Genomics and Ethics

PROFESSOR CHANTAL SIMON
Genetics or genomics?

- **Genetics** is used in discussion of single gene diseases e.g. cystic fibrosis or haemophilia.

- **Genomics** refers to a person’s entire genetic code - their genome. Variations in different parts of a genome might increase or decrease the chances of developing many common (multifactorial and polygenic) diseases such as diabetes or heart disease.

- **Genomic Medicine** refers to the application of genomics to clinical care of patients; Regional Genetics Centre have now become Genomics Medicine Centres.
But genetics is a specialist area – what relevance does it have for GPs?

- GPs have always practised family-centred care
- GPs frequently look for genetic causes of disease e.g. questions about family history of breast or bowel cancer, questions about family history of diabetes, glaucoma or heart disease
- Genetics testing in the community is commonplace e.g. antenatal testing, neonatal heel prick testing
Andrew is 41 years of age
He has advanced bowel cancer
On diagnostic genetic testing he has been found to have an inherited form of bowel cancer called Lynch syndrome
Andrew’s parents both died young but not of bowel cancer. He has two siblings but does not have regular contact with them. They have a 50% chance of having Lynch syndrome.
Andrew has been offered help from the clinical genetics department to contact his siblings so that they can have predictive testing, but has declined saying that he will contact them himself when he feels a bit better.
Case study 1

Andrew died 2 years ago
His brother, Peter, now aged 39 years, is also registered with your practice
Peter presents with a Duke’s C bowel cancer
Peter did not know that he was at increased risk of bowel cancer
Peter had not had any bowel cancer screening
Questions:

- If you know a patient is at risk of a particular disease because a relative has an inherited condition, do you disclose this to your patient or wait for the relative to inform them?
- Is this a case of a serious harm that might have been preventable if Peter had been told of his risk?
- If you think this is the case, then what level of risk, and what level of evidence regarding interventions would be required to justify disclosure?
- Does this raise different issues from those that arise when contact tracing in, for example, sexually transmitted diseases?
Case study 3

Rosie (aged 3 years) has significant developmental delay and some unusual facial features.

Her paediatrician requests comparative microarray testing and a gene deletion encompassing part of the BRCA2 gene is found.

This has no relevance for Rosie right now.

But it may have relevance for Rosie in the future and, if Rosie has inherited this from either of her parents, then they or their relatives may benefit from interventions sooner rather than later.
Questions:

- Should this unexpected result be revealed to Rosie’s parents?
- How could you ensure that Rosie is referred for screening at an appropriate time?
Case study 3

John is 25 years old. He is seen in the genomics medicine centre after a diagnosis of Huntington’s disease has been made in his 45-year-old mother.

John is informed that a highly accurate predictive test is available and that there is a 50% chance that he has inherited the condition.

After discussion, John decides that he does not wish to know whether he has inherited Huntington’s disease. His reasons are the lack of effective treatment and the long-time interval until the likely onset of symptoms.
3 months later, John’s girlfriend, Samantha, attends with their 4-year-old son, Ben.

Samantha would like Ben tested since she has observed the ‘awfulness’ of Huntington’s disease in John’s family and would like to be prepared if Ben has inherited the disease.
Questions:

- Should Ben be tested? If so, when?
- Does John’s refusal of a test have any bearing on the decision of whether or not to test Ben?
- Does the fact that the disease in question is paternally inherited mean that John has a greater stake in, or say about, genetic testing of their child?
- Would the situation be different if Samantha was pregnant and requesting antenatal testing?
Case study 5

Punit is a 47 year old business man
He is happily married and has three children aged 12, 9 and 7 years
He has undergone a commercially available mail order sputum genomic test to look for disease risk on the basis that he wants to be prepared for the future so that he can protect his family
He makes an appointment to see you to discuss the results
Genetic Health Risks (3+)

These reports tell you if you have genetic variants that are risk factors for various health conditions. Most of the time, having just one variant can be linked to higher risk for the condition.

Considerations:
- Keep in mind that having one of these variants does not necessarily mean you will develop the condition.
- These reports do not cover all possible genetic variants that could influence risk for these conditions.
- Other non-genetic factors can also influence risk for these conditions.
- Read more about 23andMe's scientific criteria for reporting genetic associations here.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Gene</th>
<th>Variant(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-1 Antitrypsin Deficiency</td>
<td>SERPINA1 gene</td>
<td>2</td>
</tr>
<tr>
<td>Hereditary Thrombophilia</td>
<td>F5 and F2 genes</td>
<td>2</td>
</tr>
<tr>
<td>Late-Onset Alzheimer's Disease</td>
<td>APOE gene</td>
<td>1</td>
</tr>
<tr>
<td>Parkinson's Disease</td>
<td>LRRK2 and GBA genes</td>
<td>2</td>
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</tbody>
</table>
Carrier Status (40+)

The reports in this category tell you if you have genetic variants that have been linked to recessive conditions. Recessive conditions occur when a person has two variants for that condition, one inherited from each parent. A person with just one variant for these conditions is known as a carrier. Carriers do not have the condition, but they can pass a variant to their children.

Considerations:

- These reports include only a subset of possible variants that may be linked to a condition. It is possible to have other variants not included in these reports.
- If you have a family history of any of these conditions and are thinking about having children, you should discuss options for testing with your doctor.
- Read more about 23andMe’s scientific criteria for reporting genetic associations [here](#).

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<tr>
<td>ARSACS</td>
<td>SACS gene</td>
<td>1</td>
</tr>
<tr>
<td>Agenesis of the Corpus Callosum with Peripheral Neuropathy</td>
<td>SLC12A6 gene</td>
<td>1</td>
</tr>
<tr>
<td>Autosomal Recessive Polycystic Kidney Disease</td>
<td>PKHD1 gene</td>
<td>3</td>
</tr>
<tr>
<td>Beta Thalassemia and Related Hemoglobinopathies</td>
<td>HBB gene</td>
<td>10</td>
</tr>
<tr>
<td>Bloom Syndrome</td>
<td>BLM gene</td>
<td>1</td>
</tr>
<tr>
<td>Canavan Disease</td>
<td>ASPA gene</td>
<td>3</td>
</tr>
<tr>
<td>Congenital Disorder of Glycosylation Type 1a (PMM2-CDG)</td>
<td>PMM2 gene</td>
<td>2</td>
</tr>
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</table>
Questions:

- Does this result mean that Punit will develop dementia in the future?
- What other implications might this test result have for Punit?
- How might you manage this situation?
Key points

- Genetic and genomic information is complex and interfamilial; a result for one person may have relevance for others. Who does a genomic test result belong to?
- There is a tension between genomic medicine - which involves families - and a modern medical framework with huge emphasis on individual autonomy
- Genomic testing may reveal unexpected information and this should be discussed before embarking on testing
- Genomic testing may give accurate information about risk, but be unable to predict when, or even if, a condition will occur
- There is a potential for stigmatization and discrimination as a result of genomic testing
Thank you

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• For more information on genomics in primary care, please visit: http://www.rcgp.org.uk/clinical-and-research/our-programmes/innovation/genomics-in-medicine.aspx

• For questions or comments please contact us at genomics@rcgp.org.uk

• For more information on genomics education, please visit: https://www.genomicseducation.hee.nhs.uk/