

## A response from the British Society for Human Genetics

### House of Lords Science and Technology Committee Call for evidence: Genomic Medicine

The British Society for Human Genetics (BSHG) represents health professionals working in specialised genetic services in the NHS and scientists and health professionals in medical research. ([www.bshg.org.uk](http://www.bshg.org.uk)).

#### Summary

- The Genetics White Paper helped modernise and network specialised genetic services but a new and resourced plan is needed if Genomic Medicine is to be successfully exploited in the NHS.
- On the ground patients and practitioners find weaknesses in the translation from research to the clinic not addressed by the National Institute for Health Research programme.
- Next generation genomic technologies will require assessment and the NHS Genetics Network, Medical Specialties and Pathology need to work more closely to find the optimum service configuration, meet the challenges of managing change and exploit the new technologies.
- Factory-style technology solutions must not damage the link between the clinic and research.
- The Human Genetics Commission provides effective oversight of legal and regulatory issues but the government must not lose focus on public engagement particularly as genomic health and data security issues begin to overlap. The public must feel it has a route to policy making.
- Effective use of genomics in mainstream medicine will require education and information resources available to all levels of the NHS. Links between mainstream medical disciplines and existing specialised genetics must be resourced and must not damage or de-focus specialised genetics as it exists.
- Genomic Medicine for inherited and non inherited conditions will increasingly focus on treatment following accurate diagnosis.
- The NHS should be cautious about the implementation of genetic risk factor tests for common diseases in a population context although these tests will be available through commercial providers. Transparent information would help safeguard the public.
- Development of Genomic Medicine is as much an informatic as a technical challenge. Success will depend on international collaboration. Informatic tools need to be stabilised for use in healthcare. Integrating genomic data into the electronic health record will depend upon developing standards. Above all the issue of maintaining public confidence in the security of personal information must be addressed.

## **Policy Framework**

The most recent statement of Government policy in Genomic Medicine was the 2003 White Paper *Our Inheritance our Future*. Its implementation strengthened the framework for specialist genetic services around the new UK Genetic Testing Network and modernised laboratory services with a round of capital funding. However the short half life of genomic technologies means that the services will be faced with a need to re-capitalise in the next 3-5 years and the Government should consider recurrent mechanisms to ensure that the NHS maintains cost effective access to appropriate technology platforms.

The Government's advisory mechanisms to anticipate developments and address regulation were rationalised under the Human Genetics Commission which remains an authoritative and respected group. From a European and trans-Atlantic perspective the UK is seen as having an organised, rational and effective approach to Genomic Medicine policy and service delivery. The UK has built on this experience leading some key international policy initiatives; helping to set a framework of standards for molecular genetic testing through the Organisation for Economic Co-operation and Development and establishing translational research networks through European Union funded partnerships.

However the BSHG is concerned about weaknesses in the chain leading to translation into clinical practice. Despite successes through the UK Genetic Testing Network the widespread experience of the Clinical Genetics community is that translation of genetic research into medical practice is slowed and access to services is geographically inequitable because of this funding gap. It is telling that many patient groups are driven to fund translation to the point where a business case for a stable NHS service can be put to NHS Commissioners. There are many examples include translating into practice new diagnostic tests for Cystic Fibrosis, familial breast cancer, genetic eye conditions and cardiac conditions. Unfortunately the strong impression of the Genetic Medicine community is that at this early stage the National Institute for Health Research does *not* interpret its remit as extending to support for the evaluation of research-based diagnostic tests in NHS service laboratories leading to their implementation in the clinic.

**Recommendation 1.** The BSHG recommends that NIHR supports a programme to evaluate and implement individual genetic diagnostic tests within the NHS and that the Government plans for the resource needs of Genomic Medicine in the NHS.

Next generation genomic technologies (micro arrays and parallel sequencing) will require a full Health Technology and economic assessment. This study should pool the valid requirements of the genetics network and mainstream medicine working with pathology. It should factor the rising numbers of clinically useful tests against falling unit costs. It will recognise that the implementation of new technology will incur an increased global cost for genomic diagnostics calculating the health benefits to patients and savings in diagnosis and treatment across the NHS.

In addition changes to the physical and organisational infrastructure and personnel requirements for information handling, transfer and storage must be considered including the need to re-skill scientists and doctors to interpret genotype data. Next Generation technologies lend themselves to high throughput, high volume settings. The optimum service configuration for these technical genotyping platforms as they become applicable will need a careful study and change management. Above all the dynamic link between research in regional academic and clinical centres and access to genomic technologies must not be lost in service re-configuration.

**Recommendation 2:** The BSHG recommends that structural links between Pathology Modernisation and Genetics should be established to facilitate the optimum service configuration for genomic diagnostics. When appropriate the NHS should commission a Health Technology Assessment of Next Generation Genomic technologies. The needs of the whole health service should be considered in this study.

