



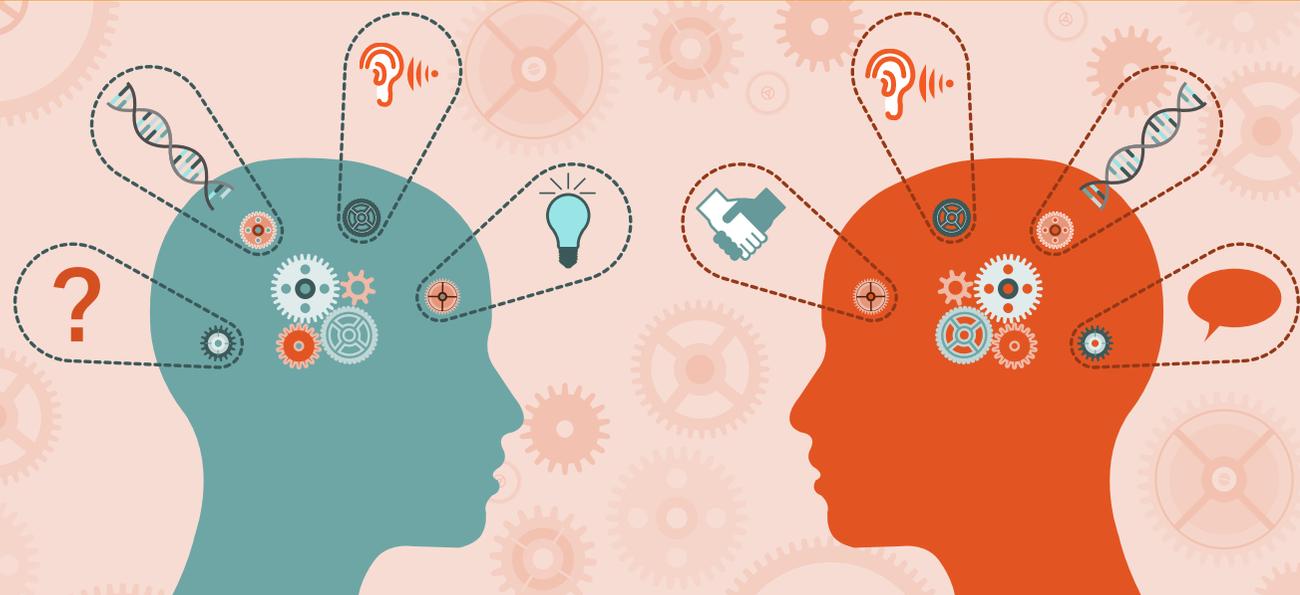
Genomics Education
Programme



Health Education England

100,000 GENOMES PROJECT

Preparing for the consent conversation



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Introduction

Genomics England and the NHS England Genomic Medicine Centres will, through the 100,000 Genomes Project, analyse whole genome sequences from tens of thousands of patients and their relatives. Healthcare professionals seeking consent from potential participants interested in joining the Project can take this training course to learn the key steps of the Project's consent protocol, what to consider when preparing for the consent conversation, and how to address patients' questions and concerns about joining the Project.

How to use this document

This document contains the full text and images from the online course '**100,000 Genomes Project: Preparing for the consent conversation**'. For those who have already completed this course, this document may be useful as a reference. It is not intended to replace the online course, which contains further multimedia content and assessments, and can be accessed at www.bit.ly/100kconsent.

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Unit 1: Genomics in healthcare

Lesson topics

- **1.1 Introduction to the course**
- **1.2 100,000 Genomes Project**
- **1.3 Whole genome sequencing**
- **1.4 Genetics and inheritance**



1.1: Introduction to the course

Welcome to this training course on preparing for the consent conversation with potential participants interested in joining the 100,000 Genomes Project.

The course is aimed at healthcare professionals working in NHS England Genomic Medicine Centres and their local delivery partners who are recruiting patients and, where appropriate, their family members onto the Project.

The main purpose of this course is to help you understand and undertake the required process for consenting eligible participants to the Project, and highlight approaches that will help you address some of their concerns or questions. The course will also cover some of the relevant ethical issues and provide best practice guidance on the consent process.

Note: This course is designed to support the diverse range of healthcare professionals who will be consenting patients into the 100,000 Genomes Project. Much of Unit 1 will be familiar territory for anyone from a genetics or genomics background. Nonetheless, it provides some of the wider context to the Project, so will still be useful for experienced healthcare professionals to review.

Learning objectives

By the end of this training course, you will be able to:

- **effectively prepare** for the patient-clinician conversation;
- **identify the needs** of potential participants to enable them to engage in the consent process;
- **confidently discuss** the details of the Project with potential participants;
- **address possible concerns or questions** about the joining the Project and the possible consequences for them and their family; and
- **recognise** when they are equipped with the knowledge they need to make an **informed decision**.

1.2: 100,000 Genomes Project

Key messages:

- Genomics has the potential to improve patient outcomes.
- The 100,000 Genomes Project spans both research and clinical care.
- The Project will leave a lasting legacy for the NHS.

The focus of the Project

The principal objective of the 100,000 Genomes Project is to sequence

100,000 whole genomes of eligible participants in relation to cancer, rare diseases and infectious diseases by 2017. Through this, the aim is to improve our understanding of the genomic basis for disease and create a lasting legacy for the NHS and the patients cared for by the service.



Understanding the genomic basis for these conditions is exciting, as it has the potential to improve their diagnosis and contribute to treatments and preventative strategies. This could also provide useful information to those planning to start a family or those with relatives who could be at risk of developing a condition.

The Project spans both research and clinical care; this means that participants' whole genomes will be analysed by researchers, with any reportable findings validated in NHS laboratories, from which clinical decisions can be made.

Currently, the primary focus of the Project is on patients with, or suspected as having, certain types of cancer or rare diseases, and this training course mainly relates to these potential participants.

The 100,000 Genomes Project will be delivered by Genomics England – a limited company wholly owned by the Department of Health – in partnership with NHS England, Public Health England, Health Education England and the NHS England Genomic Medicine Centres.

The aims of the Project

Genomics England, with the consent of participants and the support of the public, aims to create a lasting legacy for patients, the NHS and the UK economy. Its key aims are to:

1. Create an ethical transparent programme based on consent



3. Enable new scientific discovery and medical insights



2. Bring benefits to patients and create a genomics service for the NHS



4. Stimulate UK industry and investment





1.2: 100,000 Genomes Project cont.

What do you think?

Consider the questions in bold, and compare your ideas to our suggested responses below.

Consider your patients. Can you think of any particular benefits for them of participating in the Project? What might be their main concerns?

The potential of genomics to improve outcomes for patients is huge, including:

- Better insight into the cause and development of diseases, meaning that effective and targeted treatments can be developed; for example, for patients with prevalent types of cancer.
- For patients with unidentified rare diseases, the Project may lead to more accurate diagnosis to enable better management of the disease.
- Your particular patients may or may not benefit directly within the lifetime of the Project. However, as a minimum, they will be contributing to our knowledge bank that will ultimately lead to improved healthcare for patients with similar conditions.
- As genomic technologies improve, it is hoped that results, particularly where interventions are possible, will be available to more patients in a timely manner. Genomics England estimates that, by the end of the Project in 2017, it will be able to complete initial analysis within a matter of weeks.

In Unit 3 some patient concerns are highlighted together with suggested responses.

1.3: Whole genome sequencing

Key messages:

- The technique used by the Project is whole genome sequencing (WGS).
- WGS has the advantage of reading an individual's entire genome.
- The type of sample required for WGS depends on the participants' condition.

The 100,000 Genomes Project uses a technique called whole genome sequencing (WGS), sometimes referred to as next-generation sequencing. This means that the participant's entire genome will be sequenced and analysed in detail to explore what it is made up of.

Genetic tests undertaken in the NHS so far have used techniques that focus on specific parts of the participant's DNA, looking at areas in the genome already known to be associated with a particular

disease, such as cystic fibrosis or breast cancer. These techniques continue to be used where they are successful in accurately diagnosing such conditions.

However, such tests tend to focus on a person's genes, which make up just 5% of the entire genome. We now know that the non-coding parts of the genome may have a role to play in a person's health. Whole genome sequencing looks at every part of the genome – all 3 billion base pairs.

By commissioning the sequencing of whole genomes of eligible participants, the 100,000 Genomes Project will gather and hold this data, linked to each person's health information (their 'phenotype'). Researchers will be able to submit proposals for projects that will analyse relevant data, to increase our understanding of the variants in the genome that contribute to disease. This information may also lead to development of targeted therapies and improvements in diagnosis and prevention of disease.

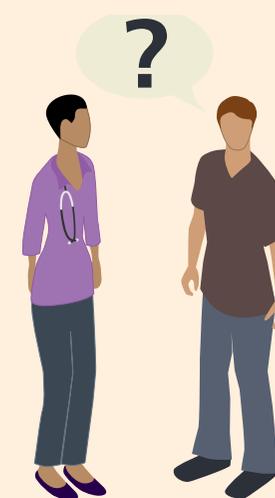
Answering participants' questions:

"I've heard of genetics, but what is genomics?"

The human genome is made up of all our DNA, which contains the information to determine how we look and how our bodies work.

Genetics typically focuses on specific parts of a person's genome, identifying a change to a gene or chromosome that has resulted in a condition, some of which are strongly inherited.

Genomics typically looks at how the entire genome influences a person's health, how individual parts of the genome relate to each other and in relation to the person's environment or lifestyle.



Whole genome sequencing in the 100,000 Genomes Project

Once the participant has consented to join the Project (see Unit 2.2 for the details of what they are agreeing to), their samples are taken for processing and DNA extraction.

For patients with a rare disease,

a blood sample is required from them and, in some cases, some of their blood relatives in order to make a comparison for diagnosis. Choosing appropriate family members for recruitment is covered in detail in Genomics England's document 'Guidelines for Rare Disease Family and Proband Selection', available at: www.bit.ly/100kGMCinfo.

1.3: Whole genome sequencing cont.

What do you think?

Consider the question in bold, and compare your ideas to our suggested responses below.

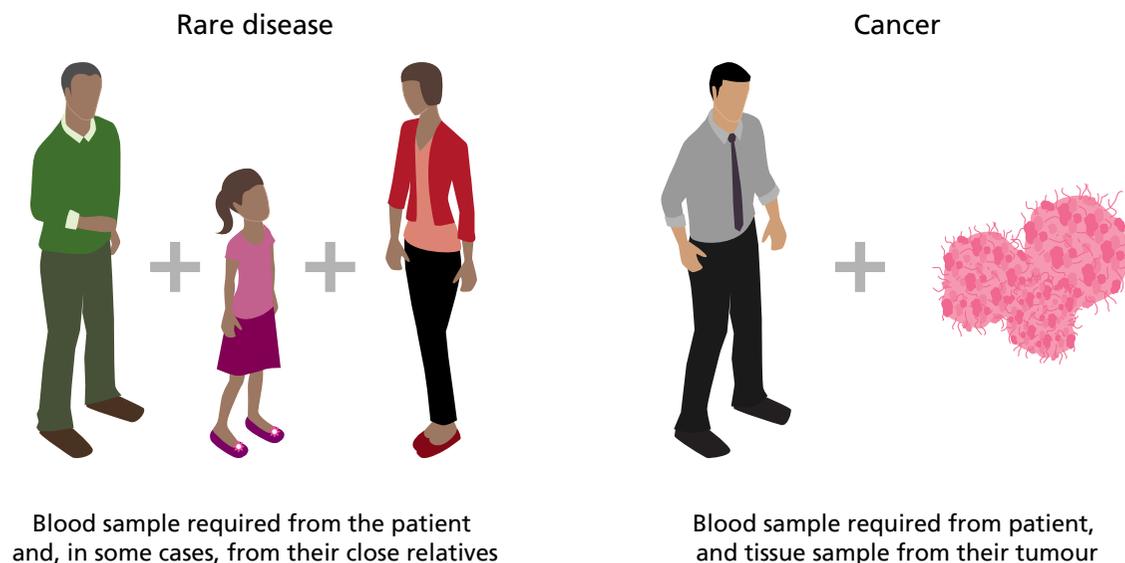
What do you think might be some of the challenges of whole genome sequencing and its output for an initiative such as the 100,000 Genomes Project?

