

# Medical Genetics, Law and Ethics

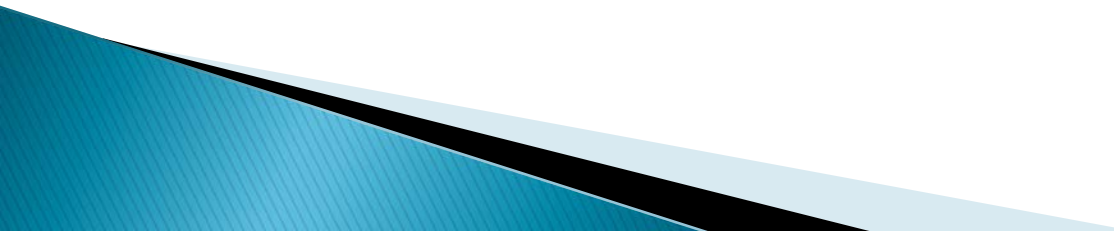
Genetic Conditions and the Family



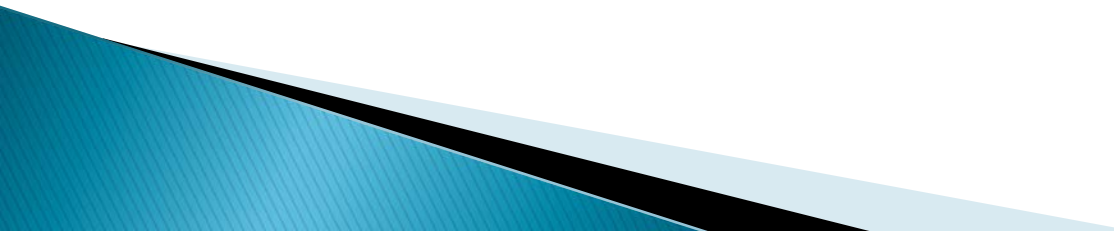
# The patient is embedded in a family...



# What are some of the issues?

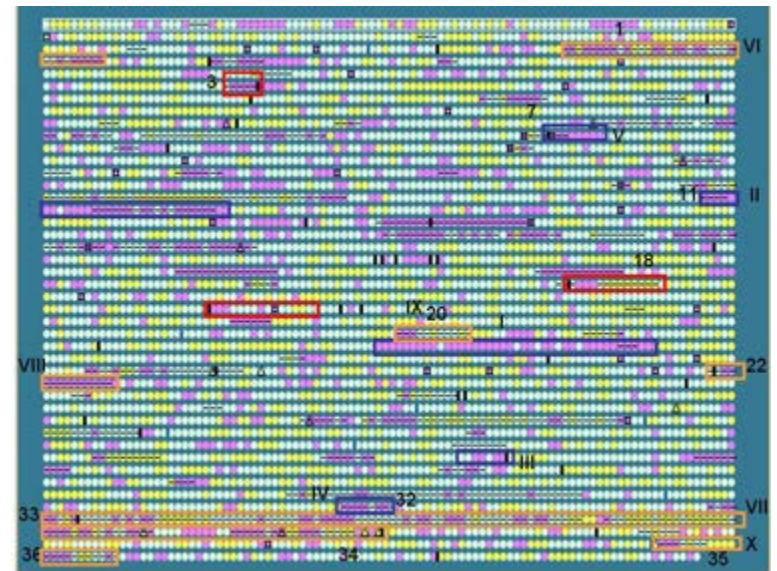
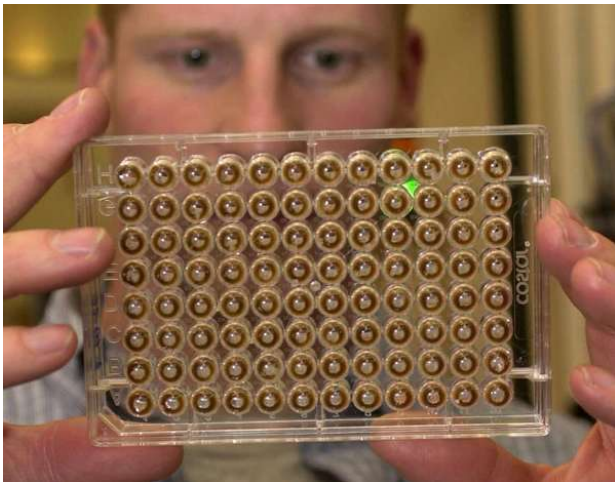
- ▶ Who is your patient?
  - ▶ Future responsibilities – for how long and to whom?
  - ▶ Are there limits to what must be interpreted?
  - ▶ What is known about the findings?
  - ▶ Should data be stored?
  - ▶ What about genetic testing and children?
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# Case scenario #1