## **Social Ethical and Legal considerations**

Science and clinical policy decision making is embedded in ethical practice under the oversight of the Human Genetics Commission. The UK has a strong framework for training and education and the governance of clinical practice. This has been developed through professional bodies under the umbrella of the British Society for Human Genetics representing Doctors Counsellors and Scientists. In addition guidance is available through focussed efforts (the Genethics club) and specialist research (the Genetic Knowledge Parks, Ethox centre and the Economic and Social Sciences Research Council genomics network)

Genomic medicine offers the promise of better diagnosis, treatment and care, yet it also challenges the very nature of the relationship between the clinical community and the public. We believe that it is the duty of the genetics community to help empower citizens to make personal health management decisions.

In 2003, in the Genetics White Paper, the Government recognised the power of genetics in a post-genome NHS along with the possibility of its rejection by the public, through lack of trust or understanding.

“Realising the full benefits of human genetics will require public acceptance and public confidence...The Government is committed to ensuring openness and transparency in genetic policy making. We want to engage in a genuine dialogue on genetics issues. We recognise that developments in genetics will present new ethical and social challenges. We need to be alert to the potential adverse consequences and prepared to take action where necessary.”<sup>1</sup>

In order to fulfil this aspiration, Government should uphold these sentiments, by developing the infrastructure and funding a national programme of rigorous public engagement that will bring about informed input into health and healthcare policy decisions surrounding genetic and genomic medicine. To achieve a mature public dialogue, we would expect such a programme to contain the following:

- Effective knowledge and information dissemination about genetic and genomic medicine
- Use of imaginative and novel modes of engagement
- Understanding what the public thinks and why they think in this way
- Informing decision and policy-making through the use of extensive valid and reliable public and patient consultation:
- Aiming towards public and patient representation at committee level.

The House of Commons Health Select Committee report on Patient and Public Involvement in the NHS<sup>2</sup> highlighted the problems of conflating involvement of patients with that of the public, and criticised the Government and the NHS for not making changes in the light of public views. These concerns echo work in the realm of ‘personalised’ medicine that has shown there is scepticism and mistrust in some quarters of the general public. Such attitudes require further exploration to reveal the likely response to ‘personalised’ medicine delivered routinely in the NHS.

In view of the above the BSHG regrets the Government decision to prematurely end support for the Genetic Knowledge Parks as short-sighted and damaging to the effort to address public concern over the implementation of genomic medicine.

**Recommendation 3.** The BSHG recommends that the Government facilitate an adequately resourced programme of engagement between health professionals, policy makers and the public.

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<sup>1</sup> Our Inheritance Our future – Realising the potential of genetics in the NHS; June 2003

<sup>2</sup> Patient and Public Involvement in the NHS: Third Report of Session 2006–07. House of Commons Health Committee (March 2007).  
[www.publications.parliament.uk/pa/cm/cmhealth.htm](http://www.publications.parliament.uk/pa/cm/cmhealth.htm)

## ***Developing Genetics in mainstream medicine***

Over the last five years the theme of developing genetics in mainstream medicine has developed rapidly and requires a policy response addressing health service configuration commissioning and education of health professionals.

In our view, the scale of development of genetics within many areas of mainstream medicine will be such that the current paradigm of 'joint management' between genetics and the specialist department will become untenable. This means that people with 'genetic disease' will largely be looked after in the relevant specialty (cardiology, lipidology, ophthalmology etc) by those with special education and training in genetics and with access to expert genetic referral to deal with more complex issues (such as diagnosis of rare syndromes, interpretation of complicated test results and counselling about prenatal testing).

If mainstream specialist services are to increase their input to the management of genetic disorders, there must be a significant improvement in expertise within each medical specialty. Consideration should therefore be given to the development of the following:

- Inclusion of genetics aspects in all areas of specialty training (e.g. medical, nursing and other associated specialties such as dietetics)
- Establishment of sub-specialty training programmes
- Access to specialist genetics departments for mentoring and continuing education of genetic and nurse counsellors working within medical specialties
- Access to specialist genetics departments and ethical groups (eg Ethox) for discussion and education around ethical dilemmas and other aspects of genetic counselling.

**Recommendation 4.** The BSHG recommends that the current efforts to embed genetics in specialist medical education be continued and that access by medical specialties to the Clinical Genetics network be adequately resourced.

## ***Research and Scientific Development***

A major challenge of 21st century genetics is to understand how the mutations and polymorphic variants that cause/predispose to disease act functionally. This information will inform rational therapeutics for many monogenic and complex diseases. This objective was not the focus of the White Paper (except for gene therapy, which may have very limited utility). We need to move the field on from diagnostics, counseling and risk assessment towards treatments.

This will require focused investment in cell biology, biochemistry etc, in animal modeling and in development of therapeutic targets/strategies. Genetics will then need to learn how to interface with treatment specialties requiring new types of multidisciplinary clinics and different counselling approaches.