Some of the key challenges include:

- ensuring the DNA that is extracted from a patient sample is of sufficient quality and quantity for WGS;
- interpreting, annotating and validating the results, and being confident in their veracity to enable decision-making on patients' healthcare;
- commissioning equipment capable of storing the massive amounts of data securely, as well as accurate retrieval as necessary;
- allowing secure sharing of data between approved bodies; and
- the education and training of professionals to enable them to undertake the essential work required to ensure successful output.

Did you think of any others?

Sample requirements



Blood sample required from the patient and, in some cases, from their close relatives

Blood sample required from patient, and tissue sample from their tumour

For patients with cancer, a blood sample is required from them, plus a small sample of solid tumour tissue. The exception to this is some types of blood cancer, where different types of sample may be required, for example saliva.

The samples will be processed and the DNA extracted by NHS England Genomic Medicine Centre (GMC) laboratories. The processed samples will then be sent to the Genomics England biorepository at the National Institute for Health Research (NIHR) National

Biosample Centre for quality checking and storage before being sent to Genomics England's sequencing centre to carry out whole genome sequencing.

The sequence is then carefully analysed and annotated. Any reportable findings will need to be validated by the NHS England GMC before being reported to the participant's clinician for discussion with their patient. (For more details of the 100,000 Genomes pipeline, see Unit 2.4.)

1.4: Genetics and inheritance

Key messages:

- The consent conversation may require an underpinning knowledge of genetics and inheritance.
- There are many easily accessible sources to develop your knowledge.
- Use the self-assessment quiz to determine your learning needs.

Participants in the 100,000 Genomes Project must agree to receive any pertinent results in connection with their existing condition (main findings), and can also opt in to receive results for a list of selected inherited genetic conditions (additional looked-for findings). (See Unit 2.3 for further details on the types of findings.)

The results might be relevant to not just their own health, but that of other family members' as well. Therefore, it is important that you are able to discuss various aspects of genetics and

inheritance with your patient.

You may already be familiar with genetics and genomics through your professional experience, or perhaps you have knowledge of genetics but have not previously worked on a project involving whole genome sequencing. Or you may never have worked in genetics or genomics.

In all cases, it is essential that you are confident of your knowledge and understanding of the fundamental aspects of genetic inheritance, and have ways of communicating these to your patients so that they are able to understand the implications.

Recording a genetic family history is not a required part of the consent process. However, it is required as part of Genomics England's data collection process. If a family history is not recorded at the time of consent, it should be taken by the proband's clinician. Follow the local guidance set by your NHS England Genomic Medicine Centre.

Resources for learning

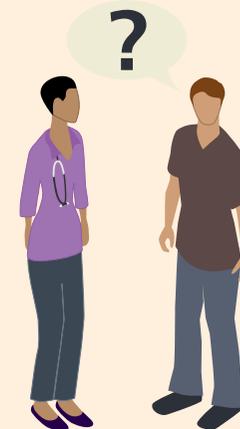
There are many resources available that cover the

Answering participants' questions:

"Are all genetic conditions inherited?"

Not all genetic conditions are inherited from a parent. It may be that the person has a *de novo* genetic alteration, ie one that has occurred for the first time in that family member.

It is important for the patient to understand that they can develop an inheritable genetic condition even if there is not a history in their family of that condition.



fundamentals of genetics that can help you to develop, review or refresh your knowledge, including those below from the NHS National Genetics and Genomics Education Centre:

DNA, genes and chromosomes
www.geneticseducation.nhs.uk/mededu/genes-to-genome/dna

Causes of genetic conditions
www.geneticseducation.nhs.uk/mededu/changes-to-dna-affect-gene-dosage-or-function

Inheritance of genetic material
www.geneticseducation.nhs.uk/

mededu/the-basis-of-genetic-conditions

Modes of inheritance
www.geneticseducation.nhs.uk/mededu/modes-of-inheritance

Taking a genetic family history
www.geneticseducation.nhs.uk/mededu/identifying-those-at-risk/taking-a-genetic-family-history

For a basic introduction to genomics and to learn about its growing importance in healthcare, you can also take HEE's 'Introduction to Genomics' online module:
www.bit.ly/IntroGenomics



Unit 2: The Project protocol

Lesson topics

- **2.1 The consent process**
- **2.2 Details of the Project protocol**
- **2.3 What results might be received?**
- **2.4 What happens next**

2.1: The consent process

Key messages:

- There is a defined pathway for recruitment and consent.
- Specific participant information sheets and consent forms must be used.
- Participants should be able, informed and willing to give consent.

As detailed in the graphic opposite, the consent process for the 100,000 Genomes Project begins with identifying suitable participants based on a set of inclusion / exclusion criteria.

Patients with, or suspected as having, certain types of cancer and rare diseases will be referred to the Project by their healthcare professional. Family members – for example, parents or first-degree relatives of a child or adult with a rare disease – may also be asked to participate.

The types of cancers currently

being researched by the Project include breast, bowel, ovarian, prostate, lung and, in collaboration with existing clinical trials, chronic lymphocytic leukaemia (CLL). You can access the full list on the Genomics England website: www.bit.ly/100kGMCinfo.

The list of rare diseases being researched by Genomics England is also available – www.bit.ly/GE-RDlist – and will be added to as more conditions are reviewed over the course of the Project.

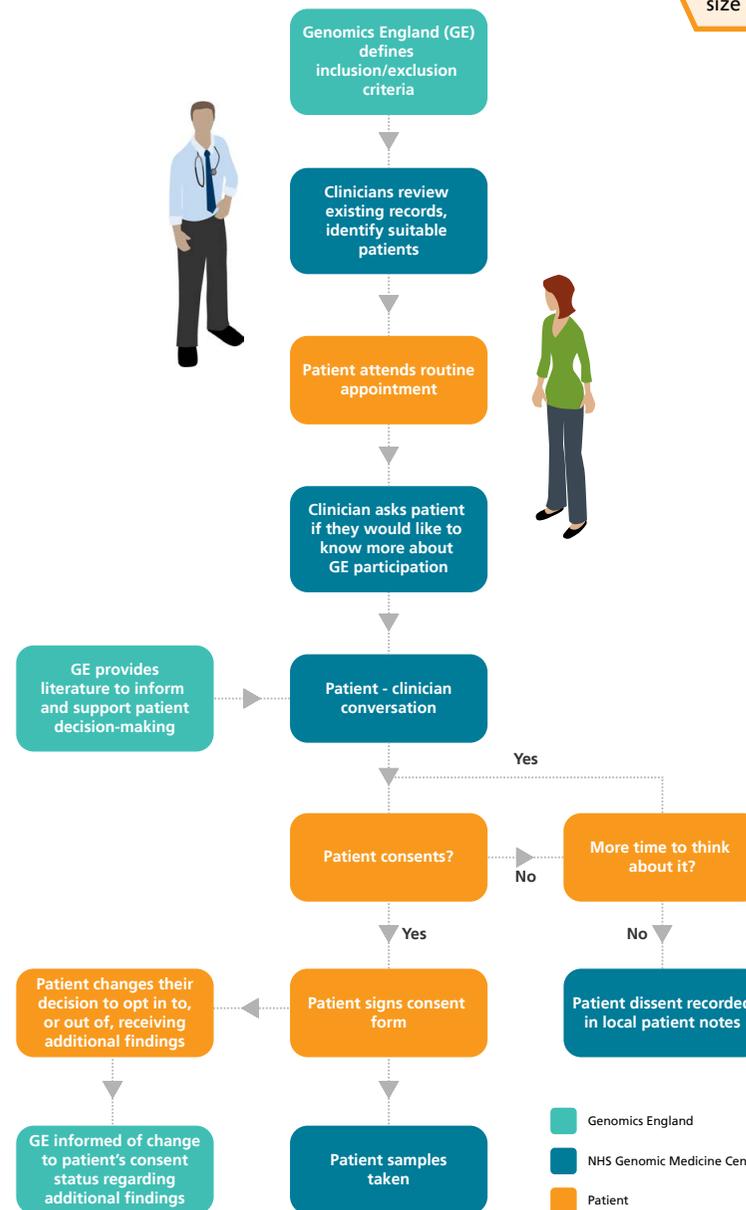
This course focuses on the consent conversation that takes place after the potential participant has been identified. The patient attends a routine appointment, and at that stage the healthcare professional asks if they would like to know more about the Project, and in doing so initiates the consent conversation.

Information for participants

Genomics England will provide eligibility criteria, participant information and consent forms to each NHS England Genomic Medicine Centre, and there will be local procedures in place to

100,000 Genomes Project consent process

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2.1: The consent process cont.

co-ordinate the distribution of consent forms to healthcare professionals. This may involve printing of documents and scanning of signed consent forms.

There are different sheets and forms for different participant groups, listed right and available at: www.bit.ly/genomes100kdocs. In the context of the Project, *proband* is the person with the disease that means they are eligible to join the Project, and *personal consultee* is the friend or relative invited to give their advice as to whether or not a person, who does not have sufficient capacity to make the decision themselves, would want to participate in the Project.

The personal consultee should know the proband in a personal capacity, and be able to advise on the person's wishes or feelings. This could be the person's friend, family member or a court appointee. Where someone is identified as a possible consultee but they do not believe they will be able to do this objectively (for example, because they are a blood relative and are worried about implications for themselves from the findings), then a different consultee should

be approached. The personal consultee must not be someone who is paid to look after the person who has lost capacity.

Using the appropriate participant literature, you will be able to offer potential participants relevant information to help them decide whether or not they would like to participate in the Project.

It is likely they will have questions. Therefore, it is essential that you are fully briefed about the Project and its protocol, so you can address these to help the potential participant reach a decision. The participant should be given as much time as they feel is necessary to consider whether to take part or not.

What makes the participant's consent valid?

First, the potential participant must have the **capacity** to provide consent. This means they are able to understand and assimilate information given to them, and make a considered decision.

Secondly, consent must be **voluntary**; that is, the participant

List of documents for participants and consultees

Available to download from Genomics England: www.bit.ly/genomes100kdocs

INTRODUCTION

- Introduction to the 100,000 Genomes Project

CANCER

Information sheets:

- C1 For adult patients with cancer (or suspected cancer)
- C2 For a personal consultee regarding a patient with cancer (or suspected cancer)

Consent forms:

- C1 Participant consent form - for patients with cancer (or suspected cancer)
- C2 Personal consultee declaration form - for personal consultees of patients with cancer (or suspected cancer)

RARE DISEASE

Information sheets for adults:

- R1 For adult patients with rare genetic diseases
- R5 For parents of a child with a rare genetic disease
- R6 For parents of a (deceased) child with a rare genetic disease
- R2 For family members of patients with rare genetic diseases
- R8 For the nominated representatives, relatives or friends of a deceased adult with a rare genetic disease
- R7 For a personal consultee regarding a patient with a rare genetic disease

Consent forms for adults:

- R1/R2 Participant consent form – for patients with a rare genetic disease and their adult relatives
- R5 Consent form for a child participant – for parents of patients with a rare genetic disease

R7 Personal consultee declaration form – for personal consultees of patients with a rare genetic disease and their adult relatives

R6 Consent form to include the sample(s) and information of a child who has died in the Project – for parents of a (deceased) child with a rare genetic disease

R8 Consent form to include the sample(s) and information of an adult who has died in the Project – for the nominated representatives, relatives or friends of a deceased adult with a rare genetic disease

For children and young people:

- R3 Information for children aged 6 to 10 years
- R4 Information for young people aged 11 to 15 years
- R3/R4 Assent form for children and young people with a rare genetic disease, aged 6-15 years

FOR BOTH CANCER AND RARE DISEASE

Withdrawal forms:

- Withdrawal information and form – for adult or child participants
- Consultee declaration of advice regarding adult participant withdrawal information – for consultees (withdrawal)

Opt in/opt out forms for additional findings:

- Information sheet and form to OPT OUT from receiving additional findings. For adult and/or child participants
- Information sheet and form to OPT IN to receive additional findings. For adult and/or child participants

2.1: The consent process cont.

must not feel pressurised by any healthcare professionals, family members or friends to take part in the Project.

