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making science work for health

# Genomic Medicine

## An Independent Response to the House of Lords Science and Technology Committee Report

May 2010

UNIVERSITY OF CAMBRIDGE

CSaP

This report can be downloaded from our website
**www.phgfoundation.org**

**Published by PHG Foundation**
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*May 2010*



*ISBN 978-1-907198-04-5*

Cover photo: http://www.sxc.hu/photo/914335

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The PHG Foundation is the working name of the Foundation for Genomics and Population Health, a charitable organisation (registered in England and Wales, charity no. 1118664; company no. 5823194) which works with partners to achieve better health through the responsible and evidence-based application of biomedical science.

*This Report is the product of five expert workshops held between November 2009 and March 2010, co-organised by the Foundation for Genomics and Population Health (PHG Foundation) and the University of Cambridge Centre for Science and Policy (CSaP), as a forward-looking critique of the House of Lords Science and Technology Committee Report on Genomic Medicine.*

*The meetings were organised and funded by CSaP, in line with its remit to create channels for scientists to consider and communicate the implications of their work for policy makers. The Report was written by PHG Foundation staff, and although it reflects the views and recommendations of the workshop participants (listed at the back), the PHG Foundation takes full responsibility for the content.*

*The PHG Foundation and CSaP are gratefully indebted to all the workshop participants for their time and expertise.*

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## Foreword

The PHG Foundation (formerly the Public Health Genetics Unit) is an independent, non-profit organisation working to achieve the responsible and evidence based application of genomic and biomedical science for the benefit of health, with a focus on policy research and health service development. In 2000, in collaboration with the Nuffield Trust, we led the *Genetics Scenario Project* to '*assess the impact of advances in genetics and molecular biology on the organisation, funding and provision of clinical services, on changes in clinical practice, and on the potential for disease prevention and public health action'*. Many of the recommendations were adopted and taken forward by the Government in subsequent years, culminating in the publication of a Genetics White Paper *Our inheritance, our future: realising the potential of genetics in the NHS* in 2003. This paper outlined a number of important initiatives and strategies which have allowed the application of genetics for health to develop and flourish within the UK.

However, enormous technological progress has since been made in basic genomic science and is continuing at a staggering rate. In response to these developments the House of Lords Committee on Science and Technology launched an inquiry in 2008 into genomic medicine to '*provide an assessment of genome technologies and their actual and potential impact on clinical practice in the post-genome era.'* Following the publication of the House of Lords Report on *Genomic Medicine* in July 2009, the PHG Foundation led an initiative to formulate an expert response to this Report that was explicitly independent of government.

In collaboration with the University of Cambridge Centre for Science and Policy (CSaP), the PHG Foundation hosted five invited workshops to gather expert opinion from scientists, clinicians, epidemiologists, informaticians, lawyers, philosophers, social scientists and policy makers. Within each stakeholder group, our aim was to reflect a spectrum of expertise, including early adopters as well as those who were somewhat sceptical of the opportunities brought by these technologies. In order to focus our inquiry, we limited the formal inputs to this process to the House of Lords *Genomic Medicine* Report and the Government's official response, published in December 2009. We initially posed a simple question: *"What are the key issues that should be part of a strategic vision for genomic medicine in the UK?"* The discussions of the first four data gathering workshops were synthesised and presented to the final strategy workshop, where the recommendations were formulated; in the interests of brevity, we have not explicitly detailed the rigorous deliberations from all the workshops, but copies of a summary synthesis document are available from the PHG Foundation.

Here we present our recommendations for action, which represent the views held by the majority, and a brief analysis of the diversity of views expressed in the workshops. These recommendations are aimed at relevant Government bodies, including the Department of Health, the Department for Business, Innovation and Skills, and the newly established Human Genetics Strategy Group (HGSG), as well as the House of Lords Committee on Science and Technology and other interested policy groups. In the main, we have not sought to address specific recommendations from the House of Lords Report or from the Government's response, nor have we chosen to re-iterate important policy initiatives with which there was broad agreement. **Instead, we seek to highlight issues that are confused or absent in the current discourse, but are nonetheless critical to deriving short and long term benefits from genomic medicine. To this end, we have made a small number of specific recommendations, with a clear requirement for immediate and direct action.**

## Executive Summary and Recommendations

The development of novel, fast and inexpensive genome sequencing technologies has created an urgent need to develop a strategy for their implementation within the UK for the benefit of health. However, while the rate of scientific and technological progress has been underestimated, the importance of genomics for the prediction and prevention of common complex diseases has been overestimated (though there is little doubt about its potential to provide a better understanding of disease mechanisms).

