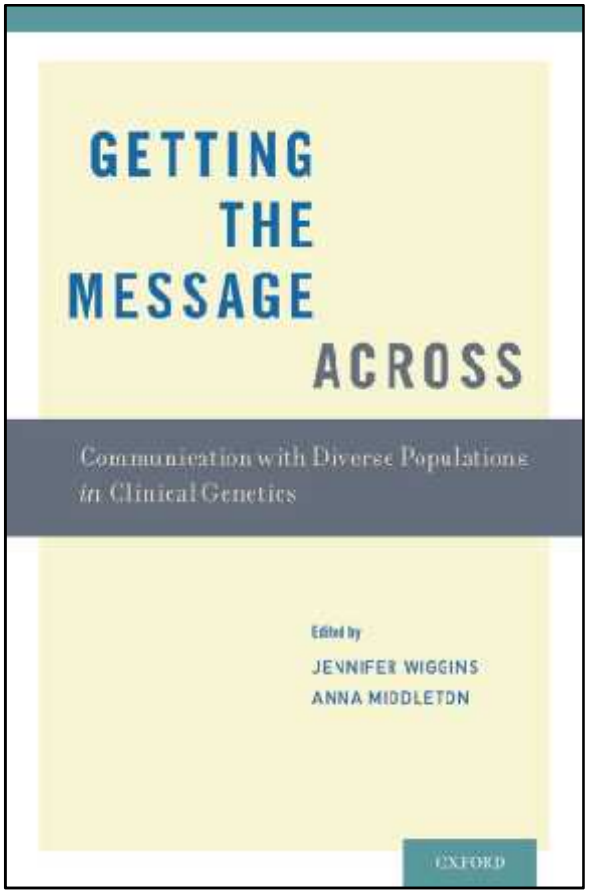
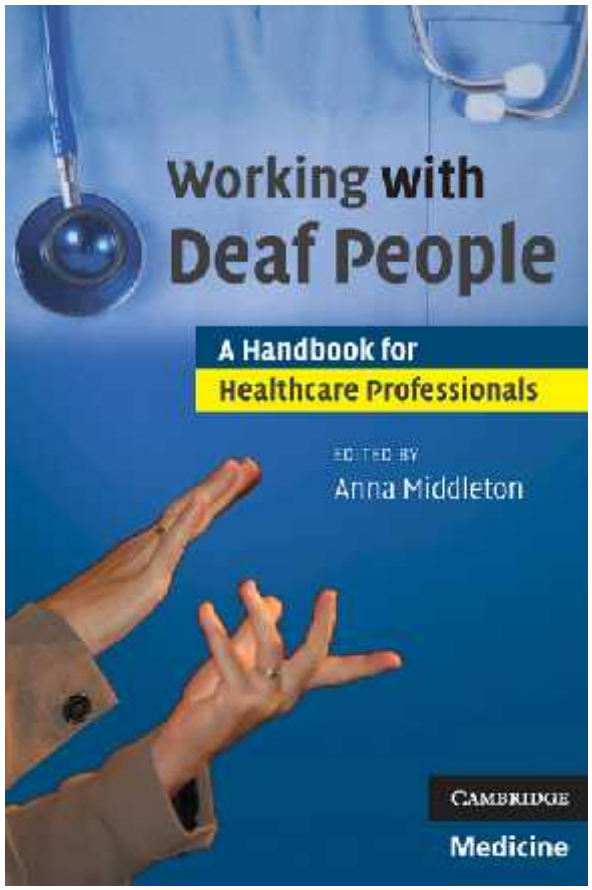
What is genetic counselling?

Dr Anna Middleton
Principal Social Scientist
Genetic Counsellor
Cambridge, United Kingdom