Finally, the participant must also be making an **informed** decision. This means they have been told what the Project is about, what it involves, and the potential benefits and risks of taking part. They will also have had the opportunity to ask questions, and know where to find more information if they need it.

Considering the needs of all participants and appropriately supporting their decision-making are central to ensuring the consent process is valid. We will look at this in more detail in Unit 3.

Assent or dissent

If the person chooses to participate in the Project, they will need to sign a consent form.

A record should be created for the participant using the Genomics England data capture tool, and arrangements made to collect samples, which might include one or more of the following: blood,

Valid consent is...



- voluntary
- informed
- with capacity to make a decision

saliva and/or a tissue sample (for example, a section of tumour that had already been removed during a routine surgery).

If, after discussing the Project, the potential participant does not wish to give their consent, and does not indicate that they need more time to think, their decision should be respected. You should record their decision and, where possible, any reasons for not giving consent in their clinical notes. Genomics England will not store this information, as no consent has been taken.

Each NHS England Genomic Medicine Centre will have its own local guidance relating to recording dissent, so it is important that you fully understand and follow this.

What do you think?

Consider the scenario and question in bold, and compare your ideas to our suggested responses.

Mr Gregor has recently been diagnosed with a form of lung cancer and you have booked time with him to discuss the 100,000 Genomes Project. He has listened to your thorough outline of the Project and wants to sign the consent form, but you are not confident that he has understood all of the implications. Mr Gregor starts to get agitated as his son is picking him up from outside the hospital in a few minutes and he doesn't want to be responsible for his son getting a parking fine. What will you do in this situation?

If you are not confident that the potential participant has understood all of the implications of the Project, and therefore is not fully informed, it may not be appropriate for the patient to sign the consent form at this time.

Your NHS GMC will provide guidance on what you can and cannot do when issues arise with the consent process, and it is essential that you follow these. As always, you will want to be confident that you are acting in the best interest of the patient and any family members involved; sometimes this will prolong the process and provision will need to be made for this.

2.2: Details of the Project protocol

Key messages:

- The protocol is detailed and will take time to discuss.
- Potential participants must decide on their options.
- You must determine participants' capacity to make a valid decision.

This part of the course covers some of the key aspects of the Project's protocol that you need to know when seeking consent from eligible participants.

What is the participant consenting to?

To take part in the Project, potential participants must be willing to say 'yes' (consent) to the following:

- **Appropriate samples being taken** and used in research on their whole genome, proteins

or other components of cells. (If additional samples are required at a later stage, the clinician will ask for consent each time.)

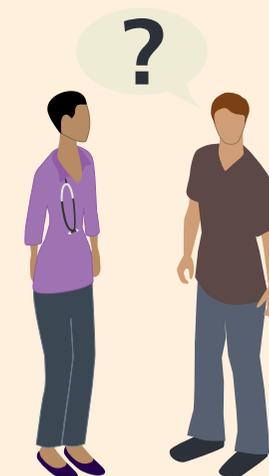
- **Ongoing access to their health records** alongside their samples, unless the participant subsequently withdraws.
- **Access by approved researchers and selected commercial companies** to use their data, which will be pseudonymised (de-identified and assigned a unique code).
- **Receiving future contact** by their healthcare team or by a Genomics England representative to consider the option of participating in other genomic research.
- **Receiving results:** any clinically relevant information relating to the main condition that made them eligible for the Project. (These results may suggest a cause for the condition or offer indicators for treatment. There is also the chance that there may be no results.)

If they are not willing to consent to all of the above, then they

Answering participants' questions:

"What will I gain from taking part?"

The participant may receive some important information about their health that could be relevant to their diagnosis and treatment. Such results may also offer information that is relevant to the health of their relatives. Even if the participant doesn't personally benefit, the results from the Project as a whole will help to further our understanding of the relationship between the genome and disease, and this could help improve outcomes for similar patients in the future.



cannot participate in the Project. In addition, participants can opt in or opt out of the following:

- **Receiving 'additional looked-for' findings:** these are genetic variations that might be clinically significant in relation to a range of selected health conditions in addition to their main condition (see Unit 2.3 for further details).
- **Determining carrier status:** eligible adults planning

children may wish to know their carrier status in respect of a select list of genetic conditions (see Unit 2.3).

It is essential to discuss the options regarding additional looked-for and, if relevant, carrier status findings with the potential participant so that they are fully aware of what they are consenting to. As noted, Unit 2.3 provides further information on what results might be received.

2.2: Details of the Project protocol cont.

How should consent be taken?

Consent should be taken face-to-face in a healthcare environment, as part of a routine scheduled appointment. If necessary, the discussion and consent to join the Project can take place at the participant's home.

Discussion about the Project can happen over the phone, but consent must be given in person.

In exceptional circumstances, some potential participants may provide consent by returning their completed consent form via post or email. A telephone discussion with a suitably trained person should be offered to them as part of this. This route to seeking consent should only be used where the clinical team has reason to seek postal consent for the individual concerned because consent could not be sought face-to-face.

There is a lot of information to get across to the participant before they can make an informed decision, and it could raise issues they never have considered before. So it is important to not

rush through this. Unit 3 covers these considerations in much greater detail.

If participants need additional time to think about the Project, then this is acceptable. They should be given as much time as they feel necessary to consider their decision, and should not be made to feel under pressure to participate.

If participants are ready to consent, they should read over the relevant consent form, initial each box and add their signature, their date of birth and the day's date at the end of the form.

It should be noted that, in some circumstances, the participant may consent to join the Project but may not be enrolled. For example, in the case of a suspected cancer, if after investigation it is found not to be cancer, the patient would no longer be eligible to participate.

Inviting relatives to participate

For patients with a rare disease, participation in the 100,000 Genomes Project requires the

proband (the person with the disorder that makes them eligible to join the Project) and, if possible, blood relatives who are willing to take part. This is so that the relatives' genomes can be used as a comparison for diagnosis.

If the proband is a child, then (aside from in exceptional circumstances) the parents will always be involved in their decision to participate, and so you can have the consent conversation with them as part of that appointment.



If the proband is an adult, you may give them a recruitment pack to pass onto their relatives, if they are willing to take on this role of passing on information. Alternatively, the proband may also be provided with an electronic copy of the recruitment pack by email, to forward to their relative.

To indicate their response, the relative can return the slip

to say that either they:

- do not wish to take part in the 100,000 Genomes Project;
- agree to be contacted by a team member to find out more about the Project; or
- would like to take part in the 100,000 Genomes Project and give written consent to participate.

As noted previously, wherever possible consent should be sought face-to-face in a healthcare environment, and only via post or email in exceptional circumstances.

If the relative is aged under 16 and lacks capacity to consent, their parent or guardian can be provided with the recruitment pack and invited to consent on their behalf.

Age and capacity

There will be some participants with whom having the consent conversation will require additional considerations based on their capacity to consent.

2.2: Details of the Project protocol cont.

Under 16: For potential participants under 16, parents make the decision about the child's participation, unless the child is deemed by the clinical team to be able to make that decision for themselves. As noted previously in Unit 2.1, tailored participant information sheets are available for those who are 6-10 years old and 11-15 years old. Like all potential participants, they should be invited to ask questions and raise any concerns.

On reaching 16 years old, all existing participants will be asked to give their own consent to remain in the Project (unless it is deemed by their clinical team that they do not have the capacity to do so at that time).

Adults who lack capacity: Potential participants who are deemed by their clinical team to not have the mental capacity to consent, in accordance with the Mental Capacity Act 2005, cannot be enrolled in the Project under usual circumstances, unless it has also been determined by the clinical team that the person's lack of capacity is connected to their disease or its treatment.

If the reduced capacity is connected to their disease or its treatment, a personal consultee should be sought to advise on the patient's wishes in line with the Mental Capacity Act code of practice 2013.

Health emergency: In cases where participants lack capacity to consent owing to a health emergency (for example, patients being treated for sepsis), a personal consultee should be sought as soon as possible, who can give an idea of the person's likely views on joining the Project.

Change in capacity: A participant who didn't have capacity at the time of consent but who subsequently regains capacity will then be invited to provide consent in their own right at the earliest opportunity.

Some participants will have capacity at the point that they consent to join the Project, but subsequently are deemed by their clinical team to have lost capacity. Each NHS England Genomic Medicine Centre will prompt its clinical team to alert them if a participant's capacity has been lost, based on their contact with

the participant once every five years after they joined the Project. This assessment will take place in all cases, ideally as part of the participant's routine clinical care. However, if the participant is not contactable in any way, there is no obligation to exhaustively follow up in order to make this assessment.

At the point that the NHS GMC notifies Genomics England of the participant's loss of capacity, the individual's consent then fails to be valid in line with the Mental Capacity Act 2005. The clinical team should identify a personal consultee in line with the guidance available, to advise on whether they believe the person would have wanted to re-join the Project as a participant.

Participants can, if they wish, inform their clinical team of whom to approach as a personal consultee in the event that they lose mental capacity in the future.

Deceased participants

If a participant who consented to join the Project later dies, their consent will remain valid.

In some instances, consent may be sought to enrol a participant who has already died; for example, where a rare disease is the suspected cause of death in a child, or after a stillbirth, miscarriage or termination of pregnancy.

Genomics England has produced information sheets and consent forms specifically tailored to these circumstances, in relation to both deceased children and adults (see Unit 2.1).

What happens if the participant changes their mind after giving consent?

Should participants wish to revise their decision after they have joined the Project, they have a number of options available to them.

If the participant changes their mind about opting into, or out of, additional looked-for findings, they can complete a form

2.2: Details of the Project protocol cont.

(available online at www.bit.ly/genomes100kdocs), and return to Genomics England or their clinical team.

Alternatively, should the participant wish to withdraw from the Project, they have two options:

- **partial withdrawal:** they can request 'no further contact' about the 100,000 Genomes Project after receiving their results, but their data and samples can still be used as part of the Project; or
- **full withdrawal:** this means 'no further use' of their information and samples.

If they choose to withdraw partially, their pseudonymised information will remain on the 100,000 Genomes Project database and their samples will still be stored in the biorepository. They will not be contacted for further information, samples, or with invitations to join other research projects, but their clinical team can still contact them to discuss their results.

If they choose to withdraw fully, their samples will be destroyed, their information will not be used

as part of the Project, and they will not be contacted regarding the Project again.

Should the participant subsequently enquire about withdrawing, you should provide them with the relevant form (available online at www.bit.ly/genomes100kdocs). After it has been completed, copies of the form should be given to the participant, their clinical team (to be stored locally), and to Genomics England.

Participants should be reminded that they can discuss their concerns with their clinical team, or look at information from Genomics England at www.bit.ly/100kFAQs to find out more about withdrawing.

2.3: What results might be received?

