Genomics research: individuals and families

Dr Paula Boddington
Senior Researcher in Ethics and Genetics
Procardis Consortium Ethics Programme
Ethox Centre, Department of Public Health
University of Oxford
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Research ethics regulation

- Has traditionally focused on protecting the individual from harms and from exploitation
- However, much medical research has implications for family members and for communities
- This is especially the case with genetic research
- This has led to some suggesting that we make changes to research practices and recruitment to research

Genetic information and relatives

- How much genetic information do you share with relatives?
- First degree relatives – parent/child – share 50% - siblings – 50% on average
- Second degree relative – uncle-aunt /nephew-neice, grandparent/ grandchild, half-sibling, share 25%
- Third degree relative – such as first cousins – share 12.5% (one eighth)
- Certain genetic characteristics may be more common in communities and population groups
- Genetic information about one person may give certain information about another.

- This information may be probablistic – e.g. a 50% chance of sharing the same genetic status as a first degree relative
- Or it may be more certain – information on the Y chromosome is passed on virtually unchanged from father to son;
- Likewise, information in mitochondrial DNA – DNA residing in small bodies within cells – is passed on from mothers to their sons and daughters
- In some cases genetic information may be inferred with certainty – for instance, if your parent carries the gene for a rare disorder, and so does your child, and your spouse does not, you know that you also carry the gene.
- In many other cases, you only know that you have a risk of carrying genes that other family members have.
- Some genomics research involves members of the same family; checking on relationship status can reveal anomalies – such as discrepancies in reported paternity and even sometimes maternity
- Genetic information can also potentially reveal high levels of inbreeding and can, on rare occasions, indicate possible incestuous relationships

Genetic information and research concerns

- **Privacy**: this is protected in medical research by anonymization of samples and data; aggregation of samples into large groups; and by promises to guarantee confidentiality.
- **Feedback of results**: some argue that individuals should be told of any results of research that may be relevant to them; others argue that research results may be misleading, or that this may be very impractical as well as costly.

Privacy

- Recent work has demonstrated that there are various ways in which standard procedures to protect privacy may be breached
- Individuals can be identified in aggregated data – where the information from a thousand people is pooled – as long as you have the original person's DNA to compare
- Information from different sources may be 'triangulated' to identify a person – e.g. a child of donor sperm managed to track down his genetic father using a combination of sources
- It has been shown to be in principle possible to link DNA information from the Y chromosome with ancestry registers to make educated guesses about surnames
- It has been shown that reasonably accurate guesses about a sibling may be made from DNA data
- DNA data may be used forensically to track down not just the individual concerned but also close relatives suspected of crimes

Privacy concerns in perspective

- It's also important to put these concerns about privacy in perspective
- It's been shown that out of a group of 1000, it is possible to detect the presence of an individual within that group – but only if you already have their DNA – and with powerful statistical techniques
- There are routine safeguards about de-identifying and anonymising data, and legal regulations requiring safe storage
- However, opinion is still out on whether concerns about DNA privacy are alarmist or realistic
- Meanwhile, what is true, is that privacy concerns for individuals may also have implications for close genetic relatives

Feedback

- If results of genomics research are fed back to individuals, they may have implications for genetic relatives
- Information from research about anomalous family relationships – should this ever be fed back? It obviously has implications for more than one person
- Information from genomics research may have implications from population or community groups. E.g. there are concerns that certain groups may be stigmatised by information about genetic susceptibility to certain diseases or conditions; information revealing widespread 'non-paternity' may stigmatise a group or endanger individuals in it (such as wives who come under suspicion)

A current live debate:

- There is currently heated debate about what policy on feedback of findings should be for different kinds of genomics research
- However it is clear that some information that might be fed back could have implications for family members

Genetic information and individuals

- Key concept underlying much of the ethical regulation of medical practice, including research: Individual autonomy
- This grounds the practice of individual free consent to research
- But the relevance of much genetic information for relatives and to communities challenges this
- Should individuals get consent from family members who may be affected by possible privacy risks – no matter how remote – or who may be affected by any results that are given?

Consent from others?

- It has been suggested that individuals should discuss research participation with close relatives
- In some genomics research with particular relevance to certain groups such as ethnic groups or isolated communities, community consent may be sought
- For example, this occurred with the International HapMap project

  http://hapmap.ncbi.nlm.nih.gov/

Including family and community in the consent process

- Does this undermine autonomy?
- Does it enhance protection?
- Does it raise ethical standards?
- Is it the responsibility of the individual?
- Is it the responsibility of the researchers?