- ▶ Many laboratories are now switching from testing individual genes for mutations to preparing “gene panels” or even whole genome sequencing. This means that there may be information regarding mutations (and therefore increased lifetime cancer risks) involving more than one gene.
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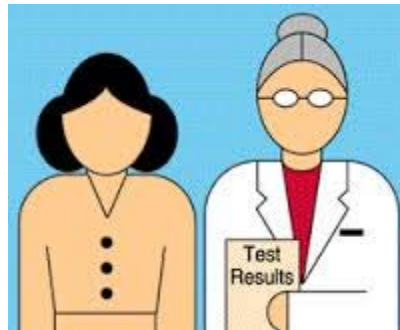
# 14 gene panel

- ▶ A combination of genes for hereditary breast/ovarian, colon cancer and polyposis syndromes

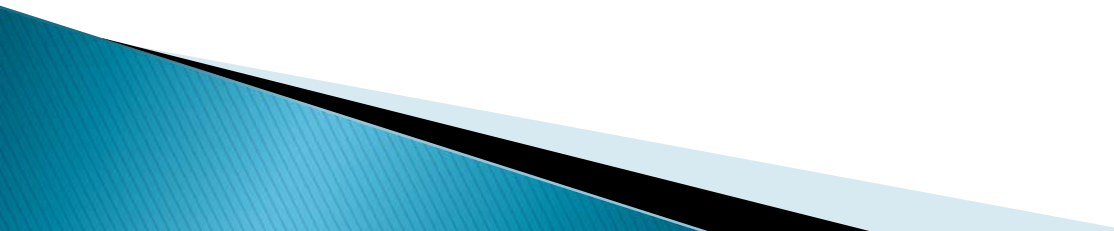


# Case scenario #1 (cont.)

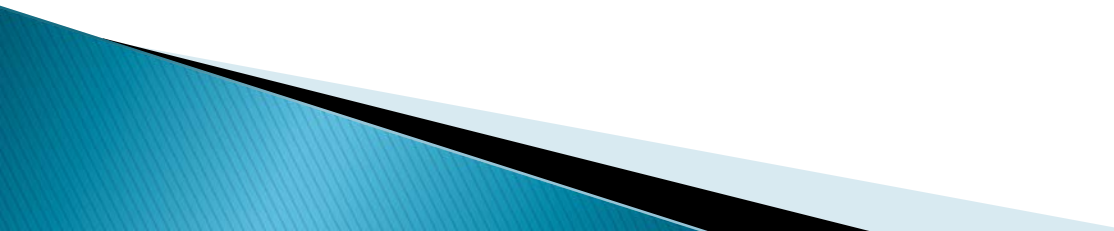
- ▶ Clinics are needing to prepare for both possible expected and unexpected results. Should all results be divulged? Should results be tailored to only the specific indication bringing the family in?



# issues

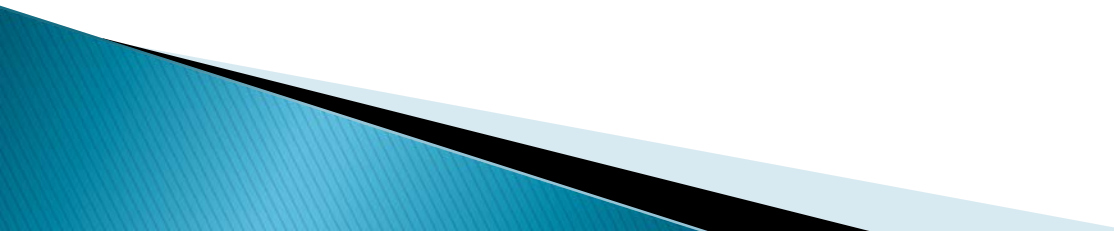
- ▶ Autonomy – could a patient choose to have directed testing only?
  - ▶ What about parents receiving results of adult onset conditions for their children?
  - ▶ Pre-test counselling will be crucial
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# Personal Oncogenomics

