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# **Does whole genome sequencing raise new ethical challenges for REC ?**

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## The claim: WGS creates unique ethical challenges

“ The nature of the data generated by whole genome sequencing (WGS) means that **conventional methods of minimising harms may be inadequate to protect subjects,** whether patients or research participants. ”

(from the report *Next steps in the sequence*)

# The claim: WGS creates unique ethical challenges

- “A recurring theme that arises when genetic or genomic data are discussed is the extent to which genomic data should be treated as **exceptional** and accorded **special protection**. Most commentators acknowledge that genomic data may have a number of characteristics that might merit special protection.” (Next steps in the sequence)

# The claim: WGS creates unique ethical challenges

From the article "Research Ethics Recommendations for Whole-Genome Research: Consensus Statement":

"These topics [the topics discussed in the article] — consent, withdrawal from research, return of research results, and public data release—were selected because they were viewed as being among the most pressing research ethics issues and as representing areas where whole-genome analysis creates **unique challenges.**"

# My sources for quotes about the unique ethical nature of WGS

1. *Next steps in the sequence*, a report published by the Foundation for Genomics and Popular Health (2011)
2. "Research Ethics Recommendations for Whole-Genome Research: Consensus Statement", Caulfield et al, PLoS Biology, 2008

(but they seem representative of the views of many)

# What are the arguments for the claim?

Some candidates:

1. WGS involves the possibility of incidental findings
2. Leaked WGS data can be used for discriminatory purposes
3. WGS can reveal information about research participants that they should not know about
4. WGS gives us information, not only about the individual research participant, but about his/her relatives as well.
5. A genome sequence is never anonymous
6. Genome data are publicly shared
7. Informed consent is impossible, since the risk of incidental findings and future use is unknown
8. A combination of the above factors



# 1. WGS involves the possibility of incidental findings

- “An IF is a finding concerning an individual research participant that has potential health or reproductive importance and is discovered in the course of conducting research but is beyond the aims of the study.”
- (Wolf et al, “Managing Incidental Findings in Human Subjects Research: Analysis and Recommendations” , *Journal of Law, Medicine and Ethics*, 2008)

## Why do IFs constitute an ethical challenge?

1. A policy of returning IFs will divert resources away from research
2. A policy of returning IFs will foster “the therapeutic misconception”.
3. Returning IFs can sometimes do more harm than good; yet, not returning them for that reason might seem unduly paternalistic
4. We cannot always respect both the participants right not to know and his right to know.

...



## Are IFs unique to WGS?

No.

“The problem of incidental findings is intrinsic to human subjects research; we simply have not focussed on it systematically.”

(Susan M. Wolf, “ The Challenge of Incidental Findings”, *Journal of Law, Medicine and Ethics*, 2008)

## Are IFs more probable in WGS? A flawed argument

1. Every person's genome contains some genes predisposing for disease or carrier genes
  - \*2. Since a person's whole genome is sequenced, these genes will necessarily be found.
- The flaw: " incidental findings are elements of belief. They are not mere items of information: information that lies latent within a blood sample, DNA sample, or gene assay is not yet "found." " (Henry S. Richardson, "Incidental Findings and Ancillary-Care Obligations", *Journal of Law, Medicine and Ethics*, 2008)

## **2. Leaked WGS data can be used for discriminatory purposes**

“Consensus Statement” :

“This is, no doubt, an exciting time for genetic research. And it cannot move forward without research participants. As such, it is important to note that the risks associated with this kind of research may be limited and controversial events rare. But history has told us that they do occur and can have a devastating impact on public trust and the research environment.”

**BUT:** such risks are common to most research projects.

### **3. WGS can reveal information about research participants that they themselves should not know about**

Contrast: "data of a nature such that, if other people knew about it, it would constitute a great prejudice to the person about whom information is leaked"

with:

"data (about the participant) which is unknown to the participant himself and which is such that *it would be unfortunate if he came to know about it* (at least if this was against his will).

**Unique to WGS?**

## **4. WGS gives us information, not only about the individual research participant, but about his/her relatives as well.**

- We must reconsider the other ethically challenging aspects of WGS in light of relatives:
  - IFs can be about relatives too
  - Relatives can also be subject to discrimination
  - Information about relatives which they would not want to know about can be revealed
- These problems are reinforced by the fact that relatives have not consented.

## **How unique is the problem of information about relatives to WGS?**

- - It is certainly shared by other types of genetic research
- Many types of research will store data which can be used to infer data about relatives (known by them) and discriminate against them
- The hard question: can other types of research reveal information about relatives that they would not want to know about?



## 5. A genome sequence is never anonymous

- “[S] single base changes in 30-80 locations in the genome are sufficient to identify a single individual from a population of 10 billion. *Thus the human genome is effectively a unique identifier.*” (Next steps in the sequence)

## **A genome sequence is never anonymous – why is that a problem?**

Case 1: When the material is not (otherwise) anonymous: the non-anonymity of the genome sequence adds nothing qualitatively new, but simply adds to the already existing risk of security breaches.

Case 2. when the material is otherwise anonymous: It would be problematic if data was treated with the degree of security appropriate for anonymous data when it is in fact not anonymous.

**BUT:** RECs and other instances are already used to assess whether purportedly anonymous material is really anonymous.

**AND:** we should apply a standard of reasonableness when we ask whether we can expect the material to be used to identify a person.

## 6. Genome data are publicly shared

- "*Consensus Statement* ":  
"International policies call for the rapid public release of all sequence data. The benefit of public data access is that it provides significant scientific utility by enabling immediate international research use of the data. However, policies that advocate unrestricted data sharing have been challenged because of the privacy risks associated with public access to genomic information"

## **Genome data are publicly shared (cont)**

Problems with public sharing:

- It is harder to withdraw consent
- It is harder to know what one consents to
- It is harder to ensure privacy

**BUT:**

- This is a contingent aspect of WGS
- These problems are primarily problems with completely open-access databases – something which does not seem required for good research

## 7. Informed consent is impossible

“Next steps in the sequence”:

“ it is unclear whether the standard models of informed consent are fit for purpose in this context. Two issues have emerged as being particularly pressing: first is the paradox that **individuals cannot be asked to consent to the discovery of risks the importance of which is impossible to assess**. Thus from a legal perspective, there is no ‘meeting of minds’ and contractually the contract between researcher and participant might be void. It is also unclear whether informed consent is sufficient to deal with the feedback of incidental findings which are not pertinent to the initial research or clinical question but that may have either clinical or personal significance.”

## Informed consent is impossible (cont)

- "Consensus statement":
- "These uncertainties [about the implications of genetic information being shared] can create unique ethical challenges. What do you tell potential participants during the consent process about risks when we still don't have a clear sense of their nature?"
- "the unique challenges associated with the research make it impractical to satisfy the norms, tools, and processes usually utilized to respect autonomy (e.g., specific informed consent). "
- "Given the uncertainty and complexity of the activity [of genome sequencing], ensuring fully informed consent will be difficult."



## **Informed consent is impossible (cont)**

- But: We never know all the consequences of what we consent to!
- If such knowledge was a requirement for valid consent, no consent would be valid.
- We already accept broad consent to an unknown set of future research projects

## **8. WGS is unique because it involves a combination of ethically challenging factors**

- The additive model
- The multiplicative model

## Concluding remarks

- There are few, if any, challenges which are unique to WGS
- This does not mean that we do not have to think more about these challenges.
- Genetics can be useful as an “ethical focalizer”, but must not trick us into missing what is really morally relevant.