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Response submitted by:

Philippa Brice  
[philippa.brice@phgfoundation.org](mailto:philippa.brice@phgfoundation.org)

Alison Hall  
[alison.hall@phgfoundation.org](mailto:alison.hall@phgfoundation.org)

# Inquiry on genomics and gene editing in the NHS: evidence from the PHG Foundation

The PHG Foundation is an independent, not-for-profit health policy think-tank that aims to make science work for health, with twenty years' experience in issues surrounding the responsible and effective use of genomics within health services.

This submission provides perspectives on the specific recommendations of Generation Genome, the Chief Medical Officer's annual report, for the mainstream application of genomic medicine in the NHS within the next five years, with a particular focus on barriers and how they should be addressed. The PHG Foundation welcomes the report and recommendations and considers that they will play a valuable role in helping to embed genomics within the mainstream NHS and deliver widespread patient access. Our comments provide perspective and highlight what we consider to be important issues relating to selected recommendations.

## Systems and services

### Recommendation 1

We support the recommendation for a new National Genomics Board. We suggest that the minister should be associated with the Department of Health (as opposed to the Department of Business, Energy and Industrial Strategy, unless the dual role of Life Sciences Minister is recreated) to ensure that patient interests are clearly prioritised at all times, noting that 'patients' in this context includes both current NHS patients who might contribute to and/or benefit from genomic research and medicine, and also potential future patients i.e. the public. We recommend that the Board include a broad range

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of stakeholders to represent the general public, NHS users, and mainstream health professionals and commissioners, as well as experts in genomic and personalised medicine and research, ethics and regulation.

### **Recommendation 2**

We support the recommendation that NHS England should continue planned reorganisation of existing genomics laboratories to create a scalable, future-proof and efficient national service with national standards and processes, based on centralised laboratories and regional hubs, and underpinned by a secure central data platform. Previous work on data sharing highlights the fact that effective genomic data aggregation and sharing within the NHS is imperative for effective delivery of clinical genomic services, and the current absence of a dedicated NHS database to facilitate this is arguably the single greatest impediment to delivery of patient benefit from genomic medicine in the NHS. It is therefore of paramount importance that in moving from the 100,000 Genomes Project (a primarily research-driven endeavour) to a national NHS genomic medicine service, the resulting infrastructure must support the collation and sharing of genomic data within the NHS.

We also wish to emphasise the simultaneous need for co-development of standardised referral processes that enable mainstream clinicians to confidently and responsibly request genomic tests, and standardised genomic test reports to facilitate interpretation and appropriate clinical decision-making. This is essential for delivery of an equitable, efficient and effective system. Although plans for the reconfiguration of genomic testing involve the development of a Test Directory, the administration of tests is dependent upon having a sufficiently skilled workforce to administer these tests. The current cadre of 'clinical champions' in genomics from wider medical specialties have developed resources and standards for their own colleagues in association with a steering group from the Joint Committee on Genomics in Medicine. These are a good exemplar of how this might best be achieved.

Experience from the ground-breaking Deciphering Developmental Disorders project should be utilised when planning for mainstreaming, notably the inclusion of a system for the reanalysis of data, yielding additional diagnoses as evidenced by published papers; the issue of reanalysis and recontact for clinical use should be addressed with respect to NHS integration

Making effective use of genomic data at scale for medicine, whilst vital, is nevertheless a monumental task. The NHS does not currently have a robust informatics infrastructure and data management processes of the kind that will be needed to deliver personalised medicine, nor is it clear how far that established for the 100,000 Genomes Project can (or should) be adapted to meet NHS needs. In particular, the new infrastructure will need to include adequate and evolving computational capacity to support the collection, analysis, interpretation and storage of genomic data; integration with clinical records; and sharing between NHS providers. Current NHS IT cannot meet these needs; efforts towards digitisation of health records are encouraging, but must be complete to allow efficient transfer of patient clinical and genomic data and equitable access to genomic medicine

Whilst genomics should not form part of screening practices unless it offers demonstrable benefit, in some conditions there is likely to be significant opportunity for improvements.