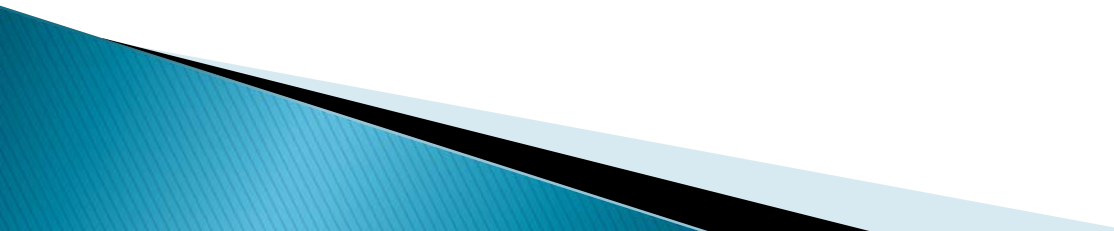
- ▶ goal is to stratify a tumour with molecular profiling to offer individualized treatment
  - ▶ research also helps in understanding the biologic pathways perturbed in a cancer
  - ▶ genome sequencing \$30,000 per patient
  - ▶ team of basic researchers, oncologists and bioinformatics group; ethics panel
  - ▶ participants have metastatic disease
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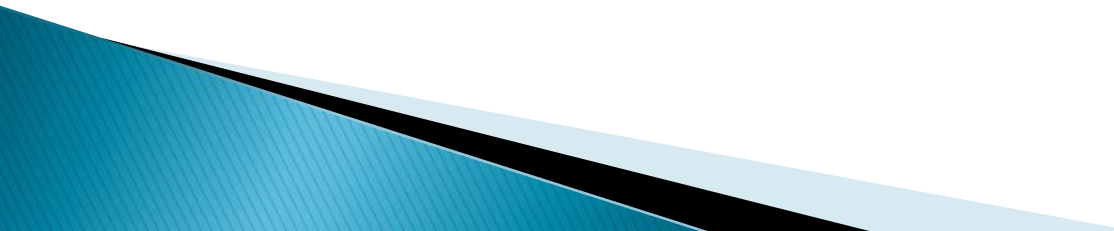
# results

- ▶ mutations in a number of oncogenes (in the tumour) – individual research results (IRR)
  - ▶ VOUS – reviewed in a separate rounds
  - ▶ possible germline mutations
  - ▶ what else? – 14 gene panel genes
  - ▶ a further 56 genes recommended by American College of Medical Genetics for clinical testing
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# Consenting process

- ▶ taking 60 to 90 minutes
  - ▶ does participant want results:
    - somatic variants with clinical significance
    - possible germline mutations
    - mutations in the additional genes (incidental findings – IF)
  - ▶ should raw data be given out?
  - ▶ use of banked data
  - ▶ how long does analysis last?
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# Incidental findings

- ▶ information unrelated to the aim of a study
  - ▶ there is an emerging legal obligation to disclose significant findings
  - ▶ Issues:
    - ▶ 1. how carefully to search
    - ▶ 2. what is the threshold of significance
    - ▶ 3. for how long does the researcher have responsibility?
    - ▶ 4. are there duties to family members?
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# Is there guidance?

- ▶ **ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing (March 2013)**
- ▶ **Clinical labs to seek and report mutations for a list of genes (56)**
  - Preventative measures available
  - Pathogenic mutations might be asymptomatic
- ▶ **Children, adults but not prenatal**

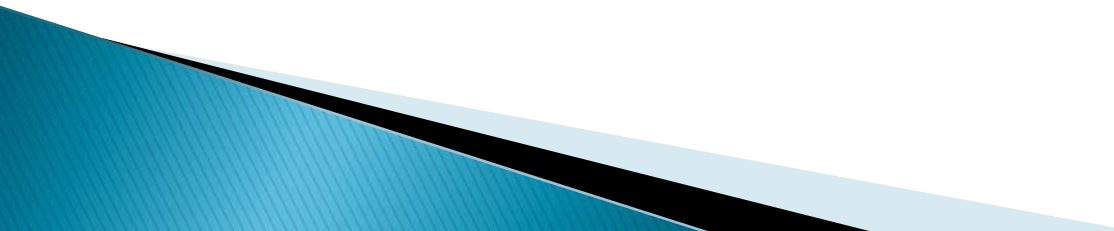
# Core Requirements of an Appropriate Plan for Managing Incidental Genomic Research Findings

1. Define the threshold for disclosure.
2. Articulate who will have responsibility for determining what information will be disclosed.
3. Outline a plan for the responsible disclosure of information, including the involvement of professionals with relevant expertise.
4. Address logistics and cost to researchers of a plan for managing incidental findings.