We conclude that 'genomic medicine' should focus on diagnostic and cascade testing for single gene disorders and inherited subsets of complex disease, for which ample evidence of demonstrable health benefits already exists. In addition, there will also be specific instances where utility will be (or has already been) shown for the prediction, diagnosis and management of complex disorders, such as the use of pharmacogenetic tests to predict and monitor individual drug response.

This has implications for the NHS (both within and outside the traditional boundaries of clinical genetics), academia, industry, policy-makers and the public. The effective implementation of new genetic tests and genomic technologies within the NHS requires:

- establishing and maintaining appropriate IT and informatics structures to allow targeted, up-to-date and evidence-based interrogation of the genome and its functions associated with health and disease;
- developing and funding a mechanism for generating and evaluating evidence for the validity and utility of different genetic tests or genomic analyses;
- creating an organisational infrastructure and funding mechanisms to allow genetic information to be available where appropriate;
- formulating an ethical code that addresses issues of consent, incidental findings and duty of care, as well as data sharing, access and governance;
- cultivating an appropriate regulatory environment that encourages investment and innovation, whilst protecting the vulnerable in society from harm;
- training and educating the professional workforce to deliver genomic services effectively and to engage at an appropriate level with the public.

Failure to address these issues will severely hinder the progress of translational research and the effective implementation of new genomic technologies in the longer term. We therefore make the following 12 recommendations for the strategic development of genomic medicine within the UK. We believe that implementing these recommendations is critical to realising the benefits from developments in genetic and genomic science, for health, wealth and society.

*Recommendation 1: Scope and Vision*

**The long-term vision for genomic medicine in the UK should, first, concentrate on establishing interventions of proven clinical utility that will contribute to addressing unmet medical needs amongst those with inherited disorders, and second, be realistic in its assessment of the likely benefits from new technologies and novel findings.**

*Recommendation 2: Evidence and Evaluation*

**The Department of Health should establish an evaluation and decision-making body, *as a matter of urgency*, to direct research funding towards important strategic questions and ensure evidence-based implementation of both new diagnostic technologies and informatics systems within the NHS.**

*Recommendation 3: Information and Interpretation*

**The Government should invest in establishing and maintaining a biomedical informatics infrastructure (including both hardware and software) to allow targeted interrogation of the genome, and ensure IT compatibility between research and clinical communities.**

*Recommendation 4: Data Storage and Access*

**The Human Genomics Strategy Group (HGSG) should liaise with relevant stakeholders to ensure that clear policy guidelines are developed outlining why, and under what circumstances, DNA samples and genomic information can be stored, accessed and used for clinical and research purposes.**

*Recommendation 5: Health Service Organisation*

**The HGSG, together with the Department of Health, need to put in place an appropriate infrastructure to deal with integrated clinical services and laboratory organisation in light of new genomic technologies.**

*Recommendation 6: National Formulary for Tests*

**The Department of Health should support the establishment and maintenance of a 'National Laboratory Medicine Catalogue' to provide up-to-date guidance on offering, performing and interpreting tests.**

*Recommendation 7: Barriers to Commissioning*

**The HGSG, together with the Department of Health, should review how NHS funding mechanisms act as a barrier to the utilisation of new tests, and should seek to eliminate budgetary silos in order to realise cost savings from genetic testing throughout the healthcare economy.**

*Recommendation 8: Implications for Industry*

**The Government should work with industry and research funders to establish systems, strategies and funding mechanisms for evaluating the clinical validity and utility of diagnostic tests.**

*Recommendation 9: Regulation of Tests*

**The Government and the Medicines and Healthcare products Regulatory Agency (MHRA) should resist attempts to reclassify all genetic tests into the same risk category under the European Directive on In Vitro Diagnostic Medical Devices.**

*Recommendation 10: Translational Research*

**The Government should continue to support and expand funding for translational research, and should direct research focus towards immediate problems, such as evaluating new tests, while maintaining a broad base.**

