Anti-Discrimination Working Group

Meeting #4

Friday 18 August 2023

10.00, NCRR main meeting room (and online)

Agenda

1. Introduction round (5 min)
2. Recap: Polygenic embryo screening (5 min)
3. Thought experiments & discussion (35 min)
4. Ideas for next meeting (5 min)

Introductions

Recap: Polygenic embryo screening

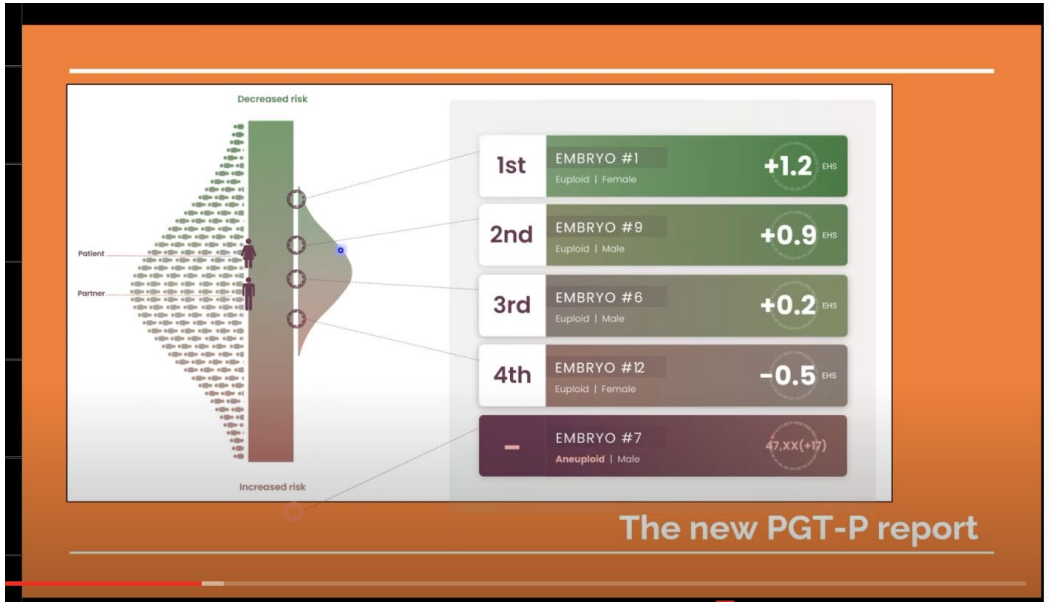
Discrimination in genetics research →

Intertwined history of eugenics and (psychiatric) genetics →

Genetic testing and polygenic embryo screening

Polygenic embryo screening (PES)

- The application of polygenic risk scores in the context of PGT, in order to determine each embryo's liability for one or more diseases/traits, and to guide selection of an embryo for implantation *(Lencz et al., 2022)*



Screenshot from Genomic Prediction presentation [Online image]. (2021). Center for Genetics and Society. https://www.geneticsandsociety.org/biopolitical-times/first-polygenic-risk-score-baby

Polygenic embryo screening (PES)

Genetic Screening Now Lets Parents Pick the Healthiest Embryos

People using IVF can see which embryo is least likely to develop cancer and other diseases. But can protecting your child slip into playing God?

PHOTOGRAPH: ALBERT MARTINE/GETTY IMAGES

At 18 months old, Aurea Yenmai Smigrodzki is inquisitive like any other toddler. She likes peanut butter, the beach, and mobile phones—or any toys that look like phones. She likes to copy her mum and dad, Thuy and Rafal, when they are using theirs. Aurea doesn't know it yet, but her birth was very special: She is the world's first PGT-P baby, meaning she is statistically less likely than the rest of us to develop a genetic disease or disorder throughout her life.

https://www.wired.co.uk/article/genetic-screening-ivf-healthiest-embryos

Why should we be concerned about PES?

PES

Practical/scientific issues about efficacy

Ethical issues

There are many issues with PES.