Association of Genetic Nurses and Counsellors

Vice-Chair Association Genetic Nurses and Counsellors



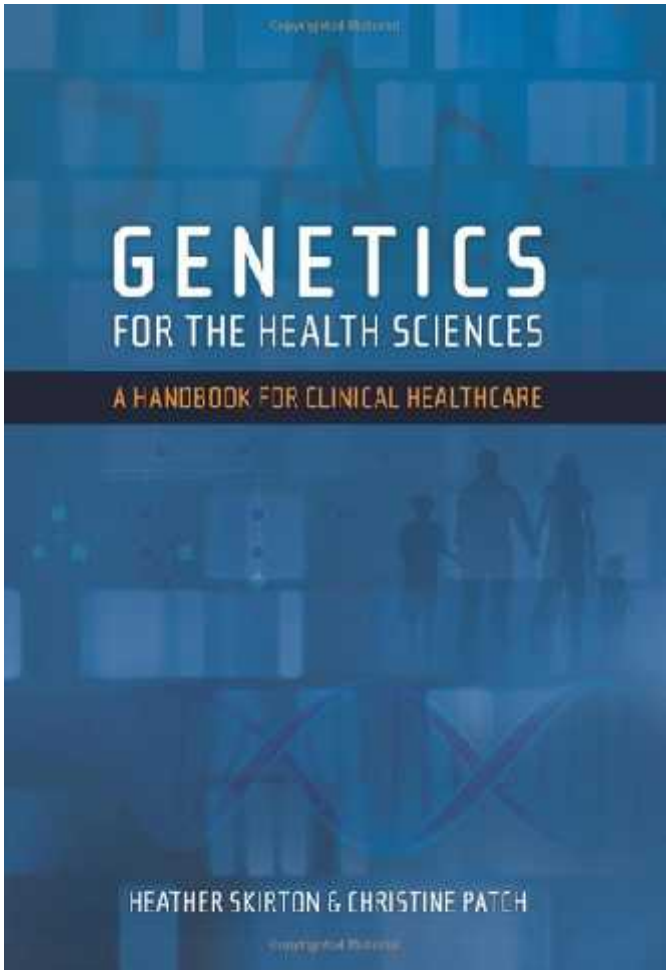


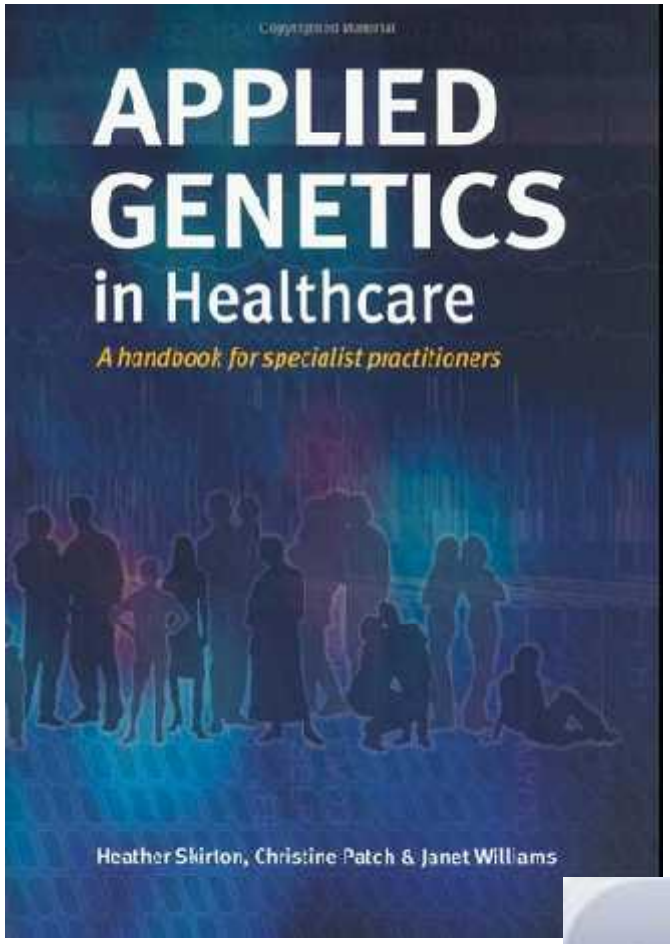
www.annamiddleton.info

@genomethics

www.genomethicsblog.org

wellcome trust sanger institute



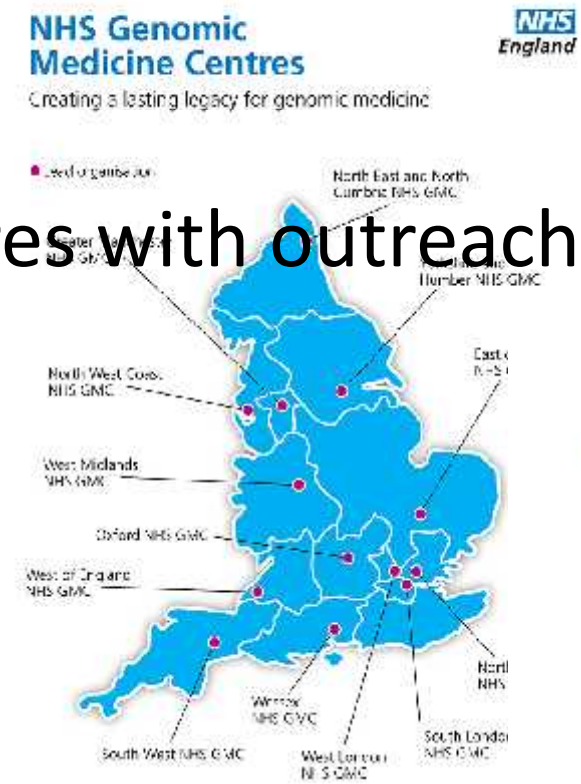


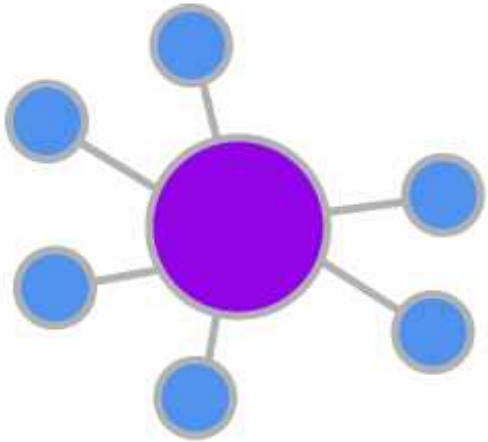
KING'S College LONDON

NHS
Guy's and
St Thomas'

Genetic counselling

- In the UK it is done in Regional Clinical Genetics services and Genomic Medicine Centres
- Specialist centres with outreach clinics
- Team of staff





The team

See patients

- Clinical Geneticists (doctors)
- Genetic Counsellors

  (nurse or MSc Genetic Counselling)
- [Research nurses, clinical nurse specialists,
- psychologists, social workers]

Don't see patients

- Lab staff (arrays/sequencing/other)
- Research teams

Train to be a Genetic Counsellor

- MSc Genetic/genomic counselling or nursing route (i.e. not via a laboratory training)
- Registration (ensures competency and standards across profession)
- Recognised profession internationally

ASGC
Australasian Society of Genetic Counsellors

National Society of Genetic Counselors

GC SA
GENETIC COUNSELLORS SOUTH AFRICA

GCRB
Genetic Counsellor Registration Board

Genetic counsellors see whole families

- Starts with the ‘proband’
- Information is shared in the family
- Relatives may then be seen
- Separate hospital notes

Reasons for genetic counselling

My mum had ovarian cancer at a young age, am I at risk?

I've had an abnormality picked up on pregnancy scan, the obstetrician thinks the baby has something genetic, please do testing

I've got a family history of Duchenne Muscular Dystrophy, am I at risk of having an affected child?

Aims of Genetic Counselling

Information

Support, empathy

Aims of Genetic Counselling

- Provide information about a genetic condition
- Explain how the condition is inherited and the chance of it occurring
- Provide testing to clarify risk
- Understand the options available for management