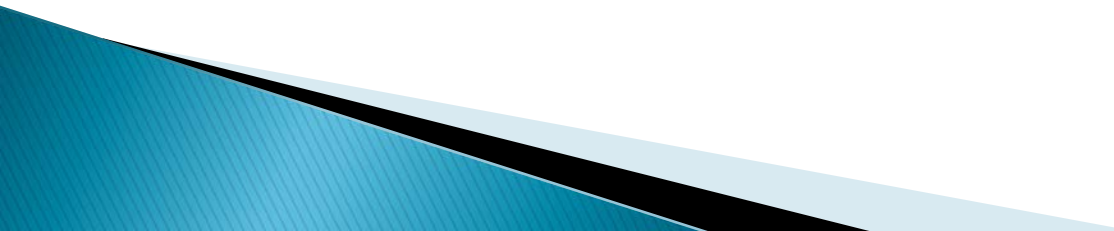
Ruqayyah A-K et al Disclosure of Incidental Findings From Next-Generation Sequencing in Pediatric Genomic Research

*Pediatrics* 2013;131;564

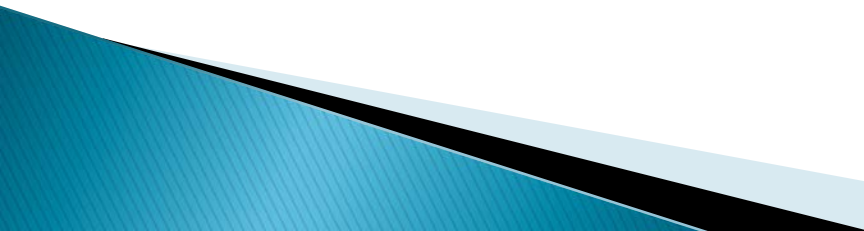
# Case scenario #2

- ▶ Prenatal diagnosis is not an acceptable option for all couples at risk to have offspring with serious genetic disorders. For these couples, pre-implantation genetic diagnosis may be preferable. Early embryos, comprised of a small number of cells, can safely have a cell or supporting cells removed for genetic testing. Those embryos free of the family mutation can then be implanted.
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# Case scenario #2 (cont)

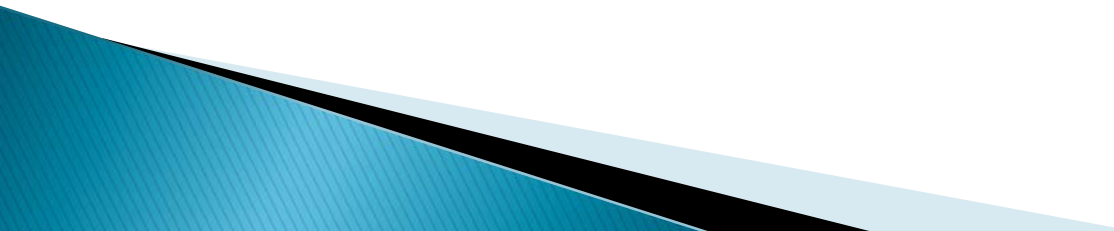
- ▶ Should this type of testing be available for adult onset disorders (for example, Huntington Disease) or be restricted to serious childhood onset disorders?
  - ▶ What about progressing to “more complete testing”?
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# What might be the issues?

- ▶ Woman's right to reproductive decisions vs right to life of unborn child
  - ▶ Rights of disabled against the promotion of public health
  - ▶ How serious is the disorder?
    - Offit et al – age of onset, penetrance of disorder, severity and risks, availability of interventions or cures
  - ▶ Number of affected in the family
  - ▶ Emotional impact of potential mother; suffering of future child
  - ▶ Moral difference between future young child and future adult?
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# Other issues?

