Genetic screening and the “not yet” born..

Prevention Or Perfection?

Karen Fiegen
UCT Human Genetics

SAMA 2018
“It's a history book - a narrative of the journey of our species through time. It's a shop manual, with an incredibly detailed blueprint for building every human cell. And it's a transformative textbook of medicine, with insights that will give health care providers immense new powers to treat, prevent and cure disease.”

Francis Collins
Genetic screening in and for pregnancy

Screening is a **public health service** in which members of a **defined population**, who do not necessarily perceive they are at risk of, or are already affected by a disease or its complications, are asked a question or offered a test, to identify those individuals who are **more likely to be helped than harmed** by further tests or treatment to reduce the risk of a disease or its complications..

(UK National Screening Committee http://www.nsc.nhs.uk)

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**Who?**

“**reproduction**”

*peak in both social and genetic concerns for parents and medical care providers*

**When?**

**When?**

**What?**

*the most neglected genomic screening tool...*
Carrier screening

Risk stratification based on ancestry
(ethnicity.....race...??)
ACOG recommend that **ALL** pregnant women be offered carrier screening.
Genetic screening in pregnancy

Screening for **Down syndrome** / Edward syndrome / Patau syndrome “aneuploidy” ~ 1 in 3-400 conceptions

<table>
<thead>
<tr>
<th>Method</th>
<th>Gestation</th>
<th>Detection rate</th>
<th>False pos rate</th>
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<tbody>
<tr>
<td>Maternal age</td>
<td>Any (16-20 wk)</td>
<td>35-50%</td>
<td></td>
</tr>
<tr>
<td>2\textsuperscript{nd} trimester triple test</td>
<td>16-20 wk</td>
<td>60%</td>
<td>5%</td>
</tr>
<tr>
<td>1\textsuperscript{st} trimester combined test (NT scan, PAPP-A, B-HCG)</td>
<td>11-14 wk</td>
<td>90-95%</td>
<td>5%</td>
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</tbody>
</table>
Non Invasive Prenatal “testing”

Aneuploidy screen

including sex chromosomes (OPTIONAL)
And more?

**Noninvasive whole-genome sequencing of a human fetus.**

“the rapid uptake of cell-free DNA screening indicates that noninvasive exome or genome sequencing will be _highly desired_ by women....the question is not _whether_ prenatal _noninvasive genome sequencing_ should be performed, but how to optimally implement it...”

Genomic Medicine for Reproductive, Prenatal and Neonatal Health
April 2018: NHGRI / NICHD
Prenatal diagnosis
“SPECIFIC”

Screen “positive”

**Known** genetic disorder

Possible genetic disorder

**Potential Benefits**

TOP (legal)

“Preparing” for this baby
  psychosocial
  medical

Preparing for the future
  extended family too

Amniocentesis
Preimplantation genetics

**PGS**creening
aneuploidy ...+?

**PGD**iagnosis
known genetic abnormality

**Preimplantation genetic “engineering”**

Mitochondrial genetic disorders

*3 parents*

- ovum donor (mt DNA)
- mom and dad – nuclear DNA

IVF

→ embryo biopsy

→ genetic testing

HOW THE EMBRYOS ARE MADE
Variant interpretation:

3 outcomes:

- **Found a problem** *(pathogenic variant)*
- **Found no problem** *(benign or no variant)*
- **Found a “no idea if a problem or not”** *(variant of uncertain significance)*
Ethical considerations

Please understand that Company Policy is that the results of the Pink or Blue® test are aimed at being used for curiosity, bonding and preparation for the new born baby. The results are not to be used for the purpose of gender selection.

Sex selection?

The “new” eugenics?

Lawsuit: Ohio’s Down syndrome abortion ban violates women's right to privacy
Genomic testing beyond health

The results describe their personal odds to have a destiny certain trait, but do not reflect a deterministic.

http://www.easydna.co.za/childrens-dna-discovery-test/
Some more ethical considerations

Informed consent
Autonomy
Confidentiality
Emotional distress
**Misinformation**
False reassurance
Discrimination
Genomic sovereignty
Commercialisation
Equity
**Genetic determinism**
The advances of genomic medicine are impacting prenatal diagnosis, just like any other medical field... offer exciting new opportunities and can empower families with increased knowledge about their reproductive risks and with decision-making autonomy, ......an evidence-based and ethically responsible manner ......many of these innovations are driven by for-profit companies, professional societies will play an increasingly important role in providing objective guidance to patients and providers. 

So what to do in this “brave new world”? 

**Just care.**

“watchful or protective attention, caution, concern, prudence, or regard”


**Principles to follow:**

*Nothing “magical” about genetic disorders*

Ask the right questions

Asses your patient in their “whole” context

Do your homework (your patient will do theirs!)

Provide information in understandable language (not medical jargon)

Be honest

Partner with parents

AND Listen

AND HEAR..