Aims of Genetic Counselling

- Make decisions appropriate to personal and family situation
- Make the best possible adjustment to the disorder or risk
- Place factual genetic information into the family context
- Integrate lay knowledge with factual information

Genetic Counselling Consultation

- Find out the **patient**'s reason for referral

- Draw pedigree
- Assess genetic risk
- Explain inheritance patterns

When drawing the pedigree…

- Listen, pick up cues especially when taking family history
- Can be intrusive process
- Visual impact of pedigree
- Surprises, e.g. TOP, adoption, non-paternity
- Grief and loss

Working out who is at risk….

- Use pedigree to work out pattern of inheritance
- Work out risks of inheriting family condition (e.g. 50/50 chance of passing on or 1 in 4 chance of passing on)
- If passed on, work out risks of disease (‘penetrance’ and ‘expression’)

Mutations in genes don't always equal disease

- Deletion in Duchenne Muscular Dystryophy = disease
- Deletion in breast and ovarian cancer gene = increased risk of disease
- Deletion in CCR5 gene = resistance to HIV
- Deletions can just be polymorphisms

Genetic Testing

- Discussion about practical and psychological implications of test result

- Diagnostic testing (adult, child, foetus, embryo)
- Predictive/presymptomatic testing
- Carrier testing

Genetic Screening

- Different to ‘genetic testing’
- Testing across a population group
- Testing of ‘healthy’ person to try to predict disease
- E.g newborn screening
- Prior probability of disease low
- Opportunistic screening with sequencing

Genetic Counselling is not Therapeutic counselling

- Considers the ‘patient’ and the extended family
- Often only seen once
- Focus is around the condition, not broader, e.g. not relationship counselling
- Advice not given but plenty of information
- May be referred on for therapeutic couns

Summary

- Given overview of genetic counselling
- Role play a genetic counselling session
- Explore how genomic technology has impacted on practice
- End with some case studies