*Recommendation 11: Public and Media Engagement*

**The strategy of the HGSG should be to engage the public *at the point of need*; in addition, the HGSG should put in place a media strategy to ensure high quality coverage of genomics in the press.**

*Recommendation 12: Public Involvement in Research*

**The Government should support public involvement in genomics by encouraging voluntary enrolment in population-based research.**

## Introduction

Over the last decade, our understanding of the genetic basis of disease has increased dramatically, and numerous genetic tests are now available to patients both within and outside of the NHS. In addition to thousands of targeted genetic tests for known monogenic disorders, which offer an often accurate diagnosis to the affected individual and their family, genome-wide array technologies are also improving the diagnosis and treatment of individuals and families affected by larger chromosomal imbalances. The increased understanding of the role of genetic variation in individual drug response (pharmacogenetics) is also leading to the development of targeted treatments and diagnostics which promise to improve drug response and reduce adverse drug reactions.

Over the same time period, the exponential development of new high-throughput DNA sequencing technologies has radically reduced the cost and time required to sequence a human genome. The first reference human genome took around five years of sequencing time and cost several billion dollars; today, a full human genome can be sequenced within weeks for tens of thousands of dollars, and experts predict that within a few years, it will be possible to sequence a full human genome for less than a thousand dollars in a matter of days. **It will therefore soon be cheaper to accurately sequence an entire genome than to selectively sequence a single gene, or genotype a series of known mutations.**

Whether or not this will happen is no longer in contention. In addition to existing tests with established medical benefit, whole genome analysis and high throughput 'omics' measures will provide comprehensive physiological profiles that are beneficial in specific clinical contexts. For example, sequencing of pre-cancerous and tumour tissue genomes is likely to have clinical utility in the not too distant future. However, two questions remain: when will it happen, and how will we deal with it when it does? We cannot predict the future, but we can plan for it. By developing a strategy that acknowledges a number of different possible futures in which rapid and cheap whole genome sequencing is available to all, we can ensure that we maximise the benefits for health whilst minimising the potential harms to society. To illustrate the breadth of possible opinions, we outline two alternative scenarios below:

*SCENARIO 1*

- Individuals' genomes are only *sequenced at the point of need* to answer a specific clinical question
- Clinical utility is limited to diagnostic and cascade testing for inherited disorders, including single gene subsets of complex disease
- Common, low penetrance genetic variants are not used for diagnosis or risk prediction
- Consumer genomics plays a minor role and individuals access their genomes primarily via healthcare professionals

*SCENARIO 2*

- The entire adult population is routinely offered *pre-emptive full genome sequencing*, outside of a specific clinical context
- Genomic information is widely used throughout medicine, *e.g.* for susceptibility testing, carrier screening and guiding treatment
- Risk models based on polygenic and environmental factors play an important role in the practice of clinical and public health medicine
- Individuals purchase, access and interrogate their own genomes directly

Although these two scenarios are somewhat hypothetical, and perhaps represent two extremes, it is likely that reality will fall somewhere in between. There is also little controversy about the fact that a greater understanding of genomic, molecular and cellular biology will indirectly lead to better healthcare interventions that stem from greater knowledge of disease pathogenesis. However, these scenarios concern the **direct** clinical application of genomic information, such as diagnosis of single gene disorders, prediction of disease susceptibility or resistance, and pharmacogenetic profiling. It remains unclear whether genome sequences will be securely stored, either centrally or by individuals, for future interrogation, or deleted following use and resequenced along with their epigenome(s) as required. Similarly, there is continuing debate (which draws upon notable parallels with the computing industry) around whether genome sequencing will ultimately be undertaken by large centralised laboratories, or by desktop sequencers in every hospital.

Irrespective of which of the various possibilities becomes reality, experts agree that some points are common to all likely futures:

(1) Many existing tests for certain rare genetic variants (associated with single gene disorders and single gene subsets of common diseases) have demonstrable health benefits and should be implemented immediately;

(2) Tests for common genetic variants are unlikely to have clinically useful predictive ability for complex diseases at an individual level;

(3) It will become affordable to repeatedly resequence entire human genomes within the near future;

(4) If whole genome sequence data are stored, we will need to decide who has access and under what circumstances;

(5) Proven clinical utility and cost-effectiveness should drive the strategy for implementing new genomic technologies in the NHS;

(6) Knowing the genomic sequence is not of value in itself; interpretation is critical to ensuring utility and cost benefits over existing tests.