Approaching 2,000 genes have been associated with single gene disorders many of them very rare. Patients with these conditions represent a significant aggregate health burden especially as they include the mendelian subset of common cancers and cardiovascular disease. Their care represents the major part of the workload of Regional Genetic Centres. New technologies, for example micro array comparative genomic hybridisation, will rapidly uncover genes for rare disorders and help explain and accurately diagnose significant numbers of patients referred to neonatal and paediatric services including unexplained birth defects and learning difficulty.

Whole Genome Association studies are uncovering variants in genes for common disease which will first lead to a better understanding of the biology of disease mechanisms, then aggregate into predictive tests and later still lead to better treatment.

The BSHG considers that in the NHS the utility of predictive tests should first be evaluated in specific patient groups defined for example by a sign, symptom or family history. These tests should not be considered from the outset as population based screens.

This is because of the complexity of evaluating their utility in a population context. An evaluation would measure the individual and public health benefits realised through people at higher genetic risk changing their life-style. It would need to balance these gains against the potential harms amongst those given a low genetic risk result considering this a 'licence' for high risk behaviour.

However curiosity will lead people to order a genetic test through a commercial provider possibly through the internet and based overseas. Unless specific harms are demonstrated this sector should not be over regulated. However the government should inform the public of existing international guidelines for example those adopted by the OECD. The guidelines recommend that genetic testing is offered in a medical context and that

counselling should be available and be proportionate to the level of genetic risk that may be revealed by the test. Importantly governments are asked to ensure that providers should be transparent about the characteristics and limitations of the test offered. The Foundation for Genomics and Population Health (PHGF) and the Royal College of Pathologists have recently recommended that test evaluation information be made publicly accessible. If adopted failure to provide data by a commercial or public sector provider would be apparent.

**Recommendation 5:** The BSHG strongly supports the recommendation of the Foundation for Genomics and Population Health and the Royal College of Pathologists for an expanded mechanism to evaluate the validity and utility of laboratory tests and to make this data public. NHS Commissioners should consider these evaluations before funding genetic tests including new predictive genomic risk factor tests.

### ***Data Use and Interpretation***

At present genomic data are not presented usefully in that they are not coordinated in terms of entering, storing, integrating and searching for data. European projects led from the UK such as *Gen2Phen* will develop tools, resources and standards to help address these issues. In our view a common public database is not the answer as the design, scope and abilities of existing databases are so varied and there are already many initiatives to collect and publish data. Genomic databases are often international. As rare phenotypes and genotypic combinations are recognised and common disease phenotypes are stratified through genotype to a finer level of detail it will be essential, if we are to realise benefits for patients, that the UK participates and benefits from international collaborations.

One difficulty for health services is the sustainability of informatic resources. Funding methods include grants, sponsorship and subscription. However the remote nature of many internet-based resources means that the user is completely reliant on the supplier maintaining the service. There are examples where service failure due to a break in the funding continuity to an informatic resource provider has caused problems. In the near future this could be potentially catastrophic for healthcare users who have little or no fall-back position. Informatic tools are increasingly integrated into NHS care pathways. The government must consider how the NHS can contribute funds, data and expertise, and how it might have an input to the provision and management quality and standardisation of key resources to ensure that they remain available, current and suitable for use as tools in healthcare.

**Recommendation 6.** The BSHG recommends that the Government should plan for the integration of genomic data into the electronic health record. Planning should include the transitional phase during which partial genomic data is collected up to and including the point where a complete genome sequence on each individual is an economic possibility. It is essential that the sustainability and quality of informatic tools for interpreting genomic data is addressed. Critically the government should address public confidence through public engagement with the issue of genomic information in electronic health records.

### ***The utility of genomic information in a healthcare setting***

The issue with non genotypic medical information is with the coding and classification of phenotype data. The principle aim of projects including *Gen2Phen* is to combine genotype and phenotype data. Underlying this are issues of coding and classification, and definitions of phenotype, which at present are not standardised. As the NHS National Programme for Information Technology has developed Genetics has considered some of these issues and found that clinical centres all use their own classification of diseases. Mandated coding standards like Snomed-CT and HL7 require, and are in the process of, extensive development in order to be applicable. Elsewhere the Rare Disease Task Force led by Orphanet in Paris are beginning projects concerning rare genetic diseases including input to the International Classification of Disease. This recognises that the current version ICD-10 does not provide sufficient detail and accuracy for unambiguous classification of inherited diseases. With coding standards in place it should be possible for genomic medicine to converse fully with the NHS medical systems that are being developed and avoid remaining an isolated speciality. One specific issue that must be addressed is the representation of family data which is not possible within the current NPfIT systems.

**Recommendation 7.** The BSHG recommends that the Government support a programme to modernise the information technology available to genetic centres. This should focus on piloting phenotypic coding designed to be compatible with the emerging standards of SnomedCT and ICD11. In addition it should trial secure methods within a governance framework of storing and making accessible genomic data for healthcare purposes.