Practical/scientific issues with PES

Issues with accuracy

1. PES depends on accuracy of polygenic scores (sample size and trait heritability).

2. Variance explained by a polygenic score is much lower than SNP-based h2 (which, in turn, is much lower than broad-sense H2).

3. Polygenic scores are based on GWAS results which may also capture genetic nurture.

4. Polygenic scores are inherently probabilstic and capture risk for multiple phenotypes.

Health disparities*

5. Polygenic scores are not transferrable across genetic ancestries.

Regulatory issues

6. The goals of PES are not clearly defined. What do parents want?

7. No established guidelines on communication of results of polygenic scores, what they mean, and what parents can expect from PES.

8. Regulations differ across countries. This could lead to reproductive tourism.

*Practical and ethical

Ethical issues with PES

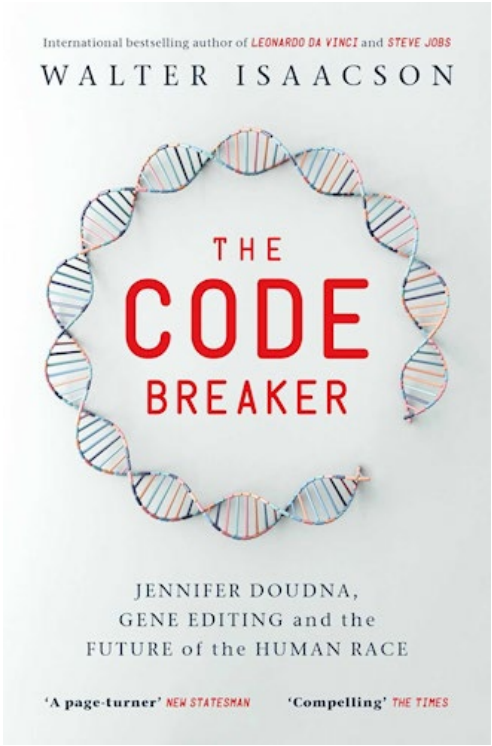
Costs to society

1. Encouragement of eugenicist beliefs.
2. Encouragement of genetic essentialism.
3. Encouragement of fatalism.
4. Increased stigma around certain disorders/traits.

Costs to research

5. Need to take into account views of research participants (e.g., in GWASs).
6. Researchers feeling that their contributions have been misused.
7. Distrust of genetics research community.

Bioethical thought experiments



Taken from Chapter 40 "Red Lines" in *The Code Breaker* by Walter Isaacson

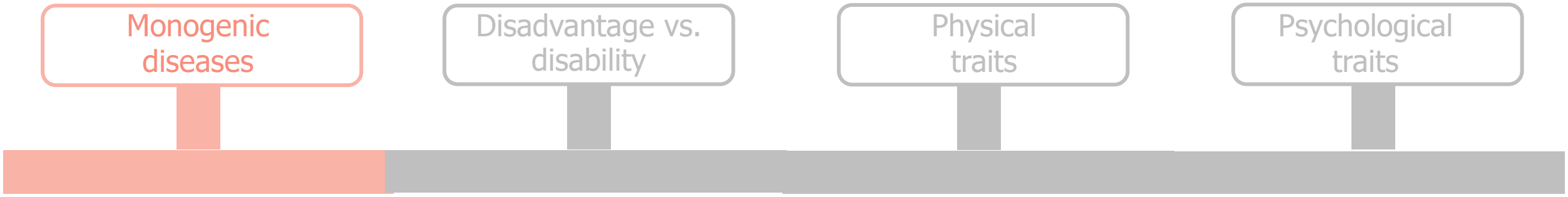
Context: Gene editing with CRISPR

Also applicable to genetic screening

Thought experiments

Huntington’s disease

- Autosomal dominant disease (50% chance if one parent has it)
- Caused by an abnormal repetition of letters in a DNA sequence
- Leads to the death of brain cells
- Uncontrollable twitching, personality changes, progressive loss of focus and motor function, sometimes dementia
- Symptoms usually arise only after childbearing years = No natural selection



Deafness

Scenario: Deaf lesbian couple wants to have a baby who is also deaf.