Lessons from the clinic

- Much work in clinical genetics shows the difficulties and complexities involved in family communication about medical matters in general and genetics in particular
- This work can be drawn upon to help to address the issue in genomics research

Communication within families

- Much research has shown that communication within families, in particular about medical conditions, is a very complex process
- Indeed, the idea of who counts as family, and what the different roles and responsibilities are of family members, varies across time and between different cultural groups
- In fact, genomics research can potentially unsettle notions of family – should unexpected results about relatedness be returned to participants (this is not general practice)

Understanding health, disease, and risk

- It's well known that lay people may understand health, disease, and risk of disease, in ways that differ from health professionals
- Often their understandings are based upon practical experience of living and coping with conditions within the family
- But even within the same family, different members may have different experiences – the situation is highly complex

Variations in experience of disease and variations in understanding

- An example is the X linked condition of haemophilia, which nearly always affects males and which is carried by women.
- It has been found that girls growing up with a brother affected by haemophilia typically have a greater understanding of the condition, and of their chances of passing it on to the next generation, than girls who have a father with haemophilia. This seems to be because they have more first hand experience of how the condition affects everyday life – seeing their brother get medical treatment etc. Fathers more frequently protect children from the impact of their own condition.
- First hand experience of the disease provides opportunities in the family to discuss it and to discuss genetic risk.
- Some genetic conditions are such that many family members have the condition – and then understanding of the disease may be greater. In other genetic conditions, few family members are affected or an individual may be the first known in that family.

Blocks and flows in family communication

- It's also been found that within families, certain individuals may take on responsibility for communicating about health
- Often it is found that women take on this responsibility although there are individual and cultural differences
- And certain individuals may be seen to be able to receive and handle such information; and others may be thought – fairly or unfairly - to be less able to cope
- In many families, ethical obligations to communicate important information are taken very seriously
- But circumstances and different family relationships may make communication problematic
- And withholding information may stem from a desire to protect not from a desire for secrecy

Conclusions

- One conclusion is that simply telling potential research recruits that they ought to discuss issues with family members might be a way of skating over the difficult confluence of individual autonomy with the fact that genetic information may have relevance for others
- But it may be a weak recommendation if it does not give any guidance about the potential pitfalls and difficulties that some – not all – families may face
- Research in clinical genetics and in the sociology of medicine is important for finding ways forward in the ethical conduct of genomics research

Summary

- A key idea in the ethical regulation of medical research has been the protection of individuals, which has come to be expressed through valuing individual autonomy to make decisions and to control information
- The relevance of genetic information to related individuals including family and population groups is challenging this central notion of individual autonomy
- We will need to think carefully whether the current model that places the individual centre stage can be adjusted or whether we may need a more radical re-think of the basis of research ethics

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http://www.genomicsnetwork.ac.uk/cesagen/

Some references

in line with a growing movement to share knowledge, some of the scientific papers referred to in this talk are available freely – including:

The paper that showed that it could be possible to identify an individual in an aggregated collection of DNA:

'Resolving Individuals Contributing Trace Amounts of DNA to Highly Complex Mixtures Using High-Density SNP Genotyping Microarrays', Nils Homer, et al, PLoS Genetics, 2008 August; 4(8): e1000167. doi: 10.1371/journal.pgen.1000167.

A paper showing that certain information about relatives could be derived from an individual's DNA:

My sister's keeper?: genomic research and the identifiability of siblings
Cassa CA, Schmidt B, Kohane IS, Mandl KD, BMC Medical Genomics 2008, 1:32
http://www.biomedcentral.com/1755-8794/1/32

Two papers assessing privacy risks in genomics research:

'Assessing the privacy risks of data sharing in genomics', Catherine Heeney, Naomi Hawkins, Jantina de Vries, Paula Boddington, Jane Kaye, Public Health Genomics, 2010, DOI: 10.1159/000294150

'Public access to genome-wide data: five views on balancing research with privacy and protection', P3G Consortium, George Church, Catherine Heeney, Naomi Hawkins, Jantina de Vries, Paula Boddington, Jane Kaye, Martin Bobrow, and Bruce Weir, PLoS Genetics, October; 5(10): e1000665.