Key messages:

- The Project can return up to three types of results.
- Participants must agree to receive findings related to their main condition.
- Participants can also opt in to receive other selected findings.

Main findings

All reportable findings will need to be validated in an NHS England Genomic Medicine Centre laboratory to check that they are accurate and reliable. Only then will they be reported back to the clinician, who will discuss the results with the participant. Some participants may not have any reportable findings arising from their genome sequencing. The clinician will be told when there are no results as part of the initial feedback report, and they will share this information with the participant.

Participants might receive information about their existing health condition (cancer or rare disease). This could include the genetic basis of the condition and/or ways their condition can be treated or managed. Alternatively, there may be nothing definitive found. In any case, the usual course of treatment will always be available.

Additional findings (health related)

Participants can opt in to receive feedback about 'additional

Types of potential feedback to participants



Main findings

All participants agree to receive results about the main condition for which they were referred

'looked-for' findings in relation to a selection of genetic variations that are known to cause diseases where treatment and/or preventative measures are available; for example, inherited breast and ovarian cancer and familial hypercholesterolaemia.

Based on current available evidence, Genomics England

Additional findings

Participants can opt in to receive feedback on a selection of known genetic alterations of high clinical significance

estimates that approximately 1% of participants could receive an additional finding in their results.

If the results show that such a genetic variation has been discovered, then this usually indicates that the individual has a predisposition to developing the condition in the future, but this is not inevitable.

Carrier status

Eligible adults can opt in to find out their carrier status for certain genetic diseases

2.3: What results might be received? cont.

What do you think?

Consider the question in bold, and compare your ideas to our suggested responses below.

How will you explain to your patients why there may be no results related to their main condition?

In some circumstances, although someone will have a clinical diagnosis of a condition, the 100,000 Genomes Project will not be able to identify the underlying genetic cause for this condition. Therefore, no findings for this will be available.

In other circumstances, individuals may have joined the Project with a condition that hasn't yet been identified (a syndrome without a name). In some situations the 100,000 Genomes Project may be able to provide answers, including a diagnosis. However, in other situations a diagnosis may still not be available. It is important for all potential participants to be aware that there may not be any findings from this Project, and part of the consent conversation will be to manage patient expectations.

If this type of conversation is a new aspect of your current role, you may find it helpful to discuss how you approach this discussion with a colleague.

They will be referred to a genetic counsellor, clinical geneticist or condition specialist to talk through the significance of these results, and explore their options.

The participant may want to embark on a screening programme intended to pick up early signs of the condition, if it is present. There may also be options for treatment or management that could reduce

the effects of the condition.

The genetic conditions that are included in the list of additional looked-for findings is available from the Genomics England website: www.bit.ly/100kresults.

Note that the list will change over the course of the Project, and the genetic variants looked for are based on the list at the time of analysis, not at the

Answering participants' questions:

"Why look for these conditions?"

If the participant opts in for additional looked-for findings, they agree to receive information about serious rare conditions. The current list comprises a number of rare inherited cancers, as well as an inherited condition that causes very high cholesterol in the affected person's body, which can cause serious health problems.

The point of looking for these, or any of the conditions on the list in future, is to give the participant information so that they can make proactive choices about screening or treatment.



2.3: What results might be received? cont.

time of consent. Therefore, it is not possible to discuss the list of conditions with the patient in complete detail during the consent conversation. Instead, the participant is consenting to the general principle of receiving additional findings about their health.

When the potential participant is making this decision, the key message for them to understand is that these are serious health conditions in which early detection could help to prevent or mitigate the impact of the condition.

It is also important to mention that only particular genetic changes associated with the conditions are being looked for. Remember, for many of these conditions, just because a particular genetic alteration has not been found does not entirely rule out the participant developing this condition.

If such a genetic variation is found in a participant, some of their blood relatives may also have inherited the same variant. Therefore, it is important that family members are offered genetic counselling, to discuss

options for genetic testing and clinical management.

Note that children whose parents opt for them to have additional looked-for testing will only be investigated for the conditions that can occur in childhood, ie not the adult onset-only conditions.

Your NHS England Genomic Medicine Centre and its local delivery partners have responsibility for caring for the family and will support any subsequent testing and counselling for family members.

If the participant decides to opt out of receiving additional looked-for findings, it is important that they are made aware that Genomics England will **not** look for these genetic variants when analysing their genome. These variants will not be looked for or recorded unless the participant chooses to opt in to receive these additional findings.

Carrier status (reproductive-related) findings

Adults who participate in the Project can opt in if they wish to

find out their carrier status for certain genetic conditions. When a person is a genetic carrier, typically they do not have any symptoms of the condition themselves, but can pass on the genetic variant to their children, who could develop the 'full' condition.

Available choices for eligible adults are to:

- **opt in to EITHER** additional looked-for findings **OR** carrier status findings;
- **opt in to BOTH** additional looked-for findings **AND** carrier status findings; or
- **opt in to NEITHER.**

Some of the carrier status conditions are 'autosomal recessive', which means the 'full' condition can only be passed down if both parents carry that gene variant, such as cystic fibrosis.

For these conditions, both parents need to be enrolled in the Project and consent to this testing (although the results can later be given if just one parent is present at that stage).

Some 'full' conditions can be passed on solely by a parent who

is a carrier; for example 'X-linked' conditions where the genetic variation is only passed down by the mother. In these cases, results will be given to the relevant individual; both partners do not need to consent together for this testing.

As with the list of additional looked-for findings listed, other conditions may also be included in the carrier status list in the future. So it is not possible to discuss the list of carrier status conditions with the patient in complete detail during the consent conversation.

Instead, the participant is consenting to the general principle of receiving information of high clinical significance that, should this be identified, could relate to the health of their children.

If the gene variants for these genetic conditions are identified, participants will be able to talk to a specialist about the significance of these, particularly around the available options with regard to any future children they may be planning.

Again, it should also be noted that



2.3: What results might be received? cont.

any genomic results – whether they are main or additional findings, or regarding carrier status – may not only be relevant to the participant, but may also have implications for their blood relatives. For more information on this, see Unit 2.4, 'What happens next'.

Findings of unknown clinical significance

As the 100,000 Genomes Project sequences the entirety of the person's genome, it is likely that there will be variations found with unknown or uncertain significance for health and disease. Typically, these findings of unknown clinical significance will **not** be returned to the clinician for discussion with the participant.

2.4: What happens next

Key messages:

- Understanding the Project stages will help you address participants' questions.
- Participants' data is securely stored and access is tightly controlled.
- Initially, results may take many months to be returned.

Once participants have given their consent to take part in the 100,000 Genomes Project, you will need to create a record using the Genomics England data capture tool, adding the participant's personal details and medical history. Their signed consent form will also need to be scanned and uploaded.

The next step is to collect the required samples, the procedures for which will be defined by your NHS England Genomic Medicine Centre.

Sample collection

Blood samples are required from all participants in order to extract germline DNA for whole genome sequencing (WGS), and to analyse proteins and chemicals in the blood.

For patients with a rare disease, a blood sample is required from them, and if possible from some blood relatives for comparison.

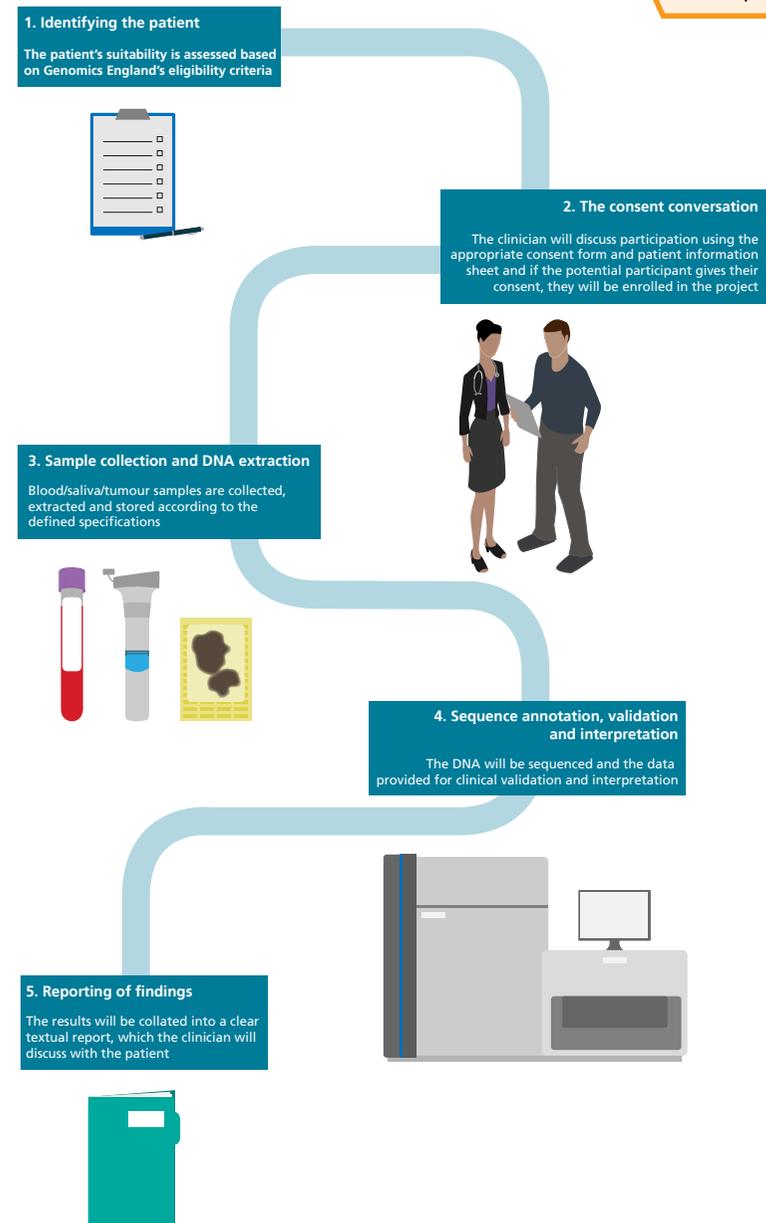
For patients with cancer, two samples are required: their germline DNA and their cancer DNA. For most, the germline sample is taken from blood and the cancer sample is taken from the tumour tissue. For patients with blood cancers, however, the cancer sample is instead taken from blood, while the germline DNA is taken from saliva.

Occasionally, the participant's sample cannot be included and therefore they will not be enrolled onto the Project; for example, in a case of a suspected cancer when it is subsequently found not to be cancer.

The samples and data will be pseudonymised; that is, they will

100,000 Genomes Project: the pipeline

View and print this diagram full size on page 43



2.4: What happens next cont.

be de-identified and assigned a unique code. After the blood and tumour samples have undergone DNA extraction, and have passed a quality control process, they will be sent to the biorepository. They will be assessed for quality, and approved samples will be sent for whole genome sequencing and analysis.

Any remaining samples will be stored in the Genomics England biorepository at the NIHR National Biosample Centre in Milton Keynes. Some extracted DNA will also be stored locally at the NHS England Genomic Medicine Centre in order to clinically validate any reportable findings.

Returning results

At the start of the 100,000 Genomes Project, it is likely to take many months for the preliminary analysis to be returned. Often this will not yield a diagnosis, and detailed expert review of the data will be required, which may take several further months.

Typically, findings in relation to the participant's main condition

will be returned first. Additional looked-for or carrier status findings will usually be returned separately, possibly at a later date.

Clinically relevant and validated findings will be communicated to the clinical team for discussion with the participant.

As the Project progresses, technology will continue to improve and understanding of the conditions being investigated will increase, leading to a faster feedback process. It is hoped that, by 2017, initial analysis will be returned within weeks.