### Recommendation 3

We strongly support this recommendation. Research is a vital element for building a robust system that optimally serves patients. Some improvements to both direct patient care and ongoing research capacity can be achieved without incurring additional costs, notably making more effective use of existing data by merging information on genomic variants currently held in separate molecular diagnostic databases. Other developments will incur additional costs; implementation research is a vital element to ensure that resources are used effectively, and especially to underpin the substitution of new technologies for existing redundant technologies (i.e. to provide a justification for changes in practice and behaviour).

Making data available for both clinical care and research is highly desirable; as genomic medicine is such a young field, clinical decision making is constantly evolving as new data linking variants and disease emerges, so that the distinction between research and direct care is often unclear. Pooling and sharing information on genomic variants is essential to understanding their clinical significance (or otherwise). As the size of genomic databases such as that of the 100,000 Genomes Project grows and research progresses, the capacity to diagnose disease and understand genomic contributions to pathology will increase. However, the insistence on restricting access to genomic data as a measure to both protect against public concerns about data security and enable commercial benefit, whilst laudable in intent, simultaneously limits the capacity for further research, knowledge and ultimately patient benefit. It will therefore be imperative to ensure that data access by researchers is maximised.

### Recommendation 6

A thorough evaluation of the new and emerging opportunities for genomic screening at individual, cascade and population levels is another excellent proposal, which the Foundation supports. Whilst genomics should not form part of screening practices unless it offers demonstrable benefit, in some conditions there is likely to be significant opportunity for improvements. At present, evidence for clinical utility of genomic data in stratifying risk only exists for forms of cancer screening.

### Recommendation 7

We strongly support this recommendation as part of improving NHS antenatal care.

## Research

### Recommendation 9

A 100,000 Genomes Project working group has been set up to explore aspects of the consent process, particularly the implications of seeking a form of hybrid consent for both clinical care and research. The PHG Foundation is represented on this group. Any consent process that is ultimately adopted needs to be consistent with existing regulation for both clinical care and

Whilst we support exploration of the feasibility of expansion of research via the 100,000 Genomes Project, we caution that not only will it continue to be important that participants understand that they may not benefit directly (i.e. findings will not necessarily influence their own direct care), but also that clinical care for those patients should not be compromised by their participation in research.

for research and the forthcoming changes required by the EU General Data Protection Regulation (and UK Data Protection Bill) as well as prevailing ethical standards. It also needs to be feasible within the wider context of mainstreaming genomic testing to multiple clinical specialties. This may require additional resources and support for health care professionals.

#### **Recommendation 10**

Whilst we support exploration of the feasibility of expansion of research via the 100,000 Genomes Project, we caution that not only will it continue to be important that participants understand that they may not benefit directly (i.e. findings will not necessarily influence their own direct care), but also that clinical care for those patients should not be compromised by their participation in research. For example, if a cancer patient chooses to participate and potentially discover genomic information about their tumour that could optimise their treatment, that is a benefit – but if the turnaround time for genomic analysis as part of the research project takes many weeks longer than it would do if ordered via other mechanisms, the delay could negatively impact their prognosis.

#### **Recommendation 13**

We strongly endorse this recommendation and further emphasise our own policy recommendations of 2015, derived through close consultation with the UK pathogen genomics community, which included that PHE should mandate deposition of all relevant pathogen genomic data in a national database with interoperable standards, to maximise data sharing for the detection and control of infectious disease threats, as well as ongoing research.

### **Data, standards, regulation**

#### **Recommendation 15**

The GDPR is broadly positive for research since it contains an exemption that allows data to be processed for research with the provision of appropriate safeguards. However, further work is necessary to allow a nuanced regulatory approach and prevent undue interference with the practice of genomic medicine or wider research. This will include setting out proportionate exemptions (which are currently under review in the Data Protection Bill). In particular, we suggest that an 'exceptionalist' approach to genomic data with correspondingly strict safeguards on data processing is inaccurate and inconsistent with other forms of predictive medical data.

