

UK Genetic Testing Network

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

Submission by: UK Genetic Testing Network (organisation submission)

The United Kingdom Genetic Testing Network: Background

The UKGTN Steering Group was established in 2002 as a sub group of the Department of Health's national Genetics Commissioning Advisory group (GenCAG). It is a collaborative group of NHS laboratory scientists, clinical geneticists, genetics commissioners and patient representatives. It aims to promote the provision of high quality equitable genetic testing services for NHS patients across the UK. This involves evaluating new tests and recommending to commissioners those appropriate for service. There are 32 member laboratories from regional genetics and other specialist laboratories. A small project team and five working groups carry out the work on behalf of the Steering Group.

The UKGTN has an internationally recognised process (commonly referred to as the "Gene Dossier process") to evaluate new genetic tests (within its scope) being proposed for NHS service from its member laboratories. Tests that pass the UKGTN evaluation process are recommended to commissioners for funding via GenCAG. A Directory¹ is produced annually listing all the tests that have been through this process and the associated testing criteria to promote appropriate referrals. The Genetic Interest Group reports that patients have recognised the increased availability of genetic tests because of the UKGTN system. Different approaches are used internationally², but the UK is seen as a world leader.

Key Points

- The UK has an internationally recognised system for assessing a subset of genetic tests and recommending them for clinical service. This system relies on co-operation and collaboration between all parties.
- Discussions about developing a policy for generating and assessing data about biomarkers and pharmacogenetic tests should be held in preparation for assessing their clinical utility and validity before being accepted into NHS service
- The UK needs a policy and mechanism for translating genetic tests into service
- There are issues to be addressed about coding genetic information and linking family data in the NHS IT system
- It is important that the commissioning and funding of genetic testing and genetic services are explicitly considered when national policies are developed that affect all aspects of health care
- Genetics education (particularly over the appropriate ordering and interpretation of genetic testing) remains a key priority

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1. *The Directory of genetic tests that have been evaluated and are available from UKGTN member laboratories is available from the UKGTN website at www.ukgtn.nhs.uk*
 2. *The evaluation of clinical validity and clinical utility of genetic tests (September 2007), authors Dr Mark Kroese, UKGTN Public Health advisor; Dr Rob Elles, Director NGRL Manchester; Dr Ron Zimmern, Executive Director PHG Foundation.*

1. Policy Framework

- 1.1 National policies are set by the Department of Health genetics branch. The UKGTN advises the Department of Health (by formally reporting to the Genetics Commissioning Advisory Group) on policy issues that will have an impact on the provision of genetic testing services

within the NHS. The mechanism for advising GenCAG is strengthened by UKGTN also regularly reporting to the National Specialised Commissioning Group Network meetings and by our Project Team being led by a Director of Specialised Services Commissioning. However the UKGTN is purely advisory and collaborative and therefore cannot, for example, enforce funding for recommended tests. Consequently there may be inequity of service provision across the UK due to local commissioning arrangements; UKGTN is carrying out a survey of testing provision for the year 2007/08.

- 1.2 A genetic test is defined for UKGTN as a test for an inherited disorder where nucleic acid is the analyte. Evaluating other genetic tests is not formally within the remit of UKGTN, for example biomarkers associated with disease susceptibility or pharmacogenetic testing. However UKGTN keeps a watching brief on these wider developments in order to provide comprehensive advice. It therefore carried out a consultation to ascertain views as to whether such tests should be evaluated for analytical and clinical validity and utility before being proposed for NHS service³. There was broad agreement that a mechanism for doing so should be identified. Based on this, recommendations have been made to GenCAG to influence future policy. The consultation has now been widened to include Royal Colleges, Professional and other organisations such as NICE, Wellcome Trust, the Centre for Evidence based NHS Purchasing. It is extremely important that a national policy be developed in readiness for when such tests become available either commercially or as part of NHS provision. UKGTN is willing to make its experience in assessing genetic tests available.
- 1.3 Another example of UKGTN anticipating technologies that may impact on future service provision and policy is its asking the PHG Foundation (formerly the Public Health Genetics Unit, Cambridge) to review the use of micro arrays to detect genome imbalance in learning disability⁴. The UKGTN made proposals against all the recommendations listed in the report.
- 1.4 Regarding genetic testing, other organisations with an interest in policy include the National Genetics Reference Laboratories (NGRL) which assess scientific validity of new technologies and make recommendations. NICE appears to focus more on treatments than laboratory diagnostics. Exceptions are when mainstream specialities with a national profile are reviewed e.g. breast cancer and cardiology. The National Horizon Scanning Centre also considers genetic technologies. UKGTN was disappointed that HTA did not take up a proposal to examine microarrays and their introduction into clinical practice.
- 1.5 It would be advantageous if policy makers in the wider NHS came to appreciate the importance of genetics and genetic testing. Genetic testing is currently of low volume but the use of genetic technologies is likely to filter into all specialties. Operational issues need addressing such as a need to develop adequate coding and categorisation (by HSCIC), currencies for tariff development (the PbR team) and family based electronic records linking with the development of coding so that genetics services can feed into PAS (Connecting for Health).