## 1. Scope and Vision

There are considerable levels of both excitement and scepticism surrounding genomics, as well as an increasing sense of urgency due to the enormous pace of technological development. However, while there are certainly significant benefits to specific groups – such as individuals and families with inherited single gene disorders, either of known or unknown aetiology, where there is currently a high level of unmet need – the potential for genomics to 'revolutionise' medicine and improve the health of the population in the near future has been exaggerated in the context of common chronic disorders.

Achieving clarity over what the term 'genomic medicine' encompasses is the first step towards creating a realistic vision. The House of Lords Report defines genomic medicine as '*the use of genomic information and technologies to determine disease risk and predispositions, diagnosis and prognosis, and the selection and prioritisation of therapeutic options*'. However, a broader conceptualisation would take into account the indirect benefits that derive from a better understanding of disease mechanisms at a genetic and molecular level, rather than just its use in determining risk and informing drug related decisions.

There is now widespread agreement that the importance of genetics for the prediction of complex diseases has been overestimated. Great progress has been made towards understanding the genetic basis of numerous complex diseases (through the development of genome-wide association studies), but the main application of this new knowledge will be to understand disease aetiology and its underlying biology, and ultimately develop new therapeutic strategies – this is a revolution in human physiology. Prediction and prevention of common diseases at an individual level is unlikely to be possible based on common genetic variants, although these technologies may nonetheless allow populations to be sub-divided to improve targeting of public health interventions.

The terms 'genetics' and 'genomics' imply differences in the way the technologies can be applied to individuals, families and populations in various contexts. To avoid confusion, we suggest that genomic medicine might better be defined simply as:

> '***the use of genomic information and technologies for the benefit of individual and population health***'.

The use of array-based technologies to analyse copy number changes throughout the genome is a clear example of genomic medicine that is already being applied within clinical genetics. Once new DNA sequencing technologies reach a critical tipping-point (*i.e.* when the cost of full sequencing is equal to the cost of performing a single genetic test), they will also have an immediate and significant effect on clinical genetics, by providing the capability for replacing and improving current technologies for diagnosing single gene disorders (including those where the underlying genetic cause is unknown).

Genomic technologies will also affect other medical specialties in the longer term, by guiding treatment options through pharmacogenetic testing and tumour genome profiling, for example, as well as diagnosing single gene subsets of complex diseases. In this situation, rather than being seen as different or special, genomic information should be used in addition to other clinically relevant information to inform and guide medical decision-making. Rather than driving a wedge between clinical genetics and other medical specialties, the application of genomic technology should thus allow the different disciplines to develop in parallel and learn from each other.

***Recommendation 1:*** **The long-term vision for genomic medicine in the UK should, first, concentrate on establishing interventions of proven clinical utility that will contribute to addressing unmet medical needs amongst those with inherited disorders, and second, be realistic in its assessment of the likely benefits from new technologies and novel findings.**

## 2. Evidence and Evaluation

Unlike 'traditional' genetic tests, which are targeted at the gene or mutation of interest, based on clinical judgement, the majority of data produced by genomic technologies will be difficult to interpret, and the relevance or otherwise to a specific clinical question will be difficult to assess. The act of sequencing a genome (the 'assay') is therefore effectively divorced from interpretation of the data for a particular purpose or in the context of a particular disorder (the 'test'). These considerations suggest that the utility of any piece of genomic information will require careful assessment, and that notwithstanding improvements in assay technology or decline in costs, knowledge and professional judgement will continue to be a limiting factor in its use.

Given this insight, an appropriate infrastructure urgently needs to be established to ensure that the clinical benefits of genomic information can be realised. Specifically, a system is needed to prioritise, commission, generate and evaluate data on the clinical validity, clinical utility and cost-effectiveness of different tests and technologies. We cannot over-emphasise the importance of, and urgent need for, evidence relating to new molecular tests and analyses; the lack of a system for generating data and evaluating tests not only prohibits evidence-based decision-making within the NHS, but also presents a barrier to innovation and realising investment within the diagnostics industry. The absence of evidence supporting the utility of testing, and the lack of a clear evaluation framework, will become even more significant once full genome sequencing becomes a clinical reality and performing additional analyses on stored genomic data becomes relatively straightforward (given an appropriate informatics framework).