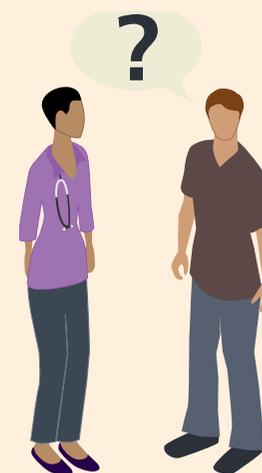
The participant will receive any pertinent findings about their main condition and, if they have opted in, information about the additional looked-for conditions and/or carrier status conditions.

Many participants will not have any reportable findings arising from their genome sequencing, but they will be told this as part of the initial feedback report. If, later on in the Project, new analysis identifies reportable findings, another report will be issued for discussion with the participant.

Answering participants' questions:

"How will my data be accessed?"

All analysis and interpretation of patient data will take place within a secure and monitored environment, similar to a reading room within a reference library, where books cannot be taken away but must be read within the library and where access to the reading material is monitored while it is being read. Use of the data will be closely controlled, audited and monitored by Genomics England to ensure it is being used for its intended and approved purpose.



Sharing results with family members

It is possible that participants will receive results that are relevant to their relatives. This may also be important if the participant or their relatives are planning to have children. In the case of participants with rare diseases, their blood relatives may also be asked to take part in the Project.

When sharing the results with the participant, the clinician

will also discuss any potential significance for their relatives. The NHS England Genomic Medicine Centres and their local delivery partners will have responsibility for caring for the family and will support the testing of relatives.

Data storage and access

Participants' pseudonymised data will be stored in a controlled-access database from which only the results of researchers' questions can be extracted (ie

2.4: What happens next cont.

researchers can't download the data held on the database itself).

Organisations that will be given access to the database can include commercial companies. Only organisations that have been approved by Genomics England will be allowed to access the data for acceptable uses and this will be applied in each case by an independent advisory committee (the Genomics England Access Review Committee).

Organisations wishing to access the data must pass a thorough identity check, and have their research proposal approved under strict conditions developed by the Access Review Committee. Once approved, they will have read-only access to the data and will not be able to download raw data to take away; only the results of analysis they carry out from their reading of the data.

All activity will be closely monitored by Genomics England to prevent any breaches to patient privacy or data security.

Participants can themselves request to receive their raw data (their genome sequence)

in addition to any results they receive, but owing to the time and cost associated with data retrieval, there will be a charge for this. As at December 2015, the process for this has not yet been defined by Genomics England because of the practical difficulties of transferring such huge amounts of data.

Future contact

Further to receiving their results, participants may also be contacted in the future by their clinician or Genomics England to provide more samples or take part in more studies.

Research companies will not be able to identify, nor therefore make any direct contact with, Project participants. You can also reassure the potential participant that other organisations, such as marketing or insurance firms, will not have access to their data or contact details.

The nature of potential recontact should be discussed as part of the consent conversation, including the fact that these requests could come from a Genomics England representative as well as the patient's clinical team.

What do you think?

Consider the question in bold, and compare your ideas to our suggested responses below.

Other than the instances noted above, can you think of any other reasons for recontacting the participant and their relatives?

Two additional reasons for recontacting the participant are to reaffirm their continued capacity every 5 years so that consent remains valid, though this should ideally take place as part of a routine appointment. Also, should it happen, participants would be contacted in case of any breach of data.

Did you think of any others? Remember, most communications between the Project and the participant will occur via the participant's clinician and healthcare team. Genomics England is the only organisation that may contact the patient directly.

2.4: What happens next cont.

Potential outcomes

You should now be familiar with the key aspects relating to participating in the 100,000 Genomes Project. Now, let's review some of the possible outcomes for the participant.

Feeding back of results

- The participant may find out the genetic basis of the main condition affecting them, or their child. But many will not receive a definitive diagnosis as a result of genomic sequencing.
- Particularly for participants with cancer, the results could be directly relevant to their treatment. But, for many, they may not be returned in time to have an impact on their prognosis or care.
- Some genetic results may also be relevant to the participant's blood relatives. Taking the participant's family history may help identify who among the family should be contacted.
- For additional looked-for findings, it should be noted that a negative result does

not rule out the participant still being predisposed to the conditions listed. It is possible that they are, but that the test did not pick up their specific gene variation.

Post-results

- If the participant consents to join the Project, they will be agreeing for their clinical team and Genomics England to be able to contact them in future.
- If the participant later decides they no longer want to be contacted, they can withdraw partially by requesting no further contact, but allowing continuing use of their information and samples.
- If the participant decides to withdraw fully from the Project, their samples will be destroyed and their information will no longer be used. However, where their information and samples have already been used up to this point, these cannot be withdrawn.

Some of these potential outcomes may be the focus for participants' questions. Others may have

different concerns or reservations. Unit 3 covers these issues in more detail, with suggestions on how you can address them.



Unit 3: The patient-clinician conversation

Lesson topics

- **3.1 Preparing for the conversation**
- **3.2 Engaging with the participant**
- **3.3 Answering participants' questions**
- **3.4 Patients FAQs**
- **3.5 Clinician FAQs**

3.1: Preparing for the conversation

Key messages:

- **Allow adequate time for the consent conversation.**
- **The Project information must be presented in an accessible format.**
- **Access to the Project must be given to all eligible participants.**

While many of the issues you need to consider ahead of time will apply to any discussion with a patient, there are particular aspects that become relevant when seeking consent for the 100,000 Genomes Project.

Time and place

There may be many aspects of the Project that may be new to your patients and their families, even those who have some experience of genetic testing for their particular condition. Some of these issues could be quite complex and difficult to explain in

a way they can understand. They may also have many concerns, such as the use and security of their data. The results they may receive could have direct consequences, not just for the individual but also to their blood relatives, including those that may not be directly involved with the Project.

Therefore, the consent conversation may take longer than you expect. In all cases, be prepared to have enough time available for a full discussion that enables the participant to make an informed decision.

It is also a good idea to consider the environment in which you are conducting the conversation. The Project protocol suggests that, where possible, the consent conversation should be carried out in a healthcare environment. In some cases, it may be appropriate to arrange a meeting in the patient's home. Wherever the consent conversation is arranged to take place, the potential participant needs to be able to discuss their concerns freely and in private, without interruption and distraction.

Written information for participants and their families

It is important that you have correct participant information sheets and consent forms ready when discussing participation in the Project. There are different sheets and forms tailored to different participant groups – see Unit 2.1 for the full list.

If potential participants want to learn more about the Project, before or after their appointment, they can also visit Genomics England's website.

Ensuring equal access

As with all interactions with patients, it is important to consider the specific needs of each individual.

Interpreter: Non-English speaking participants and sign language users will need access to a specialist interpreter, and it is your responsibility to ensure that someone appropriate is booked. Speak to the interpreter beforehand so that you can go through any complex terms or

information, and agree the best ways that these can be conveyed.

Do not rely on a family member or friend to translate – this is particularly important for blood relatives, as the participant's genomic results may have implications for them.

Lip-reading: For participants with a hearing impairment, make sure the light in the room is positioned on your face rather than behind you (which would make your face in shadow). This might mean moving the chairs in the room, opening window blinds or re-positioning a desk light.

Written information: This needs to be clear and accessible for all. Participants with visual impairment or dyslexia will need appropriately modified materials so that they are able to access the information, eg coloured paper, large print, Braille version.

Learning disabilities: When speaking with a potential participant who has a learning disability, it is important to engage with them as fully as possible as part of the consent conversation, even where a consultee is

3.1: Preparing for the conversation cont.

What do you think?

Consider the question in bold, and compare your ideas to our suggested responses below.

To enable equity of access you may need to provide participant information in other formats, such as in different languages, large print or Braille. Where will you access these modified materials?

The Project protocol states that literature may be translated by the NHS England Genomic Medicine Centres into languages appropriate to the patient groups, where needed. If there is sufficient demand, Genomics England may commission and hold a few commonly required translations centrally for electronic download.

If other formats, such as large print and Braille, are required this would also be the responsibility of the NHS GMC to obtain from Genomics England if available, or arrange themselves. Some potential participants may have their own facilities through their computer or tablet to make materials more accessible, so you could offer to email the participant information to them.

present to act as the patient's representative.

For advice and guidance on communicating with people with learning disabilities, visit Mencap at www.mencap.org.uk/about-learning-disability/information-professionals/communication/communicating-people-learning-disability and the General Medical Council at www.gmc-uk.org/learningdisabilities/25.aspx.

Discuss the Project in a quiet area without distractions. Take your time to explain, and consider using visual aids to aid understanding. Encourage them to ask questions, and observe their body language and facial expressions as well as listening to their responses carefully.

Language: Finally – and this is important for all potential participants – consider the language you use when discussing genomic sequencing and testing. Explain the Project clearly, and avoid using jargon or overly scientific terms. For guidance on effectively communicating genetic and genomic information to patients, view this online guide.

Reassurance: Patients may be concerned that if they choose not to join the Project, it may impact on their ongoing care. It is important to reassure them that this will never be the case; their care will continue as planned.

3.2: Engaging with the participant cont.

be sure they understand the information given to them? Ask them to 'play back' their understanding, for example by inviting them to say how they will explain their participation to family members or friends. Their answer will help you identify any areas you might need to go through again. Body language can also suggest how the person is handling the information.

8. **Manage expectations:** It is possible that the participant may not benefit directly from taking part in this Project. They may not receive any findings, or it could take many months for their results to be returned and so may not affect their current medical care. It is important to make this clear.
9. **Open access:** Ensure that all participants have equal access to the Project. Consent conversations may be difficult or elongated with some individuals to ensure they are consenting validly; however, all suitable participants should be offered the opportunity to take part.

10. **No means no:** If potential participants choose not to consent, then respect their choice.

Assessing understanding: visual clues

There is a lot of information for the potential participant to process during the consent

conversation. Visual clues such as body language can provide useful indicators when you are assessing their understanding.

What do you think?

Consider the scenario and questions in bold, and compare your ideas to our suggested responses.

All NHS staff tend to be under pressure in terms of time and workload, and often the patients are running to a schedule as well (for example, meeting children from school). When considering their decision to join the Project, it is essential that the patient has sufficient time to understand and assimilate the information being presented and have time to ask questions. These and other factors can put pressure on you to get the consent conversation concluded. What is your natural response to time-constrained situations and what strategies do you need to have in place to avoid pressurising your patient into making a decision?

Some of the strategies you routinely use to address pressure of time when discussing issues with patients will obviously be relevant here too. However, think about the words you use and your body language when you have limited time; do any of these need to be altered to ensure you are not coercing patients into consenting to

join the Project? Also consider whether you are inadvertently avoiding consent conversations with patients who you feel may take longer to understand complex conversations because of time constraints.

Here are some strategies to help you:

- Think about your patient, their level of literacy, understanding and knowledge about what you are going to present to them, their circumstances and their needs at previous appointments, and set aside a realistic amount of time for the consent conversation.
- Ensure that the patient and any accompanying family members are aware of how much time they may need to allow for the consent conversation.
- Can you provide the patient with any information about the Project prior to the consent conversation? This may include providing the website link to Genomics England so that your patient can look through some of the material before you meet with them.

3.3: Answering participants' questions

Key messages:

- Unfamiliarity with the Project may generate concerns for the participant.
- You need to be prepared to address potential participants' questions.
- Utilise your experience and skills to help them come to an informed decision.

A large part of the consent conversation for any research project is listening to the potential participants' concerns and answering their questions. This part of the course outlines the kind of concerns that may arise when discussing the 100,000 Genomes Project with potential participants, with suggestions on how you could approach them.

