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Genetic laboratory service redesign

The PHG Foundation is broadly supportive of efforts to harness the use of genomics and genetic technologies within the NHS, and to provide high quality, equitable and cost effective services with appropriate support for patients and families.

Are the proposed changes to regional genetic laboratory services clear and understandable?

We feel that the current service specification does not provide sufficient clarity in some key areas. In particular, the draft does not make it clear how many Genomics Centralised Laboratory Hubs (GCLHs) there would be: would this include all or most of the current regional genetics centres, or consist of a much smaller number, for example? It is our view that it would also be essential to explicitly state how the network of GCLHs and their associated Genomics Local Laboratory Hubs (GLLHs) would together provide complete population coverage.

We suggest that if there are to be significant economies and efficiencies through mass throughput, cooperation and reduction in duplication, the numbers would have to be significantly reduced from current regional centres (*e.g.* to fewer than ten). We welcome further clarification on this issue.

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We also query the specific exclusion of molecular sequencing of pathogens (para 3.5) and a number of other laboratory services that will use genomic technologies. We believe that the potential to use sequencing capacity, and the similar needs related to standards (for example around equipment QC or storage and sharing of data) would suggest that coordination and sharing of experience would be valuable and should actually be encouraged.

Will the proposed approach deliver 'state of the art' genomic laboratory facilities and improvements for patient benefit for the NHS in England?

While the proposed changes seem to be going in the right direction in order to deliver 'state of the art' facilities, the current provisions do not go far enough to ensure the necessary transition. If the 'legacy of the 100,000 Genomes Project', and genomics more generally, is to achieve benefit for NHS patients (and the population as a whole), we suggest that the following need to take place:

While the proposed changes seem to be going in the right direction in order to deliver 'state of the art' facilities, the current provisions do not go far enough to ensure the necessary transition.

1. There needs to be an evaluation from a clinical NHS perspective of the 100,000 Genomes Project with particular emphasis on its impact on clinical practice and the way that whole genome sequencing would fit, alongside other technologies, into current and new pathways of care. This needs to be followed by formal implementation processes, whereby new pathways of care are designed and commissioned by the relevant bodies

2. There will be a need to develop and maintain a secure, comprehensive accessible NHS database to undergo ongoing genomic sequence interpretation, improve clinical outcomes and support the needs of clinical services. This should be an integral part of NHS genomic testing services

3. Deposition of data into the database needs to be mandated through enhanced service specification, accreditation and commissioning

4. There needs to be a new focus on the development of healthcare systems to make the most of genomic medicine; including a shift to more preventive care, more personalised prevention and healthcare, integration of genomic and other digital health technologies to support prevention, explicit support and resourcing of practical implementation rather than placing reliance on translational research, education of a wide range of health professionals (see also Qu 4) and provision of support for patients and the public to equip them with the knowledge and opportunity to make meaningful decision about their healthcare

5. As paragraph 2.1 of the Service Specification document suggests, this is likely to involve a transition from laboratory-based testing and reporting, to increased use of point of care tests, which will enable and facilitate patients and carers to monitor treatment responses and changes in their clinical status. Funding for point of care devices and provision of appropriate support for patients, carers and healthcare professionals is a pre-requisite, before any concomitant reduction in laboratory capacity

NHS England preferred approach is to commission genetic laboratory services for patients over seven days a week in line with plans for other NHS services. Do you agree with this approach?

This depends on whatever is most cost effective and efficient. Genomic sequencing costs will be minimised if sequencing machines are run over seven days of the week at full capacity. Thus running services over seven days a week in line with other plans may offer some advantages. However, this will depend on the demand for sequencing, as well as the desired turn-around-times for results.

Are there any inequality / health equalities issues which you think should be considered in making a decision about the future delivery of genetic laboratory services in England?

Substantial inequalities already exist now and will only increase in the future, due in part to lack of awareness of physicians around the UK in the opportunities that genetic / genomic testing may provide for their patients. Inequalities arise across different specialties and in different geographic areas, and they are also likely for different patient backgrounds as defined by ethnicity, socioeconomic or educational status.

We believe that the impact of state of the art laboratory services on UK / English population patient benefit will be severely limited by the ability and competence of physicians to recognise the need for and help their patients gain access to, genomic testing. We would like to bring to the review's attention work done on Genomics in Mainstream Medicine, collaboration between Royal College of Physicians, Joint Committee on Genomic Medicine and PHG Foundation. Inequalities are also likely to arise through cross-border issues as discussed above.

Are there any other considerations which need to be taken into account, which have not been covered in the proposals?

Genomic knowledge is increasing exponentially, but significant challenges remain to generate knowledge that is clinically useful for NHS patients. Interpreting genomic variants in ways that distinguish between those that are disease causing and those that are not, in a timely and affordable manner, remains the biggest challenge. For this reason it is vital that each of the GCLH's systematically share their data, knowledge and expertise within the strategic network. It should be explicitly specified that GCLHs must work together as stated to share data, intelligence and expertise.

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Thus we strongly endorse the aim (section 3.1) of driving improved quality *"through collation and sharing of data for patient benefit by standardisation of and participation in minimum agreed datasets…."*. Indeed the clinical interpretation of genomics data and variants relies on access to pre-existing knowledge and data. In addition to genomic/genetic data, interpretation of variants also requires phenotypic information not only on the patient under investigation, but also phenotype data linked with genetic data from previous cases. As most phenotype data and genotype data are generated and recorded in different places, it will be imperative for the GCLHs to collaboratively agree and determine the level / detail of phenotype data required to support their genome analysis activities, how this can be collected and recorded in a systematic way, and how this can be shared integrated with variant data.

Another important priority is to target the application of genomic sequencing technologies at those clinical specialities and phenotypes most likely to generate clinically useful knowledge, and to minimise the generation of variants of unknown significance or incidental findings that will then require further investigation or referral, particularly arising from areas of the genome that are not pertinent to the patient's clinical presentation. This would complement the desired impact (on page 2 of the specification) of *"safe and effective targeted treatment based on the genomic profile with minimised side effects as part of the overall move towards stratified and precision medicine".*

Specifically, emerging from our report on *Realising Genomics*, which is concerned with use of genomic sequencing in clinical settings, we recommend that the network should adopt as standard the use of targeted analysis of whole genomes using 'gene lists' that are nationally agreed following genome-based sequencing as the assay and using standardised evidence criteria, unless, in a particular class of cases, there are good clinical reasons for adopting whole genome or exome sequencing as a first line test.

In order to maintain public trust and confidence in these services, it is important that services are developed in ways that are both transparent and accountable.