Ethical issues in large-scale reproductive genetic carrier screening programs: A view from Australia

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We acknowledge the tradition of custodianship and law of the Country on which the University of Sydney campuses stand. We pay our respects to those who have cared and continue to care for Country.

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Introduction

- **Carrier testing**
  - A genetic test to determine the likelihood a person will have a child with a serious, childhood onset autosomal recessive or x-linked condition
- **Until recently, this occurred in**
  - Families known to have a condition (clinical carrier testing)
  - Populations with certain ancestry/ethnicity (carrier screening, usually for single condition)

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Reproductive Genetic Carrier Screening (RGCS)

- **Now: cheaper DNA sequencing and increased knowledge of genome variation**
- **Has enabled:**
  - Government funded/offered screening
  - Commercial providers where public programs not available
  - Universal screening
  - Large gene panels

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MACKENZIE'S MISSION

- Mackenzie Casella died at 7 months from spinal muscular atrophy (SMA) in 2017
- Her parents asked - why didn't we know we were carriers for SMA?
- They appealed to members of Parliament for funding and research (on a background of years of advocacy from clinicians and support groups)
- Commonwealth Health Minister Greg Hunt advocated for a study and named it Mackenzie's Mission
- Over 8,000 couples* being recruited across Australia through specific healthcare providers
- Screening for 1,300 genes, to detect the chance a couple may have a child with ~750 inherited genetic conditions
- **To understand how to offer reproductive genetic carrier screening as a national program**

https://www.mackenziesmission.org.au/

* various family types able to participate

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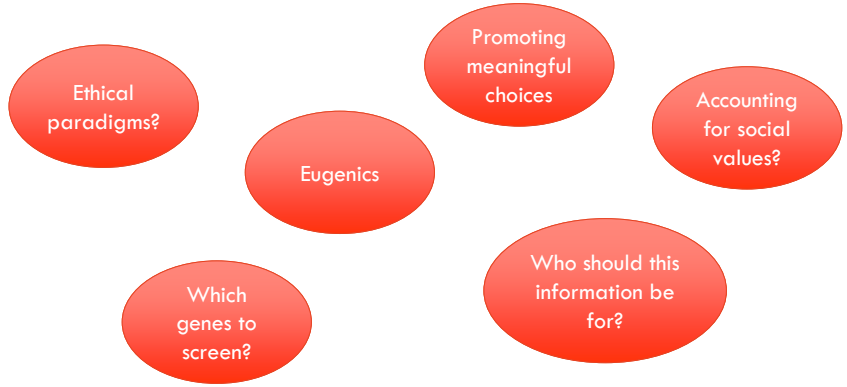
Ethical issues in population-scale RGCS



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Overview

1. **Ethical paradigms and RGCS**
2. **Eugenics**
3. **Which genes? - Severity**

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1. Ethical paradigms and RGCS (clinical or public health ethics?)

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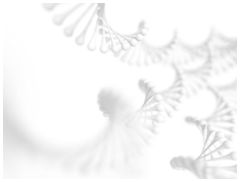
Is RGCS clinical testing, or public health screening?

- **RGCS builds on existing clinical practices and infrastructure**
  - e.g. lab services, variant interpretation, genetic counselling
- **But this is being offered at scale**
- **Participants are broad: couples of reproductive age**

- **Strong influence of clinical paradigm**
  - e.g. care not to 'miss cases' in variant curation
- **But goal also to inform future population screening**



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Is RGCS clinical testing, or public health screening?

RGCS has many features in common with a screening/PH paradigm

- Single test offer
- Made at population level regardless of background
- Standardised pre-test information provision
- Public funding (legitimacy/influence)
- No clinical triage or family history prior to testing
- Interpretation and reporting of gene variants of genes likely be more limited c.f. clinical practice

RGCS should be seen as a (certain kind of) public health intervention

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Public health ethics

- **Recognises that individuals live in a social context**
  - Our public and private spheres are interdependent
  - Social determinants are health determining
    - Education, income, housing, employment, SES etc.
  - Individuals cannot always control these

- **Health interventions can both benefit individuals and contribute to collective good**

- **Values such as equity, reciprocity and solidarity are important**

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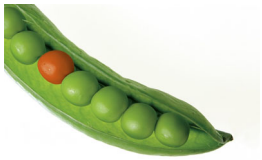
RGCS as promoting autonomy in a screening context

- **Neither clinical nor PH ethics paradigms can provide whole justification for RGCS**

- **Promote reproductive autonomy while also recognising the social context of RGCS, including:**
  - Barriers to services
  - Other social and health inequalities
  - Normative implications of the test offer
  - Collective values



Credit: Magnascan | Pixabay

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Public Health Ethics and RGCS

- **Embed PHE values into design and offer of RGCS**
- **Promote 'public health pluralism', with multiple goals**
  - Avoiding suffering
  - Promoting health of mothers, newborns and families
  - Respecting autonomy
    - On a broad understanding, e.g. social constraints on choice
  - Reducing inequity in access to RGCS
  - Recognizing and responding to social determinants and constructions of health, including disparities

