Genomics Education Programme

NHS
Health Education England

Clinician's guide for requesting whole genome sequencing: rare disease

Introduction

This guide has been developed to support clinicians who will be requesting whole genome sequencing (WGS) for patients with certain rare diseases. The guide highlights key points to cover during conversation(s) with patients about WGS and contributing to the National Genomic Research Library (NGRL), based on the statements in the record of discussion (RoD) form.

Further information to support this guide can be found at www.genomicseducation.hee.nhs.uk/supporting-the-nhs-genomic-medicine-service/.

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... for a handy pre-appointment checklist

Key points to cover when discussing clinical WGS

Introduction and context of the test

- Test is diagnostic (to identify an underlying cause for the individual's presenting condition).
- Sequencing of the whole genome will take place, although diagnostic analysis will focus on known genes associated with the clinical presentation.
- Samples from other family members may be required for whole genome sequencing, or after results.

Results

- Test may not yield any significant finding; this would not exclude a genetic diagnosis.
- Interpretation and knowledge about results may change over time.
- Main findings: results in connection with the patient's existing condition. They may or may not affect current/future care, or provide insight to prognosis or other health conditions.
- Variant(s) of uncertain significance: uncertain findings that may require following up now or in the future.
- Incidental findings: unexpected results not related to reason for the test (including family relationships).
- Results will not inform all health conditions (currently no additional looked-for findings).
- Confirm approximate timeline for results and communication process (how any results are fed back, by whom, and with whom they would be shared).

Implications for the patient

- Onward referrals may be made for screening or management based on results.
- Potential psychosocial impact of receiving results and support available.
- Implications for family planning and reproductive choices.
- Association of British Insurers' code for disclosing genetic test results vs medical/family history.

Implications for family members

- Opportunities based on results or family history where relatives could have access to preventative screening, predictive testing, and/or information about reproductive choices.
- Discuss importance of sharing results with family members, as they may impact blood relatives, and strategies that may be used (such as 'To whom it may concern' letter).

Use of samples

- Samples: typically blood; may be saliva or tissue, or previously stored DNA.
- Samples are stored and accessed within the Genomic Laboratory Hub, other local labs (such as pathology) and other labs within the NHS Genomic Medicine Service.
- Stored samples may be used for further genomic tests in the future with appropriate consent.
- Sample can be used as a control for testing other individuals, including family members.
- De-identified samples may be used for lab test development or quality control procedures.

Use of data

- Data includes patient's health and genomic information, which can be securely accessed on an ongoing basis by NHS healthcare professionals.
- National (identifiable) and international (not identifiable) comparison of data for greater understanding of significance of results.
- Genetic variant(s) may be shared (with limited identifiers) for relatives to access testing.
- Genomic data may be reanalysed in future as new evidence can occasionally change results over time.

Key points to cover when discussing the NGRL

Introduction and context

- The NGRL is a collection of data from patients and family members that can be accessed by researchers.
- Aim and potential benefits of having a large dataset and access to research to improve diagnostic potential of genomic information.
- Patient can request to withdraw at any time, either partially (no future contact) or fully (no future data use) at any time.

Implications for the patient

- Individuals would be giving permission to Genomics England to manage access to their health and genomic data.
- Each individual may or may not benefit, but increases the chance of a diagnosis in future.
- Wider benefits of learning more about rare diseases to guide management.
- Individuals may be re-contacted for further information, regarding new findings or other studies.

Use of samples

- Genomics England can access samples stored in the NHS if this would not otherwise affect clinical care.
- Samples are held securely within the UK and not sent outside without explicit consent.
- Patient may be invited to donate additional samples for research.

Use of data

- Data and samples will have name, contact and other personal identifiers removed.
- Data includes genomic information as well as other health and social care records.
- Controlled, read-only access by approved researchers both in and outside of the UK including not-for-profit and commercial (for-profit) organisations.

PRE-APPOINTMENT CHECKLIST

- **Is your patient eligible for WGS?**
  Check the National Genomic Test Directory (www.bit.ly/NatGenTests), which specifies which patients may be offered a WGS test. Tests should be targeted primarily at situations where a genetic diagnosis will affect the healthcare of a patient or their family members.
- **Should other family members be included?**
  This will depend on the suspected inheritance pattern of the condition. In general, for childhood-onset conditions it is best to test the affected individual and both parents (where possible). For adult-onset conditions, it is usually best to test just the affected individual. If you need advice, you may wish to discuss with your local GLH or appropriate clinical team, such as clinical genetics.
- **Do you have the forms you need?**
  A WGS order form must be completed with relevant clinical and family history information. There are also nationally standardised RoD forms to record each individual (patient and relative)'s choices to have clinical WGS and take part in the NGRL:

	Individuals aged 16+ years with capacity	Children (less than 16 years)	Adults without capacity)	Individuals who are deceased
Clinical test	RoD reviewed with individual	RoD reviewed with parent/guardian	RoD reviewed with person acting in best interests of the patient	RoD reviewed with appropriate relative
NGRL	The research choice is captured within the RoD. There is an additional 'Participation in the NGRL' form to note the individual's choice if this was not made at time when the clinical test was discussed.			
	No additional forms	OPTIONAL assent form signed by child	MANDATORY form signed by consultee	No additional forms

Notes: For results to be released to the GLH, an RoD must be received for each individual undergoing WGS. The process may be adapted for local needs, so do check with your GLH.
When recording patient choices in exceptional circumstances:

- If the RoD is not submitted when WGS is requested but discussions have taken place, the 'Form to follow' box can be selected at the bottom of the WGS order form. An RoD form is required before results can be released.
- Where patient's choices have been obtained through phone or video consultation, the clinician may sign the RoD and note that the patient has agreed to this remotely. This should be recorded in their notes, and a copy of the form sent to the patient.
- Where it may not be possible for the patient to provide consent, the clinician may decide to proceed with clinical WGS in patient's best interests. This should be noted on the RoD form and an appropriate record kept locally of the basis of this decision.

Additional points to consider

- The patient may decide to not proceed with the clinical test and/or research offer, or may wish to have more time to consider following the initial discussion.
- You may wish to draw on or refer for additional support from your clinical genetics service. For example: if there is a complex phenotype; for further discussion about managing risk and/or a diagnosis; or where there are complex social, family communication or ethical issues.
- Patient information has been developed by Genomics England, NHS England and NHS Improvement, and charities to support your discussions. Additional materials and support may be required for patients who are non-English speaking, hearing impaired, visually impaired, or have learning disabilities.