Establishing an overarching strategic evaluation body, and a funding mechanism for clinical trials and health economic assessments in diagnostics, would provide a solution to this problem and have major implications for research, industry and health services. Rather than setting strategy or doing research, this body would be charged with commissioning or requesting clinical trials through existing funding bodies (*e.g.* Medical Research Council (MRC), the National Institute for Health Research (NIHR) and Clinical Research Organisations) for novel diagnostic tests or genomic analyses, and evaluating the evidence. Given the lack of clarity over the future of genomic and molecular tests, the group would need to be able to respond flexibly and proportionately to new developments in research and technology. This evaluation and strategic decision-making function is vital to ensuring that evidence for genomics is generated and assessed prior to implementation, and to determining the clinical utility and cost-effectiveness of different tests, analyses and strategies.

This proposed strategic evaluation is much wider in scope than those currently undertaken by the UK Genetic Testing Network (UKGTN), the Health Technology Assessment (HTA) programme, or the National Institute for Health and Clinical Excellence (NICE). Although the HGSG appears to be the appropriate group to take on this function, its remit is currently limited to developing strategy, rather than evaluation and implementation. Therefore, unless

the terms of reference can be altered, a new body may need to be established with clear links to the HGSG.

> ***Recommendation 2:*** **The Department of Health should establish an evaluation and decision-making body, *as a matter of urgency*, to direct research funding towards important strategic questions and ensure evidence-based implementation of both new diagnostic technologies and informatics systems within the NHS.**

## 3. Informatics and Interpretation

A feature of new genotyping and sequencing technologies is their power to generate large amounts of data about a single individual, including both common and rare variants of known and unknown clinical significance. Within a given clinical context, it is likely that rather than trawling through the genome looking for 'abnormalities' (*i.e.* variations from the reference sequence), a clinical question would target the analysis to specific regions of known clinical significance*. Currently it seems most likely that this targeting will be achieved computationally, through the development and implementation of informatics software that allows clinicians to interrogate specific portions of the genome sequence.

Interpreting genomic data presents a major challenge for both researchers and clinicians, and appropriate algorithms and informatics structures will need to be developed and maintained to allow efficient and targeted interrogation of the genome. IT systems will also need to be capable of transferring, archiving and mining relevant data. Effective software is also critical to allow efficient data integration from multiple sources, and ultimately facilitate the translation of genomic information into numerous clinical specialties.

Some of the necessary work towards developing bioinformatics tools and reference databases is being done by the European Bioinformatics Institute (EBI), but development of appropriate clinical systems will need additional support from other disciplines (*e.g.* statistics, epidemiology) and from clinicians themselves. These systems would need to be kept up-to-date with novel research findings, and would need to present the information at an appropriate level depending upon the clinical context and medical specialty.

> ***Recommendation 3:*** **The Government should invest in establishing and maintaining a biomedical informatics infrastructure (including both hardware and software) to allow targeted interrogation of the genome, and ensure IT compatibility between research and clinical communities.**

* For example, based on a family history of breast cancer, or a set of symptoms, a clinician might wish to know if there are any clinically relevant mutations in the coding region of the *BRCA* genes, in order to counsel their patient about the available preventative options. The same clinician would not necessarily want to know about the sequence of any other genes or non-coding regions, as this information would be essentially irrelevant to their ability to answer the clinical question posed and give appropriate advice to the patient.

## 4. Data Storage and Access

Concerns over privacy and confidentiality need to be addressed prior to full genome sequencing becoming widely available, particularly if genomic data are centrally stored. Although clear differences arise between the clinical and research arenas, many of the important questions are the same:

- who should have access to individual genomic information and under what circumstances (*e.g.* clinicians, researchers, family members, insurance companies, the police, *etc.*)?
- when and how should findings from genomic analyses (performed for either research or clinical purposes) be fed back to individuals and family members?
- should access be open or limited to specific portions of the genome sequence (*e.g.* only those that are relevant to the question being posed)?
- what, if any, measures should be put in place to prevent unfair discrimination against individuals on the basis of their genomic data (particularly by insurers and employers)?
- how can we optimally provide for informed consent to sequencing and/or analysis of personal genomic data (*i.e.* broad versus limited consent)?