Potential areas of concern

Unfamiliarity with genetics and genomics

- Although some participants will have taken part in genetic testing before and will have some awareness of what the process involves, others will have had no experience of genetics services. Some may be familiar with the term 'genetics', but have little knowledge of genomics and the distinction between the two.
- They may be worried about what the results might mean for themselves and their family. Or they may not have realised that their results could be directly relevant to their blood relatives until the moment that you start to discuss this with them.
- They may also not fully understand that the test can reveal additional health-related information relevant to them, if they so choose.

How to respond: You may need to explain the key concepts to less familiar participants in more

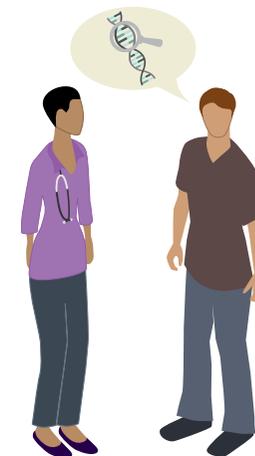


detail. Information like this may take a while to sink in, and it is possible that the consent process takes longer than you have been used to for other sorts of tests, research or trials. Allow them time to process the details, and ask questions.

Unfamiliarity with research projects

- Potential participants may be apprehensive about what the Project involves and what they will have to do as part of it.
- They may be wary of stepping beyond the usual patient pathway, and having their health information accessed by people and companies outside their clinical team.

How to respond: To help them understand how the Project works, try outlining the key stages of the 100,000 Genomes Project pipeline – you could use the graphic in Unit 2.4 as a visual aid. You could also outline the goals of the project with them – see Unit 1.2 – so they are aware of the wider aims as well as the potential benefits to their own healthcare.

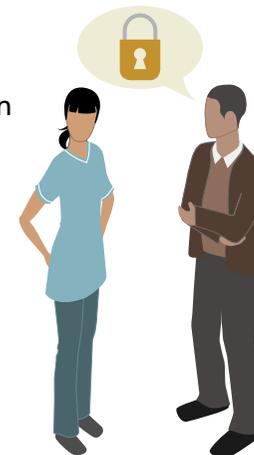


3.3: Answering participants' questions cont.



The consequences of results

- Potential participants may be concerned about what could be found out by the genomic sequencing, and how the results might affect them and their family members. Knowing that they have or could develop a genetic condition – or that they carry a genetic variation that could be passed onto their children – may be difficult to deal with.
- They may want to know when they will receive results, and whether it could affect their current treatment.
- Opting in to receive information about a list of additional genetic conditions, on top of their primary condition, may seem daunting.



positive result for carrier status, they can receive guidance about the risk of any future children having this condition. Potentially affected family members can also receive genetic counselling and testing. Ultimately, though, additional genetic information may be unwelcome for some, and they can opt out of this aspect of the Project or decline altogether. You can remind participants that they always have the option to opt in to receiving additional findings at a later date if they subsequently change their mind.

Access to data

- Selected third-party access to their pseudonymised genomic and health information indefinitely will be an issue for some participants, particularly the idea of commercial companies using their data.
- Some potential participants may have worries about how securely their data is being stored, and what will happen to it after the 100,000 Genomes Project is completed.
- Some may be concerned that the results could affect other

How to respond: Consider highlighting that a positive result could allow the participant to make proactive choices about their health, such as joining an appropriate screening programme. For parents who discover their child's condition is genetically inherited, or who receive a

3.3: Answering participants' questions cont.

parts of their lives, such as having to tell their insurer.

How to respond: Data from the 100,000 Genomes Project will not be shared for insurance or marketing purposes. Information will only be shared with organisations conducting projects that have been carefully checked and approved by Genomics England. Beyond 2017, the Department of Health will ensure that the data is held intact by a body who is mandated to ensure the ongoing security and privacy of the participants' health information. More information about data security can be found in Genomics England's FAQs.

Regarding insurance, the Association of British Insurers (ABI) has confirmed that participants in the 100,000 Genomes Project do not have to disclose their whole genome sequence results to insurers. This is in line with the Department of Health / ABI Concordat and Moratorium on Genetics and Insurance, which has been extended to 2019, with a review planned for 2016. Note that the normal rules apply with regard to disclosing treatments, family history and medical history.

For an example illustrating this, see the patient FAQs in Unit 3.4.

Key points to remember

As a healthcare professional, you are experienced in working with patients and addressing their questions and concerns. Your skills will be highly useful when taking consent for participating in the 100,000 Genomes Project.

However, there are some aspects to this Project that may require additional consideration. So here are five key points to review:

1. **Explain:** This may be the first time the participant has been asked to take part in research of this kind. They may need you to spend more time explaining the key concepts to them.
2. **Understand:** Try to put yourself in the participant's shoes. They may have just received a diagnosis they were not expecting – for example, patients with suspected or confirmed cancer – and you are asking them to make an additional important decision about their health. Be sensitive and empathetic.

3. **Keep an open mind:** Don't try to pre-empt a participant's questions as they are talking: let them finish what they are saying before you start to answer. It may not be the question you're expecting.
4. **Be honest:** Your role isn't to coerce the potential participant into joining the Project – just answer questions as accurately as you can, so they can make an informed decision that is right for them.
5. **Recognise the limitations of your role:** You won't always know the answer to participants' questions. Seek support from your colleagues and your NHS GMC project manager. It is fine if you need to get back to them with information before they can make a decision whether to participate or not.

Q&As

This Unit has outlined aspects to consider when preparing for the consent conversation, areas of concern for potential participants, and suggested approaches to take in response.

The final part of Unit 3 comprises two lists of FAQs, from the participant's perspective (Unit 3.4), and from the health professional's perspective (Unit 3.5).

These FAQs do not form part of the core course content. However, you can use them to test your knowledge by reading through them and trying to anticipate the answers based on your experience and what you've learned in the course.

3.4: Patient FAQs

The questions and answers below are intended to cover some of the common queries you may hear from potential participants in the 100,000 Genomes Project.

The answers are all in line with the Genomics England protocol.

General questions

What is whole genome sequencing?

Whole genome sequencing means analysing all your DNA – your genome. Each person has a unique DNA ‘sequence’, although some of it is shared with your relatives. By finding out what that sequence is and how it differs from others’, it is possible to find out information about your health, both now and in the future.

Why have I been selected to take part?

The 100,000 Genomes Project is inviting people with certain types of cancer and patients with a rare disease, as well as some of their family members, to participate. Later, the Project will include patients who have had certain infectious diseases.

What will I gain from taking part in this Project?

You may receive some important information about your health that could be relevant to your diagnosis and treatment. Such results may also offer information that is relevant to the health of your relatives. However, it is possible that you won’t receive results that benefit you personally.

Even if you don’t personally benefit, the results from the Project as a whole will help to further our understanding of the relationship between genetics and disease, and this will help improve healthcare in the future with respect to diagnosis, treatment, prevention and cure of disease.

What if I decide later that I don’t want to take part anymore?

You can withdraw at any point in the process – just ask for a withdrawal form from your clinical care team. You can withdraw partially, which means that you will not be contacted for further information or invitations to further research, but your clinical team can still get in touch to discuss your results, and your pseudonymised data and samples will continue to be stored by the

Project. Alternatively, you can withdraw fully, which means your samples will be destroyed, your information will not be used, and you will not be contacted again regarding the Project.

Do I have to agree to all of the conditions on the consent form?

You have to agree to most of the conditions on the consent form. If you take part in the Project, you must agree that your samples can be taken, analysed and stored. The samples include blood and/or saliva, and if appropriate a tiny section of tumour tissue removed during your routine medical care. You need to agree to be given your results and for pseudonymised data to be shared with carefully selection third-party researchers and companies. You also have to agree to be contacted about future research, but there is no obligation that you actually participate in this research; you can decide at the time.

There is one part of the consent form that offers an optional involvement: you can choose if you want the genome sequencing to look for ‘additional looked for’ findings, which are not related to the condition for which you

were referred to the Project. Adult participants may also opt in to receive information about their carrier status in relation to a select list of genetically inherited diseases.

Participants can reverse their decision about opting into, or out of, both additional looked-for and carrier status findings at a later date by completing a form available from Genomics England: www.bit.ly/genomes100kdocs.

Who can I contact if I have any questions or concerns about the Project?

You can speak to members of your clinical team, or contact Genomics England.

If I don’t take part, can I still receive genetic testing?

If you don’t take part in the Project you will have access (if appropriate) to the routine genetic testing that is available to all patients in your position. You can find out more about this from your clinical team.

Feedback

When will I receive my results?

At the start of the 100,000 Genomes Project, it is likely to

3.4: Patient FAQs cont.

take many months for any results to be returned from the analysis and validated, and then fed back to the clinician for discussion with the participant. As the Project progresses, technology and understanding will increase, leading to a faster feedback process. It is hoped that, by 2017, initial analysis will be returned within weeks.

Will I have to go into hospital to get my results?

Your clinical team should arrange a face-to-face appointment so you can receive your results: this will allow you to speak with your team more easily and you will be able to ask them questions. If you would rather discuss your results on the phone (for example, if you have difficulty travelling) then ask your clinical team if this is possible.

If you don't find any results during the initial analysis, but you do later on during the Project, will I be contacted?

In this instance, your clinician will receive an initial feedback report to share with you, which will confirm there are no initial results. You will be contacted again whenever there are results to share with you, even if these

are not found immediately.

If I change my contact details, do I need to inform you, and how?

Please inform your clinical team about any changes to your contact details.

Will I receive my raw genome sequence?

Genomics England will do its best to interpret the data from your genome sequence. But if you so choose, you can request to receive the raw sequence data so that you can seek out your own specialist software to de-code it. This is not an easy task but might be of interest to participants who are also bioinformaticians, for example. Participants can request to receive their raw data (their genome sequence) in addition to any results fed back, but owing to the time and cost associated with data retrieval, there will be a charge for this. As at December 2015, the process for this has not yet been defined by Genomics England.

Implications

How might my results affect my family members?

Our genetic information is shared

by our blood relatives, so your results might be relevant to your family (for example, your parents, siblings, aunts and uncles, cousins, grandparents and children). If this is the case we will discuss this in more detail with you, to agree how you might want to share this information.

Will I need to inform insurance companies about my results?

Insurance companies cannot discriminate against you on the basis of having a predictive or diagnostic genetic test as part of the 100,000 Genomes Project, and you do not need to inform insurance companies about having whole genome sequencing when buying insurance. This is in line with the Department of Health / Association of British Insurers Concordat and Moratorium on Genetics and Insurance, which has been extended to 2019, with a review planned for 2016.

The usual rules apply with regard to disclosing treatments, family history or medical history. Here is an example of a person who, through opting in for additional findings as part of the 100,000 Genomes Project, was told they have a genetic variant for familial

hypercholesterolemia. They do not need to disclose their result or diagnosis from the whole genome sequencing, but if they:

- 1) subsequently receive a treatment of statins, they will need to disclose this treatment to their insurer if requested;
- 2) had a strong family history of early onset cardiac disease, they would need to disclose this family history to their insurer if requested; and
- 3) have been under medical investigation for exercise-induced chest pain, they will need to disclose this medical history to their insurer if requested.

What about other organisations, such as my current or prospective employer, bank or lender, Department for Work and Pensions, DVLA, or adoption agencies? Do I have to disclose my results to them?

No, you are not obliged to disclose your whole genome sequencing results to anyone if you don't want to.

What about when giving blood or donating organs, sperm or eggs? Or if I'm considering IVF or freezing of eggs, sperm or embryos? Should I disclose my results then?

3.4: Patient FAQs cont.

If you are giving blood or donating organs or sperm, eggs or embryos, you will be subject to the usual screening or testing protocols that would apply to all prospective candidates for these procedures/treatments.