The work of a genetic counsellor in the UK

Christine Patch PhD RN Registered Genetic Counsellor

Consultant Genetic Counsellor

Guys & St Thomas' NHS Foundation Trust London

Reader

Florence Nightingale Faculty of Nursing and Midwifery KCL London

Guy's 1988

- 2 clinical GCs (both nurses)
- 1 research nurse (DMD/BMD)
- 1 Consultant, 1 Clinical SpR, 2 Research SpRs
- Majority of GC work : prenatal RMA
- Few single gene tests possible (no CF, no HD)
- Co-counselling with geneticists
- Teaching of health professionals
- Bereavement work (much post-TOP)

Guy's 2015

- 3 Consultant genetic counsellors (all RN and registered GC)
- 3 senior GC (all reg GC 1 RN)
- 7 Genetic counsellors (6 reg GC 1 RN)
- 1 cardiac genetics nurse (employed by cardiology)
- 2 Cancer risk assessment nurse
- 2 Research nurses-recruitment to and managing of multicentre studies
- 12 Consultant, 2 Clinical SpR

- GC work : 48% of appointments, predictive testing, multidisciplinary clinics, prenatal clinics, PGD.
- 60% of workload high risk cancer family history
- Teaching of health professionals

- No routine prenatal screening counselling, no post TOP beeavement, little co-counselling

Episode of care in a health setting

- Referral to Genetics team
- Patient seen by appropriate person(s) in team, according to diagnosis and issues
- May require collection of information prior to appointment
- Summary letters
- Follow up as required

What types of patients are seen by genetic counsellors

- Any who do not need a medical diagnosis
  - Predictive/presymptomatic testing-where gene mutation known
  - Cancer risk assessment and testing
  - Reproductive choice-prenatal/PGD
  - Explain genetic test results

New roles

- Multidisciplinary/specialist clinics e.g rare diseases, eye genetics etc
  - Genetic counselling
  - Management
- Clinical Nurse Specialists
  - Eg Cardiac genetic nurses

Role of genetic services

- Diagnosis
- Risk assessment
- Options
- Decision-making
- Adjustment to status

(ASHG, 1975; Harper, 2004; HGSA (1999) Guidelines for the Practice of Genetic Counselling)

What is patient's agenda

knowledge of condition's natural history
is testing available? for pregnancy? to check baby?
risks – to self and relatives (e.g. their grown up children)
management
support for family's situation

Clinicians agenda

enable patient to make informed decision
no recommendations/decision making for patient
Give accurate information
appropriate information
layman's language

support patient in their choices (non-judgemental)
alert other health carers to patients decision,
risks and management issues

What actually happens:

- Introduce self
- Summarise referral letter
- Check patients view of the situation and what they hope to gain from the session..**were they sent?**
- Explain what you, the counsellor, can offer
- Agree on a plan

What actually happens:

- **Listen**, pick up cues especially when taking family history
- **Confidentiality** –(as far as possible, discuss family communication and the need of proband to share information)
- Translate complex genetic information into lay language
- Pace the information delivery appropriately
- Common themes:
  - burden of the genetic condition/risk of it happening again
  - Guilt/blame
- Consider previous loss (loss through death, loss of self esteem, loss of control, previous abandonment and abuse) - can be reactivated through process
- Meet the **patients' needs** as well as following own agenda

What actually happens:

- Summarise and repeat key points such as risk figures and inheritance
- Allow silences, tears, talk about deceased family members
- Provide contact number
- Write to summarise details

‘Non directive counselling’

- Term derived from Carl Rogers in his writing about client centered therapy
- Aims to enable person/couple make a decision that is right for them. Particularly in pregnancy or in predictive testing for known gene mutations
- This assumes there is a choice and no pressure from public health policies

Supervision

- Technical term for counselling engagement with others
- Group or individual supervision is recommended
- Helps to be aware of own issues so that you recognise why a consultation was challenging

Genetic Alliance UK
Supporting. Campaigning. Uniting.

Find us on Facebook · twitter · home · sitemap · contact · scotland · wales

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about us • membership & support • policy & campaigns • projects • news & events • information centre • press centre •

Talking about our project SWAN UK:
"Joining SWAN UK has made a massive difference to my life. I have some great friends and always know where to turn to if I need some help"
SWAN UK member 2012

Helping those with genetic conditions

Genetic Alliance UK is the national charity of over 150 patient organisations supporting all those affected by genetic conditions.

Our aim is to improve the lives of people affected by genetic conditions by ensuring that high quality services and information are available to all who need them.

latest news

First ever UK Strategy for Rare Diseases launched - find out more here

Looking for a new Research Associate role? We have an opportunity to join the Genetic Alliance UK team

View More **News Articles....**

Our Mission

Our mission has three main elements:

- **Supporting:**
  We seek to raise awareness of genetic conditions and improve the quality of services and information available to patients and families.