In addition, given the possibility of inadvertent findings of clinical significance from genomic analyses, there will be a need to delineate clinical responsibilities and determine how far the duty of care extends within and between overlapping clinical specialties. This is likely to dictate the boundaries for medical negligence (where, for example, abnormal findings remain unreported and the patient suffers harm as a result, or where implications for other family members are not acted upon and harm arises). It will also be important to develop these principles in relation to the maintenance and use of computational strategies for interrogating genomic data.

***Recommendation 4:*** **The Human Genomics Strategy Group (HGSG) should liaise with relevant stakeholders to ensure that clear policy guidelines are developed outlining why, and under what circumstances, DNA samples and genomic information can be stored, accessed and used for clinical and research purposes.**

## 5. Health Service Organisation

Regardless of the current state of the technology and its future clinical utility, there is already a significant level of unmet need amongst individuals and families affected by single gene disorders, for whom accurate diagnosis and management of the disorder is currently feasible. In particular, diagnostic and cascade testing for single gene subsets of common disorders (such as inherited cardiovascular conditions) represents a major opportunity to derive immediate and demonstrable health benefits in terms of prevention of disease. Such benefits can only be achieved by the proper integration of clinical and laboratory genetics with other specialties. Integration will in itself provide the foundation for the further development of 'genomic medicine' within many different clinical specialties, ensuring that the transferable skills developed within medical genetics are retained – such as respecting the interests of family members, family record keeping, and a rigorous requirement for obtaining consent and maintaining confidentiality.

A strategic approach to pathology modernisation will be a further prerequisite for efficient and successful services for genomic medicine. Importantly, laboratory genetics should be considered as being part of the entirety of pathology services, rather than being separate and distinct from it. Although the technology is still developing too fast to make certain strategic decisions, it is likely that some degree of centralisation will be advantageous, by concentrating technology and expertise and avoiding unnecessary duplication of services. Genomic laboratories may need to serve numerous different clinical purposes and specialties, rather than being disease-specific.

In addition to publically funded NHS laboratories, private laboratories are also likely to offer both sequencing and/or data storage and interrogation services. Caution should be exercised by the NHS when using such services, particularly whilst the technology is in flux, to ensure that only scientifically accurate, clinically useful and cost-effective tests are offered.

***Recommendation 5:*** **The HGSG, together with the Department of Health, need to put in place an appropriate infrastructure to deal with integrated clinical services and laboratory organisation in light of new genomic technologies.**

## 6. National Formulary for Tests

In addition to developing a strategy for generating and evaluating evidence for new tests (Recommendation 2), a national mechanism is needed to decide when a new laboratory test – including laboratory and computational analyses – should be implemented within the NHS. Development of a National Laboratory Medicine Catalogue is already underway at the Royal College of Pathologists, which will act as an evidence base for tests (akin to the British National Formulary for drugs) containing guidance on testing criteria and interpretation. This open access 'pathology formulary' will summarise the evidence and clinical criteria for diagnostic tests, including new genetic tests and genomic analysis, and should provide a valuable resource for policy makers, healthcare professionals and the public.

***Recommendation 6:*** **The Department of Health should support the establishment and maintenance of a 'National Laboratory Medicine Catalogue' to provide up-to-date guidance on offering, performing and interpreting tests.**

## 7. Barriers to Commissioning

It is clear that some tests already exist that should be implemented, but remain unavailable to the majority of the public due to variations in service provision and funding mechanisms. Current NHS financial structures present a major barrier to innovation and development, and also hamper decision-making across the medical specialties, resulting in diagnostic and financial inefficiencies. The cost of an initial activity (*e.g.* a genetic test) may be controlled by a separate budget from that where potential savings may be realised (*e.g.* oncology), making it difficult to account for cost-savings generated by the use of genetic tests. Devolved commissioning tends to result in an inefficient silo mentality (where different departments are focussed on only their own services) and also leads to inequality due to regional differences in service provision.