Clinicians in the NHS who have access to participants' NHS medical records may be able to see within these records that the individual is a participant in the Project. As such, they will also be able to see if a treatment has been given or a genetic test has been validated in the NHS (both of which could have originated from information uncovered via whole genome sequencing (WGS) as part of the Project). However, NHS or other clinicians who are not connected to this Project are not able to look into the participant's WGS results or their records held as part of this Project by Genomics England.

Contact

Who will contact me in the future, and what will they contact me about?

Members of your clinical care team or a Genomics England

representative will contact you with any results, updates and requests for more information and samples.

Will you need more samples from me in the future?

It is possible that we will need another sample from you. If so, a member of your clinical team will be in touch. You do not have to provide more samples if you don't want to. In order to confirm some results, there is also the chance that we may need to collect a sample from relatives. But if this is necessary we will talk this through with you first.

Use of data

Who will be accessing my data and samples?

Your clinical team will have access to your data. People conducting research in other hospitals and research institutions, and researchers from drug companies and medical companies can also apply to use pseudonymised data from the 100,000 Genomes Project. If approved by Genomics England to undertake this work, it may help them to develop new medicines, tests and treatments.

Which third parties/commercial partners will be accessing my data?

Researchers and companies that are conducting health-related research can apply to access the pseudonymised data, and Genomics England must scrutinise and approve their request before they will be granted access. These commercial partners may be drug companies or companies that are organising clinical trials. They can access the data, but they cannot download or remove it – see the question below, 'How secure is my data?'.

Will I be anonymous? Can I be identified from the data?

You will not be identifiable to anyone outside of your medical team and certain members of the Genomics England team with special permission – your samples and data will be labelled with a code that is unique to you, and protects your identity. There is a very tiny risk that a researcher could identify you if they have enough detailed information about your health, but this is very unlikely, and anyone who does this will be committing an offence under the Data Protection Act and can be fined up to £500,000.

How secure is my data, and what will happen to it after the Project finishes?

Maintaining data security and protecting the privacy of patients is of great importance to Genomics England. All analysis and interpretation of the data will take place within a secure and monitored environment, similar to a reading room within a reference library where books cannot be taken away, but must be read within the premises of the library and where access to the reading material is monitored while it is being read. Data from the 100,000 Genomes Project will not be shared for insurance or marketing purposes. Information will only be shared with organisations conducting health research that has been carefully checked and approved by Genomics England.

After the Project finishes in 2017, the Department of Health will ensure that the data is held intact by a body who is mandated to ensure the ongoing security and privacy of the participants' health information. More information about data security can be found in Genomics England's FAQs.

3.5: Clinician FAQs

The questions and answers below cover some of the anticipated questions you might have as a healthcare professional taking consent for the 100,000 Genomes Project.

General questions

How does this differ from purely research and/or purely clinical?

Through the NHS England Genomic Medicine Centres, this Project includes clinical-grade genetic testing (to validate reportable findings that arise through whole genome sequence analysis), and also has the additional benefit of generating vast amounts of data that can be used in a research setting to further our collective understanding of genetic disease. In a pure research setting, results may not be fed back to research participants, but as this has a clinical focus, results that are thought to cause or predict disease, or influence treatment options, will be returned to participants.

How can I answer questions about genetics / genomics if I'm not trained in that area?

You will need to have an understanding of the

fundamentals of genetics in order to be able to take consent for this Project. This means that you appreciate that genes link us to our relatives and that anything discovered from the whole genome sequence might be relevant to several people in a family and not only the person in front of you. You can talk to your local training manager, review online educational resources on genetics or take HEE's 'Introduction to Genomics' online module: www.bit.ly/IntroGenomics.

Where can I go for help and guidance?

Your NHS England Genomic Medicine Centre should be able to help you with practical information and support so you can do your job effectively to consent participants into the Project.

Will the Project be expanded to include conditions other than cancer / rare disease / infectious diseases?

It could do in time, but the Genomics England protocol will be updated should the focus of the Project expand.

Where can I direct patients if they want to know more about genetics?

NHS Choices has lots of information on genetics, and includes links for further reading. Genetic Alliance UK is an excellent source of information and support, and the British Society for Genetic Medicine has comprehensive details about genetics services within the NHS. Genomics England also has lots of information about the Project and their own set of FAQs.

The consent process

Do I have to have undergone GCP training before taking consent?

It is likely that you will have undertaken Good Clinical Practice training as part of your existing role. If not, you can arrange training at the Clinical Research Network website, or contact your local training manager. This course is not intended to replace the training that a healthcare professional would normally undertake in relation to communication, consent and ethics.

Is there a set timeframe that we should give potential participants to reach a decision? And is there a defined 'cool-off' period after they have consented?

After their appointment to discuss

the 100,000 Genomes Project, the potential participant should be given as much time as they feel is necessary to consider whether to take part or not. There is no 'cool-off' period defined by Genomics England, and any consenting participant can withdraw – either partially or fully – at any point. They can also change their decision regarding opting into, or out of, receiving additional looked-for and/or carrier status findings.

How do we record dissent in local notes if notes don't exist with that service?

It should be recorded locally in the patient's medical notes. Genomics England will not store this information, as no consent has been taken.

Will I need to take a family history?

A family history, or genetic pedigree, is requested by Genomics England as part of the proband's clinical data. This may be taken by the patient's clinician separately to the consent conversation. You should follow the local guidance set by your NHS England Genomic Medicine Centre.

What happens if the list of the additional looked-for gene

3.5: Clinician FAQs cont.

variants changes? Will patients need to be reconsented?

No. When participants consent to have their sample tested for additional looked-for gene variants, they are consenting to the principle of receiving results in relation to a list of genetic conditions that may change over the course of the Project. The genetic variants all relate to serious health conditions in which early detection may help prevent or mitigate the effects of the condition, but it's not possible to give any more details at the point of taking consent. If participants are uncomfortable with this level of uncertainty, then they can opt out of having any additional looked-for findings.

What if a patient later says they want to withdraw?

There are two options for withdrawal.

Participants can withdraw partially, which means that they will not be contacted for further information or invitations to further research, but their clinical team can still get in touch to discuss their results, and the participant's pseudonymised data and samples will continue to be stored by the Project.

Alternatively, they can withdraw fully, which means their samples will be destroyed, their information will not be used, and they will not be contacted again regarding the Project.

What if a relative wants to withdraw (eg a parent of a child with a rare disease)?

Usually the proband and one blood relative can remain in the Project, though it will depend on which stage the relative withdraws. If initial analysis has not yet been undertaken, it could be beneficial to seek another relative.

At the point of consent, if only one blood relative is available to participate, what is the protocol about a replacement for the 'missing' relative?

Samples from any additional affected family members should be collected where possible. If the proband is the only affected individual in the family and only one parent, for example, of the proband is available, a sample should be collected from an additional blood relative of the proband (eg sibling or offspring). There is more information about the most informative family

structures in the Genomics England document 'Guidelines for Rare Disease Family and Proband Selection': www.bit.ly/100kGMCinfo.

What happens if a participant's sample is not accepted?

On occasion, samples may not be suitable for the Project; for example, in the case of a suspected cancer where it is subsequently found not to be cancer. In this case, the individual would therefore not be eligible to join the Project. Another example would be if it was not possible to yield sufficient high-quality DNA for whole genome sequencing from the participant's sample. In this case, where possible the participant would be invited to consent to a further sample being taken.

Feedback

If the patient's results mean that there are implications for their relatives, who is responsible for informing the relatives? Should we refer them to clinical genetics services?

The NHS England Genomic Medicine Centres and their local delivery partners will have

responsibility for caring for the family and will support the testing of relatives. Clinical genetics services will be within most NHS GMCs, and your local guidance should identify the appropriate routes for referral.

What happens when one member of a couple wants to receive information about carrier status but the other member doesn't?

Each participant can opt in individually for carrier status findings, but they will not receive results relating to autosomal recessive conditions unless both members of a couple have consented to carrier testing.

If only one parent out of a couple come back for the results session, can I give that parent the 'couple's' results for carrier status?

It is preferable if both partners in a couple come back to receive their results together where they relate to autosomal recessive conditions. However, if only one out of the couple comes to the results session, it is acceptable to give the couple results to one of the partnership. Carrier status findings that relate solely to an individual will only be given to that individual.

Glossary

Additional looked-for findings

In the context of the 100,000 Genomes Project, additional looked-for findings relate to the information generated and disclosed to participants that is not related to their existing health condition. This is most relevant for those who have opted to receive feedback about any additional looked-for findings that may appear in their results.

Autosomal dominant inheritance

A genetic condition with autosomal dominant inheritance is caused by a gene on an autosome (a non-sex chromosome) and can therefore be inherited by both males and females. The condition occurs when only one of the two copies of the gene is altered. This alteration is sufficient to impair cell function, leading to disease. If a person has this gene alteration, there is a 50% (1-in-2) chance that each of their children will inherit the condition.

Autosomal recessive inheritance

A genetic condition with autosomal recessive inheritance is caused by a gene carried on an autosome (a non-sex chromosome) and can therefore be inherited by both males and females. It occurs

when both copies of the gene are altered. An alteration needs to be present in both copies of the gene to cause sufficient impairment to cell function to cause disease. People with one copy of the gene alteration do not have the disease, and are said to be a 'carrier' for the condition. If both parents of a child carry an alteration in this gene, there is a 25% (1-in-4) chance that each of their children will inherit the condition, and a 50% (1-in-2) chance of each child being a carrier.

Autosome

Any of the 22 nuclear chromosomes other than the sex chromosomes.

Base pairs

A base is the building block of DNA. The information in DNA is present as a code made up of four chemical bases: adenine (A), cytosine (C), guanine (G) and thymine (T). The order, or sequence, of these bases determines the coded information required for building and maintaining an organism. DNA bases pair up with each other in a complementary manner; A pairs with T and C pairs with G. The human genome contains about 3,000 million base pairs.

Carrier

A carrier is a person who shows no symptoms (asymptomatic) of a condition but carries a genetic alteration that could be passed on to their children. They may have a gene alteration in one of their genes for an autosomal recessive condition (ie has one usual and one altered copy of a particular gene) or X-linked recessive condition, or a balanced structural rearrangement of their chromosomes.

Chromosome

Chromosomes are tightly packaged bundles of DNA, the chemical that encodes genetic information. Nearly all human cells have a set of 46 chromosomes, identified as 23 pairs; 22 pairs are autosomes which are present in males and females. The 23rd pair are the sex chromosomes (XX in women and XY in men) which determines the gender of a person. Human gametes (sperm and egg cells) have 23 chromosomes; one copy of each autosome and one sex chromosome. Each individual therefore inherits one copy of each pair of chromosomes from their mother and the other copy from their father.

Cystic fibrosis

Cystic fibrosis is an autosomal recessive inherited condition of the exocrine glands, most commonly presenting during early childhood. Symptoms are due to the production of abnormally thick mucus from the affected glands due to alterations in the *CFTR* gene. This causes a high susceptibility to lung infections and progressive lung damage. Pancreatic insufficiency is also common. For more information please see the condition factsheet: www.bit.ly/GEPGenFactsheets.

De novo alteration (new alteration)

A new alteration (mutation) that has occurred owing to an error in the copying of genetic material or an error in cell division. Often used to describe the gene alteration in the first person in a family to have a genetic condition. A person with a de novo alteration has their condition as a result of an alteration occurring in a gamete (egg or sperm) from one of their parents or very early in the developing embryo.

DNA

DNA (deoxyribonucleic acid) is the molecule that encodes genetic

Glossary cont.

information. The code itself is based on the sequence of four chemicals, or bases, known as A (adenine), C (cytosine), G (guanine) and T (thymine). The sequence formed by these 4 bases produces the entire instructions for growth, development and function of the human body.

Exome sequencing

Exome sequencing is the technique for sequencing all the protein-coding regions (the exome) of the genome. The exome represents less than 2% of the entire human genome.