RARE DISEASE | UK

SWAN UK

Members

Anorchidism Support Group (ASG)

Anthony Nolan

- What about your services?

Genetic counselling is a communication process that deals with the occurrence, or risk of occurrence, of a (possibly) genetic disorder in the family. The process involves an attempt by appropriately trained person(s) to help the individual or the family to

(1)understand the medical facts of the disorder;

(2) appreciate how heredity contributes to the disorder and the risk of recurrence in specified relatives;

(3) understand the options for dealing with the risk of recurrence;

(4) use this genetic information in a personally meaningful way that promotes health, minimizes psychological distress and increases personal control;

(5) choose the course of action which seems appropriate to them in the view of their risk and their family goals, and act in accordance with that decision;

(6) make the best possible adjustment to the disorder in an affected family member and/or to the risk of recurrence of that disorder.

(modified from Frazer FC: Genetic counselling. Am J Hum Genet 1974:26:636-661, Biesecker and Peters:Process Studies in Genetic counseling: peering into the black box. Am J Med Genetics 2001:106:191-198, , Resta, R. G. (2006), Defining and redefining the scope and goals of genetic counseling. Am. J. Med. Genet.)
http://www.eurogentest.org/professionals/info/public/unit3/final_recommendations_genetic_counselling.xhtml

Role play

- Anna is seen in clinic to discuss family history of breast cancer

Genomics in the clinic

(Genomic counselling?)

Christine Patch PhD RN
Consultant Genetic Counsellor
Reader
Florence Nightingale Faculty of Nursing and Midwifery London

KING'S College LONDON

Guy's and St Thomas' NHS
NHS Foundation Trust

Specialist roles

- Diagnosis
- Explanation of technical issues
- Interpretation of results
- Exomes
- Genomes
- Specialist counselling skills
- ??????

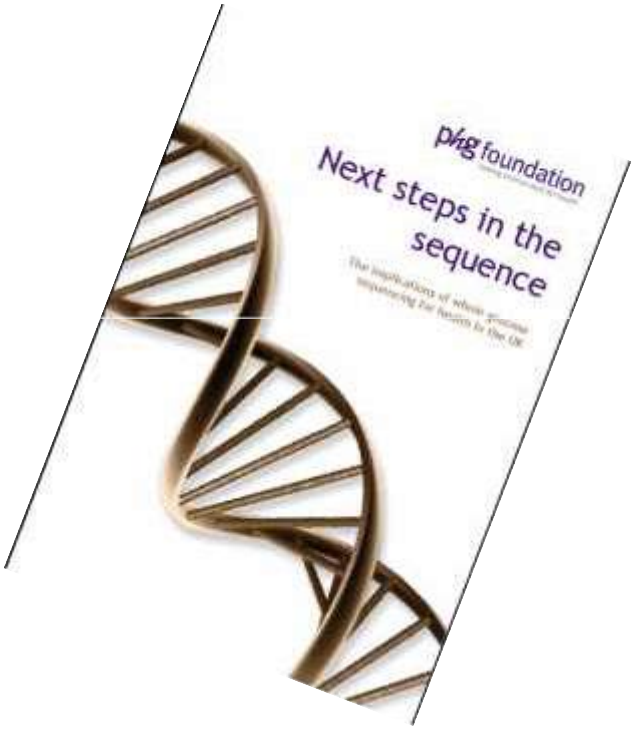
Mainstream roles

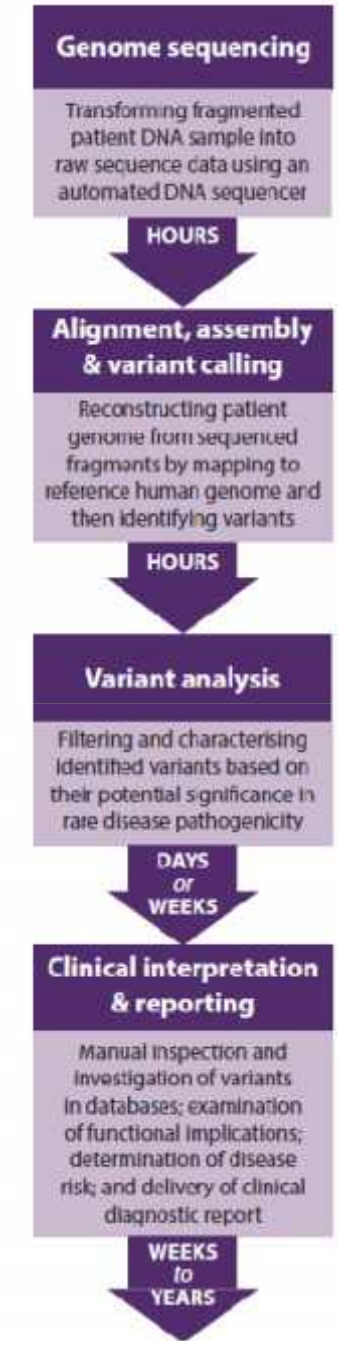
- Support
- Adaptation
- Decision-making