An important part of eliminating silos is providing evidence that testing offers clinical utility and cost-effectiveness throughout the patient pathway, rather than limiting the evaluation of cost-savings to a particular clinical specialty. A more effective commissioning model is needed across the whole NHS, not just for genetics, to reduce inequality, encourage innovation and improve service provision.

***Recommendation 7:*** **The HGSG, together with the Department of Health, should review how NHS funding mechanisms act as a barrier to the utilisation of new tests, and should seek to eliminate budgetary silos in order to realise cost savings from genetic testing throughout the healthcare economy.**

## 8. Implications for Industry

The UK should aim to be an international leader for research and development in genomic medicine and ensure that it is a competitive, attractive and rewarding place to invest. Already home to a number of leading companies offering genotyping arrays and developing sequencing platforms, the UK economy is likely to continue to benefit from this burgeoning industry. New genome sequencing technologies are likely to drive uptake of genomic medicine, and there may initially be more genomes sequenced commercially than within the NHS – including through direct-to-consumer (DTC) services – despite a lack of evidence of their clinical utility. Nonetheless, while new technology underpins many scientific discoveries (particularly in genomics), it should not drive clinical or public health practice without evidence of the direct medical benefits. A balance must therefore be reached between the commercial interests of UK PLC and the potential of genomic medicine to yield health benefits and improvements in patient care through the NHS.

Developments in genomic medicine will impact widely upon the development of diagnostics and stratified medicines. However, because tests are part of a clinical pathway, rather than an end in themselves, their validity and utility is highly dependent upon the context in which they are used; a single test may be used in conjunction with numerous other tests for multiple different applications, each with differing levels of performance. There is therefore a need to establish frameworks for generating data and develop standards for assessing clinical validity and utility, which can then be used to determine the quality, efficacy and safety of novel tests.

The traditional method of realising investment in biotechnology is to gain patents over new innovations, which allows the patent holder to restrict the use of the new product and thus secure its market and price for a limited term. One difficulty with the diagnostics industry is that the diversity of applications means that patents are often unsuited to protecting proprietary investments. Hence alternative means of protecting intellectual property might need to be explored and the diagnostics industry is likely to require an alternative source of funding from that seen in existing business models. Since appropriate clinical trials are likely to be too expensive for the diagnostics industry to fund alone, public-private partnerships may be needed.

***Recommendation 8:*** **The Government should work with industry and research funders to establish systems, strategies and funding mechanisms for evaluating the clinical validity and utility of diagnostic tests.**

## 9. Regulation of Tests

Evaluation of the benefits and harms of testing should guide the proportionate regulation of tests and companion diagnostics by the Medicines and Healthcare products Regulatory Agency (MHRA). Proportionality is needed in the regulation of genetic tests relative to other *in vitro* tests; rather than simply classifying all genetic tests as medium risk under the European Directive on In Vitro Diagnostic Medical Devices (98/79/EC) solely because they involve DNA, classification should be risk-based following a scientific assessment of the potential risks and hazards on a test-by-test basis. A simplistic framework which assigns all DNA-based tests to a medium risk category will not only provide an example of unwarranted genetic exceptionalism, but more importantly could stifle innovation and reduce the benefits that genetic testing could bring to individuals and populations.

Notwithstanding this concern, some level of pre-market assessment of the validity of any particular medical test is desirable to enable consumers (both public and professional) to determine whether a particular test is valid for the use for which it is marketed. Post-market surveillance would also provide valuable information, but would require significant investment and infrastructure to be achieved; thus, pre-market assessment may be a more practicable and cost-effective approach.

***Recommendation 9:*** **The Government and the Medicines and Healthcare products Regulatory Agency (MHRA) should resist attempts to reclassify all genetic tests into the same risk category under the European Directive on In Vitro Diagnostic Medical Devices.**

## 10. Translational Research

By combining its academic strength in genomic science, bioinformatics and epidemiology with the might of the NHS, the UK should maintain its status as an international leader in translational research. In order to fully realise this potential, appropriately powered clinical trials are urgently required to determine the clinical validity and utility of new tests and genomic analyses, as well as their health economic impact.

