Subdomains and Indicators.	"Cross-border domain: - legislation for cross border data sharing in genomics; - technical infrastructure to link up to the EHDS infra; - Education for Migrant sub-populations"

Table 10: Delphi Panel Round 2 General Comments

Generally you could consider having a level stating "under development" or "under discussion"

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The current method of looking at the subdomains and their indicators one by one misses an important point of structure of the MFM. 1/ The Domains, Subdomains and Indicators in different parts of the MLM framework are not in balance. In most parts of the framework Indicator = Subdomain, ie. there is only one indicator per subdomain. In Section VIII, there are several well used indicators per subdomain, thus keeping the number of subdomains in check. 2/ Some subdomains would not deserve to be subdomains. This is very clear in the economic analysis which has 3 subdomains, while the hugely important issues of access to genomic medicine or its financing both have only one subdomain. Similarly, there are 11 subdomains in section III. Several could be combined, but keeping the indicators. 3/ Finally, a detail, but highlighting the problem of the current method is Subdomain 1 of Domain VII. The Subdomain as such is fine but would belong to Domain VI but the only way to indicate this is to protest the Subdomain itself. There should be a meeting or a method to look at the whole once we have validated all wordings.
No. Overall good improvement after reformulations.
I think the Model as a whole covers well the national/org level, It could perhaps benefit from a domain on cross-border tools and cooperation mechanisms. This is particularly relevant as the future usage of the EHDS to foster research is envisioned.
I think one major meta thing is how to handle the national vs regional aspect. I think the key organising principle is that this maturity model should be appropriate to however a healthcare system is organised. In federal countries where healthcare is federated - Germany (Länder), Spain (autonomous regions), Italy (health care regions), UK (Scotland vs England, complications on Wales) etc the maturity model is to the highest level with full autonomy on healthcare. Otherwise looks good and although much of this is "obvious" nevertheless one needs to have a checklist and a scheme to show regions/countries on.
It is not a domain, but the difference between international standards and global standards used sometimes is not clear and would require either harmonisation for one of those terms only or precise definition of both underlying differences
Generally you could consider having a level stating "under development" or "under discussion"

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Annex 2.

Glossary

Acceptance

Perceived usefulness of genomic medicine to patients. Recognition from citizens, patients and patients' associations of a positive impact of the use of genomic medicine on patients levels of satisfaction

API

Application Programming Interface. A software intermediary that allows two applications to talk to each other.

Awareness

Public's level of understanding about the importance and implications of genomic medicine.

Centrally

Based within a national or regional node.

Clinical interpretation of genomic results

Translation of the technical output of a clinical genetic or genomic test into potentially clinically actionable information.

Cost-effectiveness assessment

Cost-effectiveness analysis is a form of economic analysis that compares the relative costs and outcomes of different courses of action.

Costed implementation plan

A multi-year roadmap that enables governments to prioritise interventions, engage stakeholders around one strategy, forecast costs and mobilise resources to meet identified gaps, namely to implement genomics in healthcare systems.

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Data protection

Certainty that personal data is used fairly, lawfully and transparently – for specified, explicit purposes – in a way that is adequate, relevant and limited to only what is necessary, accurate and, where necessary, kept up-to-date, for no longer than is necessary, and handled in a way that ensures appropriate security, including protection against unlawful or unauthorised processing, access, loss, destruction or damage.

Data reuse

Reuse, or secondary use, of health data for purposes other than the primary reason for which they were originally saved. Other purposes may include scientific research, development and innovation activities, teaching and statistics.

Data reception

Uniform processes (such as quality control and standardisation) to receive (download) or access (through API) both data and metadata in a consistent way, enabling infrastructures to adhere to global standards and principles for genotypic and phenotypic data. It includes logically describing datasets to an extent that they can become actionable on the infrastructure, even if they are stored nationally or locally. (Adapted from the 1+MG Scoping paper)

Dataset structure

The dataset is formatted in a standard way to support interoperability, i.e. via use of international standards.

Dedicated governance

The process by which decisions are made and implemented. Governance is the process by which public institutions conduct public affairs and manage public resources.

Economic model

A structured approach to help decision-makers choose between alternative ways of using resources, by weighting the cost of an action against the benefits that it provides. It is frequently used to anticipate the costs and benefits of new health care technologies, policies and regulations.

Federated model

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A distributed network of repositories for sharing genomic information.

Further processing

The processing of personal data for a different purpose(s) than the initially collected.

Genetic data

Personal data related to the inherited or acquired genetic characteristics of an individual, which give unique information about his/her physiology or health, that result from an analysis of a biological sample from the individual in question. [ref. Art. 4(13) GDPR]

Guidelines for clinical interpretation of genomic results

Guidelines for translating the technical output of a genetic or genomic test into potentially clinically actionable information.

Guidelines for clinical reporting of genomic results

Guidelines for reporting the actionable results of a genetic or genomic test to the attending clinician and/or patient.

Health data

Personal data related to the physical or mental health of an individual independent of its origin (e.g. healthcare context, research, clinical trials, the data subject directly, smart devices). [ref. Art. 4 GDPR]

HTA framework

Health Technology Assessment framework. A multidisciplinary process that uses explicit methods to determine the value of health technology at different points in its lifecycle to help decision-makers make informed decisions.

ICT (clinical) tools

Information and communication technology, such as electronic health records, telehealth or online resources.

ISO

The International Organisation for Standardisation

Locally

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Within a single institution, i.e. not beyond a lab, department or hospital.

Metadata

Data that provides information about other data. For example, the origin of the data, the processing details or the sharing permissions.

Multidisciplinary teams

Teams comprised of individuals who span across different areas of expertise to cover all knowledge areas required for genomic medicine.

No-cost access plan

Detailed set of rules that determines rights, duties and procedures to benefit from access to genomic tests at no cost

Norms

A set of principles of right action binding upon group members and serving to guide, control or regulate appropriate and acceptable behaviour. E.g. legislation, policies, professional regulations, codes of conduct.

Personal data

Data related to a living individual, who is likely to be identified by the data directly or combined with other data (e.g. through a pseudonym). [ref. Art. 4 GDPR]

Primary bioinformatics analysis

The initial analysis that turns the machine output of genomic sequencing into genomic information for clinical/research interpretation or other contexts.

Reception and interfaces

This consists of two areas.
(1) Reception. Uniform processes (such as quality control and standardisation) to receive (download) or access (through API) both data and metadata in a consistent way, enabling infrastructures to adhere to global standards and principles for genotypic and phenotypic data. It includes logically describing datasets to the extent that they can become actionable on the infrastructure, even if they are stored nationally or locally.

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(2) Interfaces. Organisations offer interfaces (APIs) following international standards that form the technically interoperable infrastructure backbone.
[Adapted from the 1+MG Scoping paper]

Record

A dataset record is a collection of fields of information about the same person, item or object in a database. It can be thought of as a row of information within a database table.

Secondary data analysis

The use of existing data, collected for a prior study, to pursue a research interest that is different to that of the original work. [ref: https://sru.soc.surrey.ac.uk/SRU22.html]

Sequence-associated metadata

Data that provides information about other data, specifically about genomic-sequence data.

Societal benefits

Any advantages, gains or improvements as a result of employing a genomic approach to a group of people (e.g. patients, citizens).

Structured dataset metadata

Metadata (data that provides information about other data) for datasets that supports data discoverability using international standards.

Vulnerable groups

Vulnerable groups of population include children, adults with diminished capacities, the elderly, racial or ethnic minorities, the socioeconomically disadvantaged, underinsured or those with certain medical conditions who are at risk for unequal healthcare access, outcomes and exploitation.

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