We support the ICO in the development of codes of conduct that enshrine context-specific safeguards that are proportionate to the potential harms resulting from data use (or misuse) in those contexts. Issues warranting particular scrutiny in codes of conduct could include approved methods for effective anonymisation and pseudonymisation; further clarification of what constitutes 'the public interest'; data security; and the information that should be provided to data subjects and the public.

Outstanding legal uncertainties with respect to data sharing (such as the interface between the National Data Guardian's opt-out, and subject access rights under the GDPR) will also have to be resolved and effectively communicated before roll-out

### **Recommendation 16**

We concur that international cooperation and mechanisms to support sharing of genomic research and health intelligence data with respect to infectious disease threats is highly desirable, and another opportunity to build on the UK's global excellence in infectious disease genomics to assume an ongoing leadership role. In our interconnected modern world, an infectious disease threat in one country is necessarily a concern for others. PHG Foundation is an active participant in GA4GH which is developing tools and processes for more effective genomic data sharing. We also reiterate our own recommendation of paragraph 13 (above), that there needs to be urgent attention to ensuring that systems, mechanisms, rules and leadership within the UK are also in place to ensure rapid sharing of research and health intelligence data with respect to infectious disease threats.

### **Recommendation 17**

Coordinated approaches to standard-setting and regulation to meet developments in sequencing bioinformatics and clinical reporting are a critical recommendation. The PHG Foundation has previously emphasised the need for recognition that capacity and resources will be needed to ensure that systems keep pace with scientific and technological developments (and corresponding clinical needs), as well as to oversee appropriate data curation, compliance with standards, and evolution of these standards. It will also be vital to co-develop supporting systems (such as IT) with the planned NHS end-users, to ensure buy-in and compliance. Outstanding legal uncertainties with respect to data sharing (such as the interface between the National Data Guardian's opt-out, and subject access rights under the GDPR) will also have to be resolved and effectively communicated before roll-out.

### **Recommendation 18**

We strongly support this recommendation and have engaged with many of the key stakeholders on this point. Although the In Vitro Diagnostic Devices Regulation will not be implemented until 2022, key elements for genomic medicine include the breath and operation of the exemption for in-house laboratory tests, the inclusion of software within the scope of this Regulation and being proactive about meeting the requirements for clinical performance for new tests. The need to provide clinical evidence of utility for each type of test process under the IVDDR may prove onerous for some types of test, especially those for rare and very rare diseases where numbers affected are so low that they will not necessarily reach statistical significance.

### **Engaging staff and patients**

#### **Recommendation 19**

We concur with the need for proper public dialogue on the shared social contract between patient, public, clinicians and academics in relation to genomic medicine. We support the CMO's recognition that concepts of genetic exceptionalism are outdated, given the potentially greater sensitivity of other forms of medical data (such as sexual history or mental health), and the arguably greater relevance of shared genetic heritage over individual differences.

We also propose that there should be a clear focus on public understanding of the need for genomic data sharing within the NHS, for both direct/individual and widespread benefit.

We also propose that there should be a clear focus on public understanding of the need for genomic data sharing within the NHS, for both direct/individual and widespread benefit. Whilst there is understandable concern to address public worries about the confidentiality of genomic data, data sharing is so fundamental to both research and practice in modern healthcare, including genomic medicine, that efforts to ensure that patients and the public understand this should be paramount.

Whilst previously many public engagement exercises in genomics have distinguished between clinical practice and research, this is not always clear in genomics, since information on one patient's genomic variation and symptoms can be crucial to diagnosing and caring for another. There should be transparency about the uses to which genomic data will be put, highlighting where data processing is a necessary and integrated part of delivering healthcare, and those instances where additional burdens or risks may arise from research: ultimately the goal should be working towards a learning healthcare system approach.