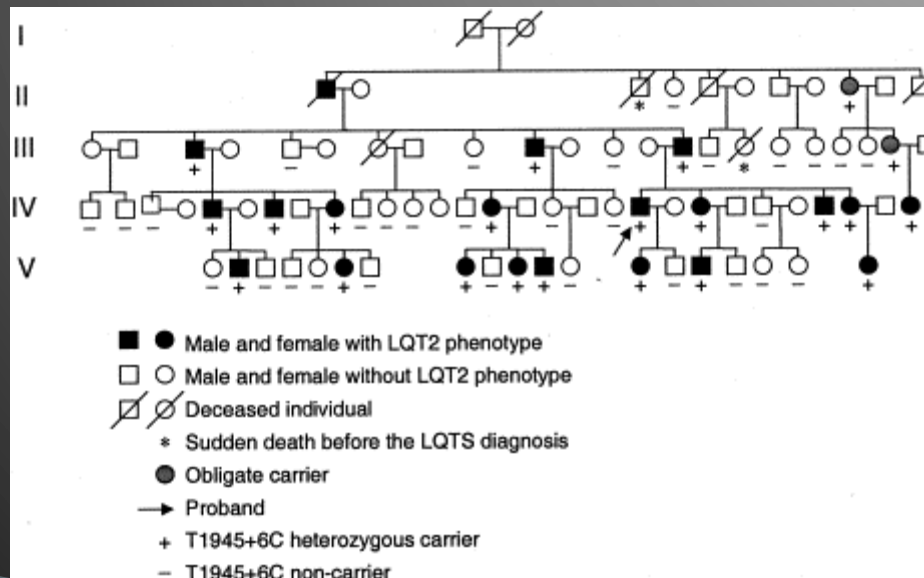
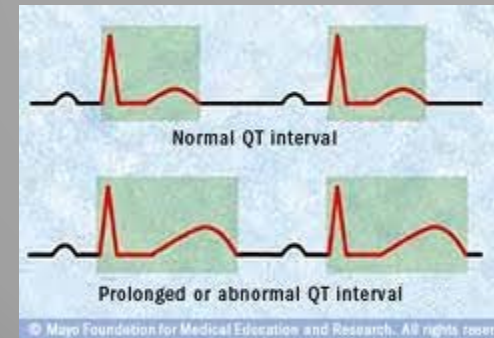
- ▶ If choose to continue an affected pregnancy – the diagnosis of an adult disorder is made in a child
  - ▶ Costs \$2500 to 7000 per cycle
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# Case scenario #3

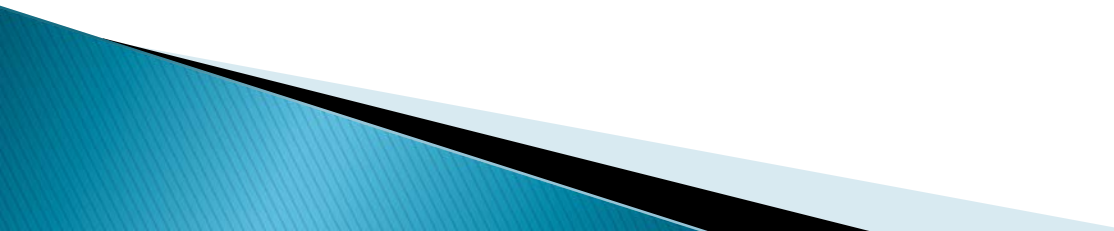
- ▶ A young man drops on the soccer field, is found to be in cardiac arrest, and is safely resuscitated. After seeing a cardiologist, the young man is identified to have a hereditary arrhythmia syndrome, Long QT, and the causative mutation is identified. Dad has the mutation as well. Both are treated with an implantable pacemaker.
- ▶ The geneticist discusses the importance of dad letting his extended family know of these results. Dad refuses, as he feels this is a private matter.
- ▶ In this situation, does the geneticist have a responsibility to the extended family?

# What is long QT?

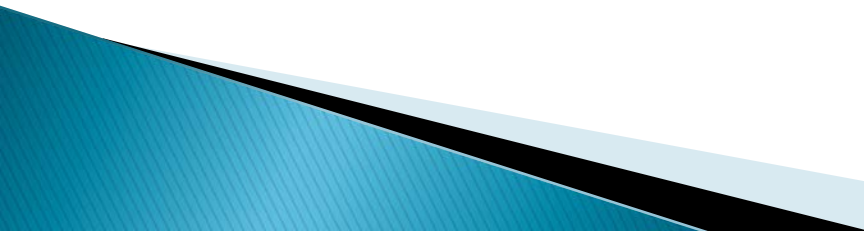
- ▶ Fainting
- ▶ Seizures
- ▶ Sudden death



National Heart, Lung, and Blood Institute states that “genetic research results should be offered to study participants if the finding is actionable with important health implications, the test is analytically valid, and the participant has consented to receive this information”



# Genetic research and children

- ▶ may be involved as part of a family study
  - ▶ may be a long term outcomes study
  - ▶ important to consider the increasing maturity of the child – parental consent → assent → consent
  - ▶ may need to build “consent to continue” into such studies
  - ▶ incidental findings in children – how to handle?
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# approaches

- ▶ What principles are in conflict?
  - ▶ Do you have all the facts?
  - ▶ Is there direction or are there developing standards?
  - ▶ What assistance might there be from the law?
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