Supplementary Appendix 2: Patient summary of guideline

Genomic testing for single gene inflammatory bowel disease

Crohn's disease and ulcerative colitis are the two main forms of inflammatory bowel disease (IBD). Crohn's and Colitis can develop when immune cells enter your gut and react in an abnormal way. We do not know exactly why this happens in most people. Many things are probably involved. This includes lifestyle factors, such as the food you eat, whether you smoke, and your stress levels. It also includes changes in your genes. Together, these things affect how your immune system reacts to the world around it.

Rarely, some people have a type of Crohn's or Colitis that is caused by a damaging change in a single gene that stops it working properly. This is called 'monogenic inflammatory bowel disease' or monogenic IBD.

Monogenic IBD usually shows up at a young age – often in babies or toddlers. They may become very ill as a result. People with monogenic IBD might also get unusual symptoms outside the gut, like repeated severe infections or inflammation in other parts of their body. Other family members might also be affected. Monogenic IBD often does not respond well to the medicines usually used to treat Crohn's and Colitis.

Knowing that someone has monogenic IBD, and exactly what changes they have in their genes, could help their hospital team to work out the best treatment to use. To do this, a blood sample can be tested to look for changes in their genes. This is called genomic testing.

Genomic testing is expensive and it can take weeks or even months to get the results. Most people with Crohn's and Colitis do not need this testing because they are very unlikely to have monogenic IBD. But some signs and symptoms make monogenic IBD more likely. So it is important to set out guidelines for who needs genomic testing and the support these people should have.

The British Society of Gastroenterology (BSG) and the British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) have put together these guidelines. They help work out who should have genomic testing for monogenic IBD. They also set out how the process should work, and who should be involved.

Nearly all people with monogenic IBD get symptoms when they are children. But some people might not have had genomic tests when they were children. They might now be adults with ongoing symptoms that started during childhood. The guidelines are relevant for paediatric and adult medicine.

Who should be offered genomic testing?

Consultants should consider genomic testing for:

- People who developed Crohn's or Colitis before they were 2 years old.
- People who developed Crohn's or Colitis before they were 6 years old, especially if they have:
    - Other immune system problems.
    - Frequent infections.
    - Diarrhoea since birth.
    - Cancer as a child or young adult.
    - A close family members with suspected monogenic IBD.
- People with Crohn's or Colitis who are so severely affected that they might need a stem cell transplant.

People who developed Crohn's or Colitis after they were 6 years old rarely need genomic testing. It should mainly be offered to people with specific immune problems or other inherited problems.

How should the system work?

Consultants in gastroenterology or immunology can request genomic testing.

- If a consultant thinks someone might have monogenic IBD, they should discuss it with a team of experts. The team should include the lead consultant, an expert in monogenic IBD and a clinical genetics specialist. It might include other specialists too.
- The team of experts should discuss the person's medical history and test results. Based on these, they should judge whether genomic testing would be helpful.
- The lead consultant should tell the person or their parent(s) what the team of experts has discussed. They should talk about the benefits of having genomic testing, as well as the things that can be difficult or uncertain.
- If the person or their parent(s) choose to go ahead with genomic testing, the expert team should look at the results and work out what they mean.
- The person's consultant should tell them or their parent(s) the results. They should explain what the results mean and if they affect the recommended treatment. If the results might affect other family members, the consultant might refer the person and/or their parent(s) for genetic counselling.

- To help scientists find out more about the genetic changes in Crohn's and Colitis, people who have genomic testing should be invited to take part in research studies. Research is important for everybody with Crohn's and Colitis but it is especially important in people with rare types. Research could help scientists find out what causes Crohn's or Colitis, and help find new, targeted treatments.

What might the results of genomic testing mean?

- In many cases, testing might not find the cause of the condition. This can still be important because it helps rule out monogenic IBD.
- Testing might find a genetic change that is the probable cause of the condition. Doctors might then suggest extra tests and different treatment options. The genetic changes might also be present in other family members and could affect their health too.
- Testing might find a change that scientists do not fully understand. The person may then be asked to participate in research to help scientists understand the change and whether it causes disease or not. Scientific knowledge may become clearer in the future. This might mean that some people who do not get a diagnosis of monogenic IBD at first might get one in the future.
- Rarely, genomic testing might find a change that is not related to gut inflammation but could have other health implications for the person or their family members. If people want to be told about these unexpected genetic findings, the clinical team will discuss them and what they might mean.

Patient visual summary of guideline

- A visual summary of the guideline is provided to aid patient understanding.