Genomic investigations: Health Care Professional (HCP) and family experiences of managing incidental information in clinical practice

Gillian Crawford
Clinical Doctoral Fellow/
Principal Genetic Counsellor
Clinical Ethics and Law at
Southampton (CELS)

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Phenotype → Genotype

Targeted counselling and testing

Low chance of uncertain and incidental findings

Genotype → Phenotype

Broad counselling and testing

Increased numbers of uncertain and incidental findings
Abnormalities of potential clinical significance that are unexpectedly discovered during routine testing, unrelated to the original purpose of the investigation.
Incidental to what?
Unexpected to whom?

Clinical question that arises from signs/ symptoms/ FH

*Duty of care in clinical practice*

Research into the sequence of genomes

*Altruistic participation; duty of contract*

Disclosure practices may differ

Clinical ethics and law Southampton: [www.soton.ac.uk/cels](http://www.soton.ac.uk/cels)
Not new…but…

- Genetic technologies will increase frequency
- Limited research on management of IFs in clinical practice (consent and disclosure)
- Pre-natal and new born screening
Terminology

Unwanted

Unanticipated/Unexpected

Off-target

Unsolicited/unsought for

Secondary Variant

Opportunistic

Incidentaloma

Not pertinent

‘One size does not fit all’

Clinical ethics and law Southampton: www.soton.ac.uk/cels
Patient perspective

Phase 1

Observations

In-depth interviews

Literature and policy review

Analysis

Phase 2

Survey

Empirical and ethical insight into practice

Dissemination and practice recommendations
Research aims

• Describe current practice in a range of clinical settings
• Explore lay and professional views and experiences of genetic IFs arising in the clinical setting
• Generate information to advise policy on the consent and disclosure practices of IFs in clinical practice
Interview sample

HCP Interviews (n=32)
- Genetic specialists: 22
- Paediatric specialists: 7
- Adult physician: 1
- Clinical scientist: 2

Family interviews (n=16)
- 16 participants from 13 families
- 3 sets of parents
- Number of families with an IF: 5
<table>
<thead>
<tr>
<th>Reason for test</th>
<th>IF discovered</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>DD aCGH</td>
<td>22qdel including SMARCB1 Schwannomatosis</td>
<td>Regular review</td>
</tr>
<tr>
<td>Muscle problems aCGH</td>
<td>FBN2 mutation Marfan’s phenotype</td>
<td>Cardiac screening</td>
</tr>
<tr>
<td>Behavioural and social problems aCGH</td>
<td>Y chromosome deletion (infertility)</td>
<td>N/A</td>
</tr>
<tr>
<td>DD aCGH</td>
<td>Deletion including MSH6</td>
<td>N/A Referral for bowel screening as an adult</td>
</tr>
<tr>
<td>RP Gene panel</td>
<td>Mutation in LRP5 gene Osteoporosis</td>
<td>Bone density screening</td>
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Findings: Consent and Disclosure

- The possibility of an IF is not consistently discussed
- No common practice when IFs are discussed
  (use of examples, consent forms)
- No discussion about the information families want
“...But you know it was a bit of a shock, because no we didn't know that they could have found anything else out. Nobody said that....No, nobody ever mentioned...I didn’t really realise and I thought they were looking for one thing; didn't know that you could sort of find all these other things out...” FAMINT013 (IF discovered)
Lay and professional experiences of IFs

Family members

- Surprised by IF result
- No regret at receiving IF (interventions/future treatment)
- Would want further IFs
- Desire for information

HCPs

- Nearly all IFs were disclosed
- HCPs found disclosure challenging
- Often used cases in subsequent consultations
- Reported that patients adjusted well to this information
“...because it’s actually a twist of fate if you like, a bit of luck, that had [son] not had these underlying problems he could have developed... this condition later in life and been unaware of it. So actually the fact that he knows about it, it gives him a kind of ... a lucky break... because he’d got the opportunity to get screened for it regularly...” FAMINT011 Father
“...it proved very hard work, explaining that [juvenile polyposis IF] and the mother getting very upset and quite angry... I mean the irony actually was that probably the risk with this single allele being deleted...was uncertain, but almost that was kind of worse because then there was the accusation that you bring something up and yet you still don't really know if it’s important or not.” HCPINT013 Consultant Geneticist
Findings: Meeting expectations

- Consensus that possibility of IFs should be discussed
- Reasonable for patients to have choice on IFs disclosed
- Challenges of offering choice:
  - Hypothetical decision-making
  - Sustained wishes
  - Recording and complying with decisions
  - Follow up and storage of information
Hypothetical decision-making

“I think it’s really difficult and I think for a lot of people they wouldn’t be able to give that [IF choices]. And I think even myself, if somebody asked me that, I think, well it would depend what it is ... and clearly you don’t know what your incidental finding is until you find it, so you can’t counsel somebody and ask them about every single eventuality.” HCPINT028

“You can get a feeling, a gist of someone’s preference, whether... someone would want to know everything, know nothing or a few gradations in between. That’s probably about as good as you can get.” FAMINT008 Father
Themes about consent and disclosure practice

What is consent?
- Information
- Information and involvement
- Permission

Who decides?
- Patients
- HCPs
- Shared
Themes about consent and disclosure practice

- What is ‘the result’?
- Clinical practice and research
- Genome as a future resource
- Patient expectations
- Mainstreaming
- Follow up and re-contact
- Familial implications
To consider…

• The place for non-directive counselling?

• The consent process?
  (who, documentation, dynamic, broad, opt-in, opt-out, mainstreaming)

• Challenges at the clinical/research/commercial interface
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