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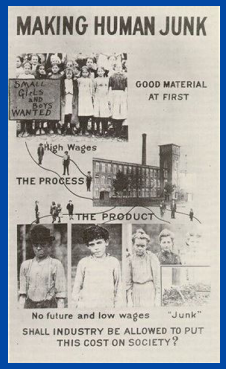
2. Eugenics



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Eugenics

- **Practices (political, social, medical) designed to use heredity to promote desirable characteristics within a population or group**
  - In the early to mid-twentieth century, a range of atrocities were committed in the name of eugenics
    - Narrow view of desirable human traits
    - Inappropriate methods, which denied bodily integrity and were racist and discriminatory
- **Much contemporary practice in medical genetics has placed great effort in distancing itself from these acts**

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Is RGCS eugenic?

- **RGCS:**
  - is a way of selecting which (future) children will be born
  - Takes place using a list of genes that are screened for (and thus 'undesirable')
- **While RGCS may not commit the same wrongs as eugenics of the past, it has been criticised as being eugenic in either intent or outcome:**

The Catholic Weekly

Home › Opinion › A mission to weed out unwanted children

News

A mission to weed out unwanted children

By **Monica Doumit** - April 28, 2021

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One response

- **RGCS is not really eugenic, because it strongly emphasises individual choice**
  - RGCS is optional
    - Individuals/ couples are supported to reflect on whether it is right for them
  - Post-result choices – different options are available

- **Is this enough?**

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RGCS does not only affect individuals

- **The response that RGCS emphasises choice is not enough**

- **Offering RGCS for certain genetic conditions → less acceptance of and accommodation for the disability and difference these conditions cause**

- **Emphasising individual choice also neglects both**
  - The collective impact of prospective parents' choices on society
  - How social norms influence prospective parents' choices

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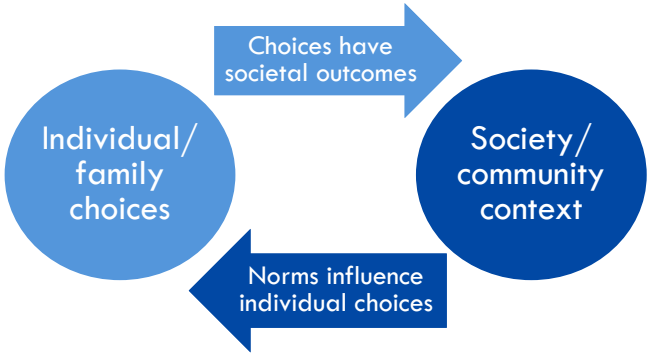
Engaging with to the eugenics critique of RGCS



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Responding seriously to the eugenics critique of RGCS

1. **Recognise the potential for reduced acceptance of disability and difference, and pay attention to how health and disability are framed in RGCS**
2. **Have a transparent, robust, revisable and representative process to identifying genes that are screened for in RGCS**
3. **(As with Public Health Pluralism) All implementation efforts must account for inequity and disadvantage**
4. **Avoid routinization through a multifaceted approach**

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3. Which genes? - Severity

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Gene selection for RGCS

- **Assembling lists of genes to screen for in RGCS often includes:**
  - Statement that conditions are **severe** or **serious**
  - 'Signal' that condition is something that a person or couple could be expected to take steps to avoid
- **A condition being 'severe' or 'serious' might be used in an attempt to separate RGCS from critiques such as eugenics and devaluing disability/difference**

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Factors associated with severity

- **Serious impairment**
  - Socio-environmental context of impairment
  - Physical / cognitive?
- **Life-limiting**
  - How limiting (life expectancy)?
  - Always life-limiting?
- **Significant suffering**
  - How to conceptualise? How to quantify?

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Existing ideas about severity

Clinical voices prioritized

Quantification prevalent, e.g. algorithms, indexes

Focus on inherent clinical sequelae rather than experiential factors or social environment

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Severity is an "essentially contested concept"

- It is appraisive / evaluative
- It is internally complex
- The concept admits of modification as circumstances change
- Modifications can't always be predicted

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Working with severity

- **Perceptions and perspective – epistemic diversity**
  - Incorporate diverse views into policy, decision-making
- **Inherent uncertainty**
  - ➢Many layers / dimensions
- **Acknowledge and respond to the complexity**
  - ➢Pay attention to the work that a determination of severity is doing, e.g. distinguish between:

classifying a condition as severe (e.g. to include on a panel);
vs understanding the impact of a condition on a person/ family for decision-making purposes

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Conclusion – Scaled up RGCS….

- **Is both a clinical offering and a public health program, so needs to draw on both clinical and public health ethics**
  - Need a nuanced public health ethics paradigm, focusing on a commitment to plural values
- **Needs to account for the eugenics critique and actively work to counter this**
- **Should screen for 'severe' conditions that reflects broad testimony and values**

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Thank you!

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Publications to date

- Dive L, Newson AJ, (2021) "Ethical Issues in Reproductive Genetic Carrier Screening," *Medical Journal of Australia* 214(4): 165–67
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