- Current drivers

  - Technological and scientific development
    - Sequencing technologies
    - Laboratory rationalisation
    - Changing business models
    - Managing expectations
    - Direct to consumer testing offers

  - Changes to health services
    - Training
    - Managing expectations
    - New ways of working
    - Strained financial resources



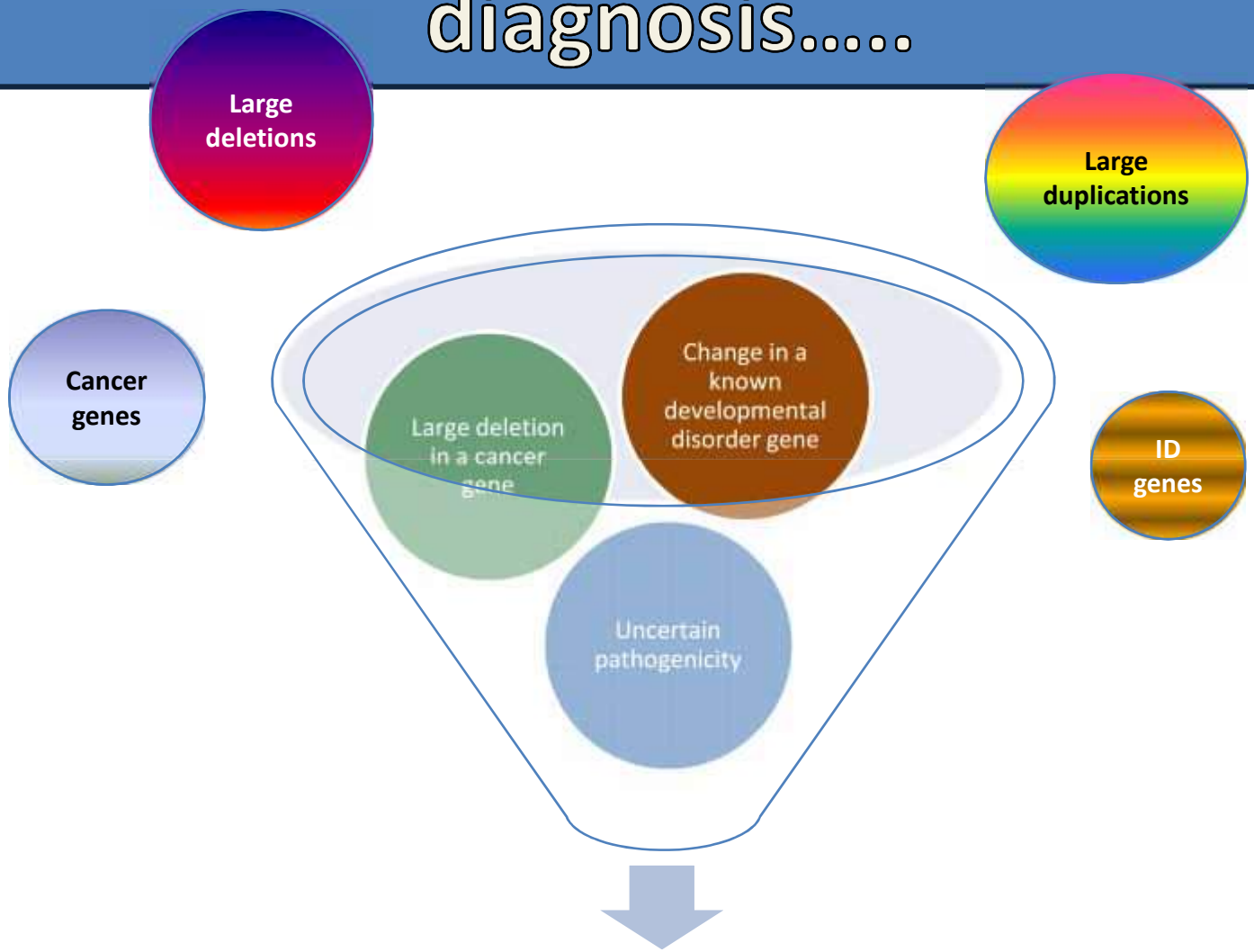


Reality of WGS

Role of genetic counsellors?