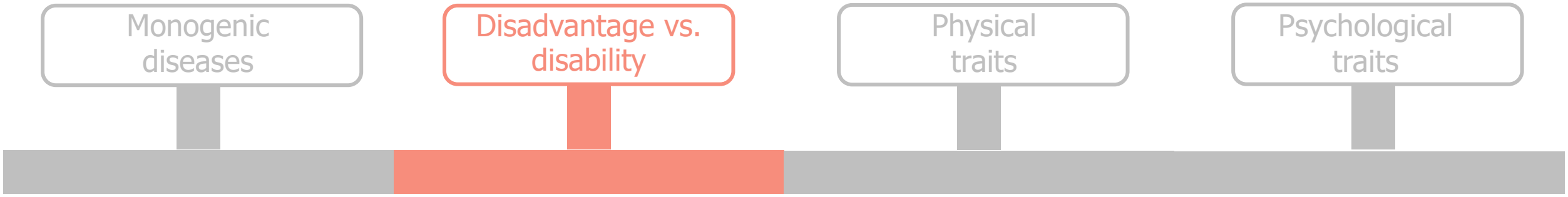
A. Find a sperm donor who is also congenitally deaf

B. Use pre-implantation diagnosis to select an embryo that had the genetic mutation for deafness*

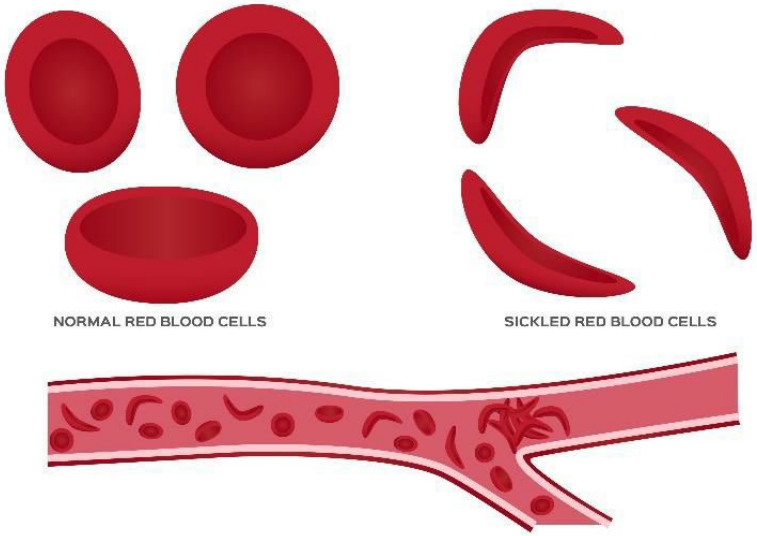
C. Gene edit a typical embryo to be deaf

D. Ask a doctor to rupture the child's eardrums after birth

*What if it was polygenic?



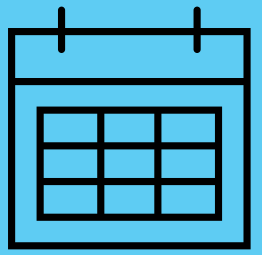
Sickle-cell anemia



- Recessive disease
- Caused by a single nucleotide variant
- Malformed red blood cells
- Fatigue, infections, spasms of pain, early death
- **But:** One copy of gene → Immunity to most forms of malaria
- Gene edit?

Monogenic diseases | Disadvantage vs. disability | Physical traits | Psychological traits

Next meeting:
September?



Thanks!

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References & further resources

- Lencz et al., (2022), Concerns about use of polygenic embryo screening for psychiatric and cognitive traits. *Lancet Psychiatry, 9*(10), 838-844. DOI: 10.1016/S2215-0366(22)00157-2
- Isaacson, W. (2021). *The Code Breaker: Jennifer Doudna, Gene Editing, and the Future of the Human Race.* Simon and Schuster.
- Fleming, J. (2021). *How to be Human: An Autistic Man's Guide to Life.* Simon and Schuster.