3. *Evaluation of novel genetic tests & complex molecular biomarkers (July 2006), authors Dr Ron Zimmern, Public Health Genetics Unit & Dr Mark Kroese, UKGTN Public Health advisor*

4. *Evaluation of the use of array comparative genomic hybridisation in the diagnosis of learning disability - Report of a UK Genetic Testing Network working part (August 2006), main author Hilary Burton, Public Health Genetics Unit.*

To contribute to these, the UKGTN ran a project to inform national tariffs for genetic testing⁵. UKGTN continues to link with the Department of Health Payment by Results team

and the Health and Social Care Information Centre and to influence policy on currencies, coding and classification for genetic testing. The UKGTN also links with the European Rare Diseases Task Force on the development of coding for genetics (ICD-10) which in turn is used by the NHS to code and group services.

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- 1.6 Commissioning policy identifies Genetic services (clinical and laboratory) as a specialised service in the National Definition set published by the Department of Health. Genetic tests are requested by the referring clinician either from a mainstream speciality or by clinical geneticists. As new tests are developed there will be a need for the national tariffs/local prices to be adjusted for these costs. UKGTN has been working to develop tariffs for genetic tests separate from clinical services. This will also require an educational initiative for referring clinicians outside clinical genetics.
- 1.7 Regarding ethical, legal and social implications, UKGTN takes these into account as part of the Gene Dossier Process but wider implications are addressed in depth by other bodies.
- 1.8 The UK may need to influence current discussions in Europe concerning the IV Directive and the possibility that genetic tests may move from category 1 to category 2. Category 1 products are self regulated whereas category 2 products need to meet formal regulations. UKGTN is concerned about the impact on tests developed “in house”. Some laboratories may have to move to use commercially available kits which are likely to be more expensive and may not provide the exact testing requirements.

2. Research & Scientific Development

- 2.1 The UKGTN remit does not include the co ordination or advice on research but because it provides advice on the likely impact of new genetic technologies and new tests on service configuration the UKGTN does have a role in horizon scanning.
- 2.2 The rate of change in genetics technologies is fast moving. The NHS seems to find difficulty in keeping up. For instance, efficiency and productivity from introduction of new technologies into genetics laboratories by the White Paper is only just being realised although some of the equipment may already be considered out of date. Currently new developments include whole genome sequencing and micro arrays. These new technologies may impact on the speed of providing test results.
- 2.3 Although core research attracts funding, UKGTN recognises a policy gap in identifying mechanisms to support funding for development and translation. Also, it is important to ensure that there is a policy mechanism not only to ensure sufficient national capacity for genetic testing but that it can be used flexibly in response to clinical demand and the advent of new technologies that could link with Pathology Modernisation.
- 2.4 There may be value for the NHS to consider laboratory configuration as the boundary between cytogenetics and molecular genetics becomes less distinct due to new technologies. It may be difficult to ensure national capacity and influence laboratory configuration, as specific Trusts manage the regional laboratories.

5. *UKGTN National Tariff Exercise – National Tariff Proposals for Molecular Genetic Testing (May 2007)*, author Jane Deller, UKGTN Project Manager in collaboration with the UKGTN Project Team

3. Data Use and Interpretation

- 3.1 Genomic information associated with clinical disorders is being collated and annotated in various databases, for example DECIPHER (**D**atabases of **C**hromosomal Imbalance and **P**henotype in **H**umans using **E**nsembl **R**esources) run by the Wellcome Trust Sanger Institute. One of the National Genetics Reference Laboratories is also taking forward a Clinical Molecular Genetics Society initiative in establishing the Diagnostic Mutation Database (DMuDB) to collate data derived from sequencing disease genes in quality assured laboratories.
- 3.2 Performing an assay (the method used to analyse a sample) may be undertaken using robotics but the clinical interpretation of the raw data usually has to be carried out manually. It is the latter which requires specific expertise and knowledge of the genetic condition. Concomitant with an increase in speed of generating test data, there has to be an increase in the capacity to provide an interpretation. Introducing new technology may therefore place a strain on genetic laboratories as interpretation of genome data demands more time. The development of software for interpretation of results would appear to be a priority.
- 3.3 Laboratory and family data from patients referred to specialist genetics services usually have to be recorded on bespoke IT systems because NHS programmes tend not to have the ability to manage them adequately. This is because of the need to link family information and the lack of nationally agreed coding. This affects not only genetic services but as patients with genetic disorders are seen in all specialties, family information may be important in management. This is a challenge for the NHS IT system.
- 3.4 The Human Genetics Commission and the PHG Foundation have considered the implications on storing genome data and on privacy. The Genetics and Insurance Committee are probably better placed to comment on the use and abuse of genetic information in insurance. The JCMG also produced a report on consent and confidentiality. Particular attention needs to be paid to direct consumer testing and how results will be stored and used.