Challenges for genetic counsellors

When exploring a clinical diagnosis…..



Diagnosis

What is 100,000 genome project http://www.genomicsengland.co.uk

Genomics england

Home | About us | 100,000 Genomes Project | GeCIP | GENE Consortium | Library & resources | News

Genomics England, with the consent of participants and the support of the public, is creating a lasting legacy for patients, the NHS and the UK economy through the sequencing of 100,000 genomes: the 100,000 Genomes Project.

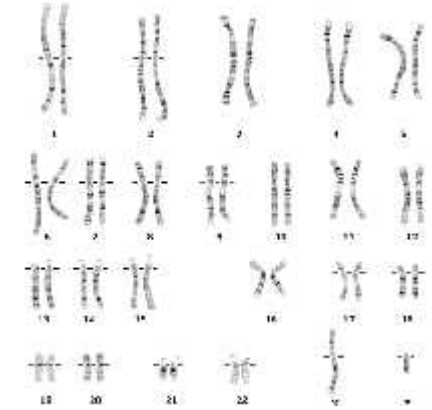
Genomics England was set up by the Department of Health to deliver the 100,000 Genomes Project. Initially the focus will be on rare disease, cancer and infectious disease.

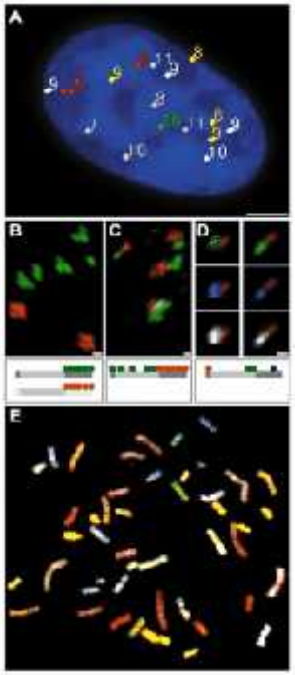
Read more...

- New technologies
  - How much (too much ?) information
  - Utility of information
- Organisation of services
  - What is role of genetic services?
  - Who should provide genetic/genomic health care
- Quality assurance
  - Technology
  - Services
  - Professional