Research is also required on managing the familial basis of hereditary disease, including understanding genotype-phenotype relationships, surveillance of disease in family members (including asymptomatic individuals who have inherited a disease-causing mutation), and developing mechanisms for cascade testing which include providing advice and medical care to families as well as individuals. As genomic analyses become more common, research funding bodies will also need to develop policies with respect to anonymisation, data sharing and reporting findings back to research participants and their families.

However, researchers need to be realistic about the likely outcomes from genomic research and the processes needed to realise health benefits. Many steps are involved in translation in order to bridge the gap between research and practice: analysis, synthesis and dissemination of knowledge, accompanied by policy and service development, are essential features of translational work. Given the pace of technological advance, it is essential that all these phases of the translation process are explicitly recognised and adequately funded, to ensure equitable and evidence-based implementation of new technologies and scientific developments.

***Recommendation 10:*** **The Government should continue to support and expand funding for translational research, and should direct research focus towards immediate problems, such as evaluating new tests, while maintaining a broad base.**

## 11. Public and Media Engagement

It is widely recognised that a simple deficit model for the public understanding of science is insufficient, and a mixed model of genetic literacy is more appropriate. Understanding of genomics amongst the public varies enormously; included in the 'public' there is a spectrum from healthcare professionals and families affected by single gene disorders, through to individuals who have had no personal contact with genetics services or inherited diseases.

In order to facilitate this process, researchers and healthcare professionals need to be adequately trained and resourced to provide appropriate contextual information to patients and research participants at the point of need. This could include supporting the NHS National Genetics Education and Development Centre to continue and expand their valuable work. Third sector organisations should also be engaged in this process, as they are frequently used by patients as trusted sources of expert information. The HGSG also needs to be adequately resourced to develop and implement a media strategy, which focuses on 'myth-busting' (rather than creating further hype around genomics) without undermining research.

***Recommendation 11:*** **The strategy of the HGSG should be to engage the public at the point of need; in addition, the HGSG should put in place a media strategy to ensure high quality coverage of genomics in the press.**

## 12. Public Involvement in Research

The potential for the NHS to gather and link anonymised information to better understand the relationship between genotype and phenotype could make the UK the envy of the world. Those using the NHS could be recruited more systematically into the research process, whether through the routine use of anonymised data and samples for research and audit, or being more actively involved through clinical trials and bio-bank initiatives.

One voluntary model for this is the Cambridge BioResource, a collaboration between the hospital, the University and the people of Cambridgeshire, in which members of the general public are approached and invited to participate in local research studies investigating the links between genes, the environment, common diseases and psychological function. Volunteers who join the BioResource provide a DNA sample as well as phenotypic data (such as age, gender and ethnicity); all samples and data are treated as confidential, and volunteers are free to withdraw from the project at any time. This type of initiative provides not only a valuable resource for researchers, but also a mechanism for voluntary public engagement in research and genomics.

***Recommendation 12:*** **The Government should support public involvement in genomics by encouraging voluntary enrolment in population-based research.**

## Conclusion

The House of Lords Committee for Science and Technology should be applauded for recognising that the enormous pace of change in genomic science and technology will require a new strategic phase for implementation into health services. However, we believe that its Report on *Genomic Medicine* overestimated the immediate importance of genomics to the prediction and prevention of common diseases, and largely ignored the synergies and opportunities to advance genomic science in the context of the improved diagnosis and treatment of inherited single gene disorders and inherited subsets of complex diseases.

Healthcare systems must respond urgently and effectively to the scale and complexity of genomics to capitalise on the opportunities presented by new sequencing technologies. Major challenges include the storage, access and interpretation of large volumes of personal genomic data, clinical and laboratory service reconfiguration, and establishing new commissioning processes and budget arrangements. Most importantly, a clear process for generating and evaluating data on the clinical and cost-effectiveness of new and existing tests and analyses is urgently needed, to ensure that policy makers and the NHS can make evidence-based decisions about the implementation of new genomic technologies for the benefit of health.

## List of Expert Participants

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The PHG Foundation is a forward-looking policy think-tank and service development NGO based in Cambridge, UK. Our mission is *making science work for health*. We work to identify the best opportunities for 21st century genomic and biomedical science to improve global health, and to promote the effective and equitable translation of scientific innovation into medical and public health policy and practice.

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ISBN 978-1-907198-04-5

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