#### **Recommendations 20 & 21**

PHG Foundation has been contributing to efforts in this area via the Genomics In Mainstream Medicine project for almost ten years and welcomes the report's emphasis on the need to develop professional training for present and future genomic areas. Currently, lack of awareness among clinicians about the available options for genomic testing limits patient benefits. In addition, the perception by some of genomics as costly and ineffective interventions in medicine and public health should be challenged, since in the longer term it offers the potential to truly understand (and hence more effectively prevent and treat) disease. However, in the shorter term the direct patient benefits will be limited, and so we support a pragmatic approach to professional education, with a focus on the potential to improve current clinical care for their own patients and populations.

Whilst we need to retain and respect the unquestionable expertise of clinical and laboratory geneticists, we nevertheless agree that routine, mainstream delivery will require change. Based on our own work supporting the expansion of genomics to mainstream clinicians, we agree wholeheartedly with the need for appropriate inclusion of genomics at all levels of specialist training.

Mainstream clinicians may lack the awareness, knowledge or confidence to offer genomic testing where it might be appropriate. Mainstreaming genomics will rely upon increasing awareness of national genomic testing criteria, genomic literacy among the clinical professional workforce, and ensuring they are equipped to capture sufficient clinical and phenotypic data to recognise when and what genomic test is warranted. It is also vital that appropriate training and support is provided in the interpretation and clinical actionability of genomic test reports.

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### **Recommendation 22**

We endorse this recommendation, with the proviso that there needs to be a clear distinction between courses offered to early adopters and enthusiasts (such as the research-oriented Masters in Genomic Medicine), those providing new forms of specialist training (such as in data science), and those aimed at mainstream health professionals at different stages.

### **Miscellaneous**

#### **Recommendation 23**

We note that genomic testing to contribute to the assessment of disease risk may be used as part of obtaining health insurance, in efforts to promote personal health and prevent disease, or both. The text of the CMO's report refers to adoption of key points from the Council of Europe's recommendations with respect to genomics and insurance; these are more nuanced than previous iterations of the UK Concordat and Moratorium on genetic testing and insurance, adopting guiding principles instead of outright prohibition, and allowing the potential for use of genomic data by the insurance industry provided it is not discriminatory.

In taking forward the CMO's recommendation for review in the light of 'the need to support a new approach to equitable and integrated care that provides elements of clinical practice and research', we refer to our response in paragraphs 19-21, above.

#### **Recommendation 24**

We agree there is a need to revisit current regulatory pathways in the light of precision medicine, using genomic testing to guide the repurposing of existing drugs (as well as new ones) for use in stratified patient sub-populations in whom benefits are maximised. Affordability will continue to be vital. Since new tests may well fall under the scope of the forthcoming In Vitro Diagnostic Devices Regulation, it will be important that NHS providers of tests and care are supported to take advantage of the exemptions for in-house development of laboratory tests, and that the challenges noted in paragraph 18 (above) are addressed.

#### **Additional comments**

We have previously commented that plans for the reorganisation of genomics services and NHS mainstreaming of genomics will necessitate action by commissioners to allocate additional resources for cost-effective genomic diagnostics that can improve the quality and volume of care delivered via the new service, particularly where this will introduce not only new testing costs but also a requirement to change existing patient pathways. Without addressing these issues, clinicians will be unable to access the tests and the changes in clinical practice required for patients to benefit from genomic medicine will not be delivered.

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In order to ensure that the legacy of the 100,000 Genomes Project is maximised, we strongly recommend a formal evaluation of its different work programmes from inception to 2017-18. Results will be critical for informing the design and implementation of future NHS healthcare services.

### **About the PHG Foundation**

The PHG Foundation is an independent, not-for-profit health policy think-tank that aims to make science work for health, with twenty years' experience in issues surrounding the responsible and effective use of genomics within health services. The PHG Foundation has no relevant financial or other interests to declare. Other recent consultation responses are freely available from our website along with related reports, briefing notes and infographics. We are happy to comment in greater depth on any issues, or to provide oral evidence.