Familial hypercholesterolaemia (FH)

Familial hypercholesterolaemia (FH) is an autosomal dominant condition that occurs from a gene alteration in one of 3 genes: *LDLR*; *APOB* and *PCSK9*. This results in abnormally high levels of low density lipoprotein (LDL) cholesterol at birth. When too much LDL cholesterol is present in the blood stream, it builds up in the walls of the arteries and increases a person's risk of heart attacks and heart disease. For more information please see the condition factsheet: www.bit.ly/GEPGenFactsheets.

First-degree relative

A person's biological parent, sister, brother or child.

Gene

A gene is the basic biological unit of inheritance. A gene consists of a segment of DNA which usually codes for a protein, a component of a protein or regulatory elements. It includes coding segments (exons), intervening sequences (introns) together with regulatory elements. Genes are arranged in linear order on the chromosomes. Genes are passed down from parents to their children. Usually an individual has two copies of each gene, one inherited from each parent. The human genome contains about 23,000 genes.

Genetics

Genetics is the study of genes, patterns of inheritance and genetic variation in relation to genetic conditions.

Genome

The total genetic information of a living organism, a complete copy of which is found in most somatic cells. The human genome is defined as one copy of each autosome, both sex chromosomes

and mitochondrial DNA, and is made up of around 3 billion base pairs of DNA. The genome includes the protein-coding genes and all the other sections of DNA. Some of these other sections of DNA are thought to have important functions in the body but the functions of many parts of the genome are unknown.

Genomic medicine

Genomic medicine (or healthcare) is the use of genomic information and technologies to determine disease risk and predisposition, diagnosis and prognosis, and the selection and prioritisation of therapeutic options.

Genomics

Genomics is the study of the structure and function of the whole genome and the interplay of genetic and environmental factors in disease. The word 'genomics' also has a broader meaning, which includes the laboratory technologies that have been developed because of it.

Germline

Egg and sperm cells are called germ cells or gametes. These cells transmit genetic information to the next generation. Other cells in

the body are referred to as somatic cells. Germline refers to a factor occurring in the egg or sperm from which that individual developed.

Germline mutation

A genetic alteration (mutation) in a gamete or germ cell, ie one that someone was born with, rather than acquired later in life.

Hereditary breast and ovarian cancer

Hereditary breast and ovarian cancer is an autosomal dominant condition that predisposes women in a family to have an increased probability of developing breast and ovarian cancer. Two major genes associated with familial breast cancer are the *BRCA1* and *BRCA2* genes. Women with an alteration in the *BRCA1* or *BRCA2* genes have a significantly increased probability of developing breast and ovarian cancer during their lifetime, and may be offered additional screening. Men with an alteration in the *BRCA1* or *BRCA2* genes have an increased probability of developing prostate cancer and breast cancer. For more information, please see the condition factsheet: www.bit.ly/GEPGenFactsheets.

Glossary cont.

Main findings

Information received by participants in the 100,000 Genomes Project about their existing condition; this could include information on how the condition can be treated and managed.

Modes of inheritance

A term used to describe the different forms of genetic inheritance.

Mutation

A change in genetic material, either of a single gene, or in the number or structure of the chromosomes. A mutation that occurs in the gametes (germline mutation) is inherited; a mutation that occurs in the somatic cells (somatic mutation) is not inherited.) In a clinical setting, the word 'mutation' is often reserved for describing a variant causing a disease (pathogenic changes). Scientifically, the word may also be used to describe non-pathogenic changes. In clinical practice, a mutation is often described as an alteration or variation.

Pedigree

A pedigree is a diagram that is drawn using internationally

agreed standardised symbols and lines that shows how family members are related to each other. Additional information about medical conditions is added to the diagram to assist in making a diagnosis about an inherited genetic condition. Clinically, it is sometimes referred to as a family tree.

Penetrance

The proportion of individuals with a mutation causing a particular disorder who exhibit clinical symptoms of that disorder.

Personalised medicine

In this module, personalised medicine is the term used when specific information about a person's genes is used to decide what is the most effective treatment for their condition.

Phenotype

Phenotype is used to describe the physical, observable and/or biochemical characteristics of a person.

Predisposition

Predisposition is the intrinsic likelihood of a person developing a particular condition.

Prevalence

Prevalence is the number of people living with a particular condition in a defined population during a specific period of time.

Proband

Proband (also referred to as the index case) is usually the first affected person with the condition of interest in a family who brings a genetic disorder to the attention of the medical community. In the context of the 100,000 Genomes Project, the proband is the person with a condition that means that they are eligible to join the Project, and who is in the youngest generation of the family being recruited to the Project.

Pseudonymised data

Patient data held by Genomics England as part of the 100,000 Genomes Project is pseudonymised. Each patient record is de-personalised and assigned a unique code.

Rare disease

In the UK a rare disease is defined as one that affects 1 in 2,000 or less of the population and is a life-threatening or chronically debilitating disease.

Sequencing

The technique used in laboratories to determine the order of the base pairs in DNA or amino acids in a protein.

Sex chromosomes

The sex chromosomes determine the sex of an individual. These are XX in women and XY in men. The non-sex chromosomes (numbered 1 to 22) are known as the autosomes.

Somatic alteration

An alteration (mutation) occurring in any cell except the gametes. Somatic alterations are not inherited and are not passed on to children. A series of somatic alterations can cause normal cells to develop into cancer cells.

Somatic cell

Any cell in the body except the gametes (sperm or egg).

Variant

A variant is when alterations are found in DNA bases that differ from a reference genome sequence. The difference may be bases that have been deleted, altered or inserted.

Glossary cont.

Variation

Variation is the differences in the DNA sequence that occurs between individuals and populations.

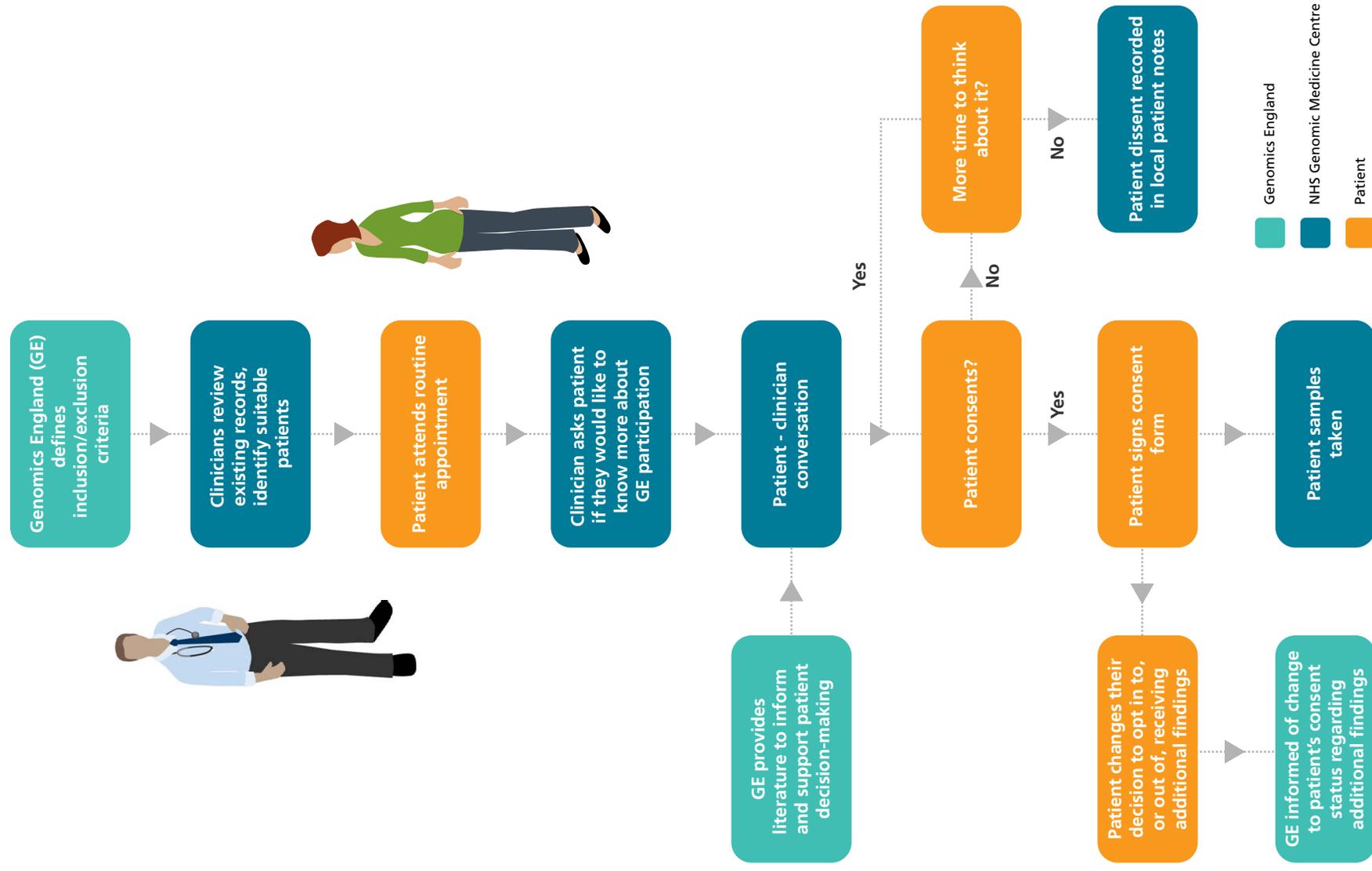
X-linked

A genetic condition with X-linked inheritance occurs when there is a genetic alteration on the X chromosome. Males only have one X chromosome; therefore, for X-linked recessive conditions, if they have an alteration on their X chromosome they will develop the condition. As females have two X chromosomes, if they have an alteration on one of their X chromosomes their other X

chromosome can 'compensate' for this alteration and they are therefore a carrier for the condition. Females who have only one copy of the altered gene most commonly do not show signs of the condition, but occasionally may, because of differences in X-chromosome inactivation.

If the mother of a child is a carrier for an X-linked recessive condition, any son she has will have a 50% (1-in-2) chance that he will inherit the condition. Any daughter she has will have a 50% (1-in-2) chance of also being a carrier for the condition. Some conditions are inherited in an X-linked dominant way but this is much more unusual.

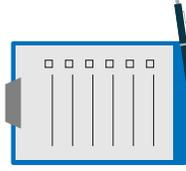
100,000 Genomes Project consent process



100,000 Genomes Project: the pipeline

1. Identifying the patient

The patient's suitability is assessed based on Genomics England's eligibility criteria



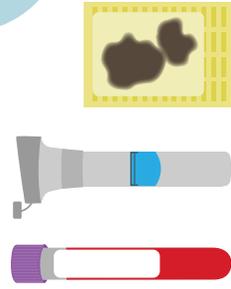
2. The consent conversation

The clinician will discuss participation using the appropriate consent form and patient information sheet and if the potential participant gives their consent, they will be enrolled in the project



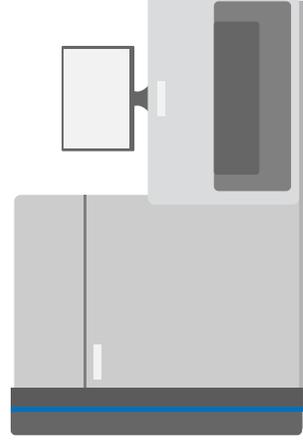
3. Sample collection and DNA extraction

Blood/saliva/tumour samples are collected, extracted and stored according to the defined specifications



4. Sequence annotation, validation and interpretation

The DNA will be sequenced and the data provided for clinical validation and interpretation



5. Reporting of findings

The results will be collated into a clear textual report, which the clinician will discuss with the patient