4. Translation

- 4.1 UKGTN has concerns about the current lack of a mechanism to translate genetic tests from research into clinical practice and validate them. There is a demonstrable gap in translation between the identification of genetic tests for genetic disorders and their development into NHS service. Currently commissioners expect laboratories to submit a business case to their hosting NHS Trust for development monies. However we are advised that the laboratories have difficulties in securing a financial commitment. Within the current research and development framework it is unclear how information about clinical utility of biomarkers will be generated to inform acceptance of a test into NHS service, and whose responsibility this should be.
- 4.2 Translation into clinical practice has often been as a result of local clinical interests. The UKGTN is concerned that a mechanism is developed to ensure tests are introduced into service where no laboratory has a prior interest. In addition, the UKGTN has been encouraging laboratories and clinical services to develop “portfolios” of testing, concentrating either on several diseases associated with a particular gene, or a particular disease.

- 4.3 Investment from the White Paper for English laboratories provided an opportunity for laboratories to modernise. However there is no rolling programme of investment unlike Scotland which has a rolling capital programme for molecular genetics. Left to each individual organisation the investment will differ by organisation and pace of change will differ and consequently the levels of service will not be equitable. Due to the fast pace of technological change this is a particular issue for laboratories using genetic technologies.

5. Biomarkers and epidemiology

- 5.1 The current remit of UKGTN does not include evaluation of genome-wide association data, but UKGTN does have a role in evaluation of tests for high genetic risk biomarkers as used to identify subsets of common disease presentations where there is high hereditary risk, (e.g. in hereditary breast or bowel cancers, or in sudden cardiac death).
- 5.2 There is an urgent need to determine how the UK is going to collect epidemiological data for assessing tests for rare single gene disorders and biomarkers. It may be difficult to gain epidemiological data about many single gene disorders because of their low frequencies. Data that could be collated are not being captured on NHS systems. In addition, it is vital that studies are undertaken when biomarkers are identified to assess their utility in clinical practice before being accepted into NHS care. As discussed earlier, it is not clear how such studies are going to be developed and funded.

6. Use of genomic information in a healthcare setting

- 6.1 As inherited conditions are researched, many are found to be genetically heterogeneous, with mutation in more than one gene causing the same, or a very similar clinical presentation (eg. Spinocerebellar ataxias [SCA1-17]). Conversely there are now several examples of genes where different mutations in one gene can cause very different clinical conditions (eg. FilaminA, Lamin A/C, and a calcium channel gene CACNA1A – including SCA6 as one of its presentations). The classification, or sub-classification of such conditions for coding purposes is a challenge, but will probably require some form of dual approach. The UKGTN is involved with Orphanet and the Rare Diseases Task Force in Europe in developing a standard approach for coding rare disease including ICD-11.
- 6.2 The UKGTN currently uses OMIM for disease nomenclature and the HUGO database for gene nomenclature.
- 6.3 Although UKGTN evaluates proposed new genetic tests for NHS service for inherited disorders, there is no assessment of tests made available where non UKGTN laboratories are providing the testing. An opinion is not available to the UK population on the merits of direct to consumer testing either, increasingly freely available through the internet. There appears to be little evidence base on the utility of these tests and information about test results direct to consumer are not always clear in explaining relative risks. This could have an impact on the NHS if anxious consumers enter the NHS system to ask advice.
- 6.4 UKGTN wanted to explore the issues of introducing genetic tests into a “mainstream” specialty, and commissioned the PHG Foundation to explore the issues taking ophthalmology as an example⁶.

6. *Genetic Ophthalmology in Focus, A needs assessment and review of specialist services for genetic eye disorders – Report for the United Kingdom Genetic Testing Network (March 2008), authors Professor Tony Moore, Professor of Ophthalmology, Institute of Ophthalmology, University College London & Dr Hilary Burton, Consultant in Public Health Medicine, PHG Foundation, Cambridge.*

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It is likely that not all clinicians within a particular specialty will need to develop in-depth genetics expertise, but all clinicians should be able to recognise when it would be appropriate to refer a patient to a genetics specialist either within the specialty or to clinical genetics. Clinical genetics would continue to see patients with very rare conditions but would also provide information and support to other specialties. The report gives an excellent overview of policy and organisational requirements necessary for “mainstreaming” genetics.

- 6.5 As the number of appropriate genetic tests increases, the current role of the specialised genetic services in “gate-keeping” will need to be reconsidered. Some colleagues in other specialties increasingly will want to use genetic testing. Funding will need to take account of test costs within these other specialties and there will also be a need for education and information. The requesting or reporting of a genetic test requires education in genetics and therefore UKGTN is working closely with the NHS National Genetics Education and Development Centre in Birmingham. With Skills for Health, the Centre developed core competences for non genetics healthcare professionals, including competences regarding ordering and interpreting genetic tests to patients. This is likely to a long term task, and requires the involvement of education providers, statutory bodies responsible for professional training and policy makers.
- 6.6 There will be a particular need for some in the NHS workforce to develop skills in differentiating between genetic test results that offer certainty, and those that give a relative risk. This may have particular relevance to direct to consumer testing where UKGTN believes that those providing the tests have a duty to ensure that consumers are given sufficient information. We are aware that some people believe that this should be made mandatory.