Genetic technologies evolution

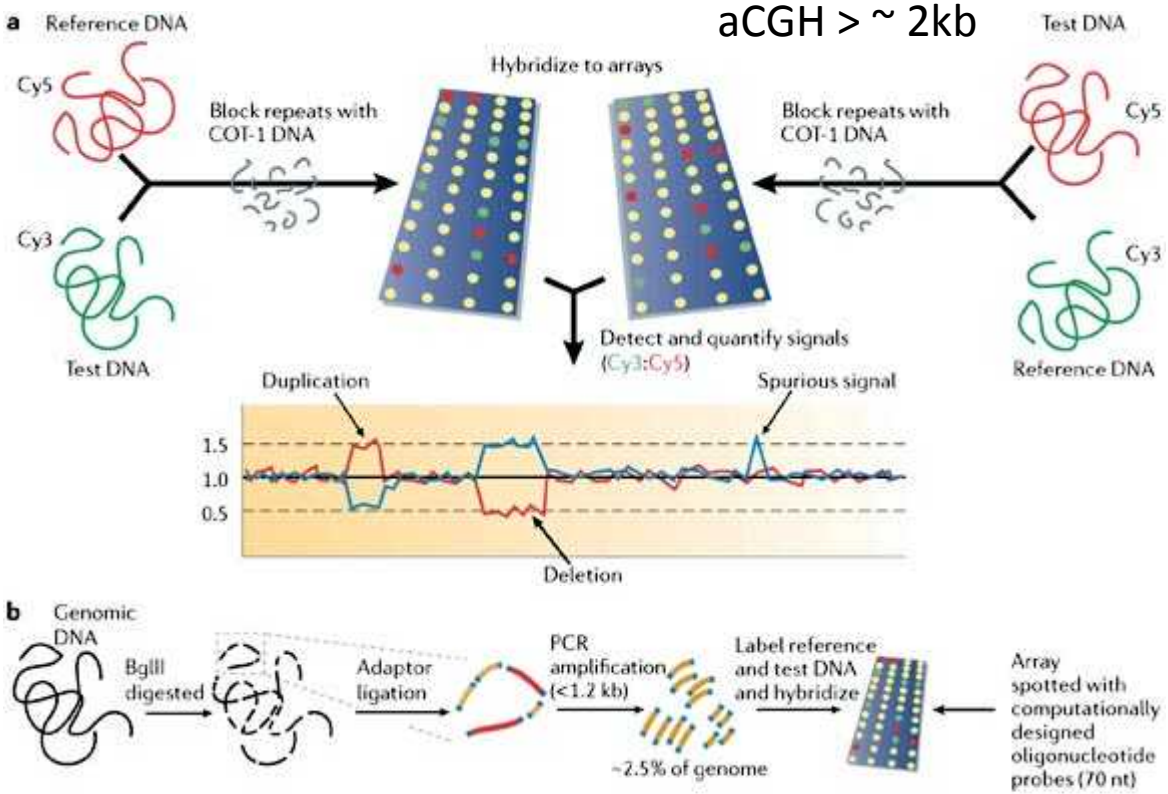
Karyotype >3-5Mb

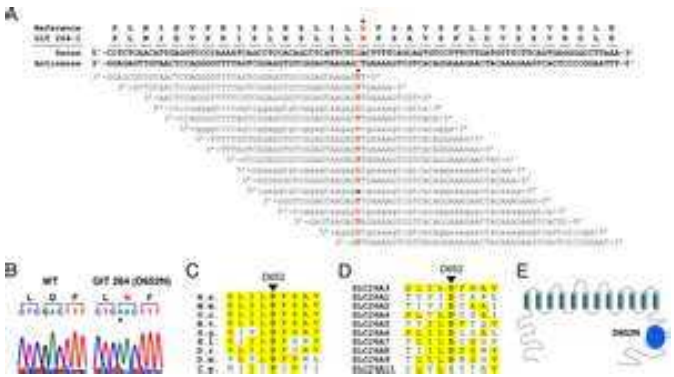




Fluorescent in situ hybridisation

aCGH > ~ 2kb





Sequencing

1bp

- UK - Arrays recommended as first line test since 2010.
- Varying technologies
- Varying algorithms for determining pathogenicity
  - NB does not detect balanced rearrangements

  - best practice guidelines
    www.cytogenetics.org.uk/prof_standards/ACC_array_bp_dec2011_2.00pdf
    American College of Medical Genetics Genetics in Medicine 2011 13 676-679, 680-685
    ISCA

CNV detection rate=25%

87% too small to be detected by G-banded chromosome analysis

33% of imbalances are definitely pathogenic

34 different established genomic disorders detected in 430 patients

Imbalance for 6 different susceptibility loci detected in 205 patients

Most common genomic disorder: 22q11.2 deletion syndrome (n=64)

Most common susceptibility locus imbalance: 16p11.2 (n=60)

Ahn et al.(2013) Array CGH as a first line diagnostic test in place of karyotyping for postnatal referrals – results for four years clinical application for over 8,700 patients

- Challenges
  - Interpretation

    - 4 year old boy learning difficulties
    - Parents mild learning difficulties

Great Maze Pond, London SE1 9RT
Tel: 020-7188-1709
Fax: 020-7188-1607

CPA Accredited Medical Laboratory
Reference No: 1993

ARRAY CGH REPORT		DNA	
NAME	[redacted]	SPECIMEN NO	[redacted]
		PRU No	
		Date Taken	
DOB		Date Rec'd	
		Hospital No	
Referring Physician	[redacted]		
Hospital			

INHERITED CHROMOSOME IMBALANCE DETECTED

arr del(3)(p26.2p26.2)(4,331,005-4,553,093)mat,dup(6)(q22.31q22.31)(123,581,324-124,208,360)mat

Follow-up report:

Array CGH analysis of DNA from [redacted] has been carried out using oligonucleotide arrays with ~44,000 probes across the genome. This test identified two regions of imbalance:

i) in the short arm of chromosome 3. The imbalance comprises approximately 222kb of material from band p26.2 and lies between 4,331,005bp and 4,553,093bp from the chromosome 3 short arm telomere.

ii) in the long arm of chromosome 6. The imbalance comprises approximately 627kb of material from band q22.31 and lies between 123,581,324bp and 124,208,360bp from the chromosome 6 short arm telomere.

The deletion, duplication and sample identity have been established using custom MLPA probes specific for loci within the regions of imbalance.

No other imbalance was detected (excluding previously published polymorphisms).

Follow-up studies on DNA from [redacted] parents [redacted] using the same custom MLPA probes, have shown that Alan's mother carries both the chromosome 3 short arm deletion and the chromosome 6 long arm duplication. These imbalances are therefore likely to be polymorphisms of no clinical significance; however any unusual features shared by Alan and his mother may be associated with either of these imbalances.

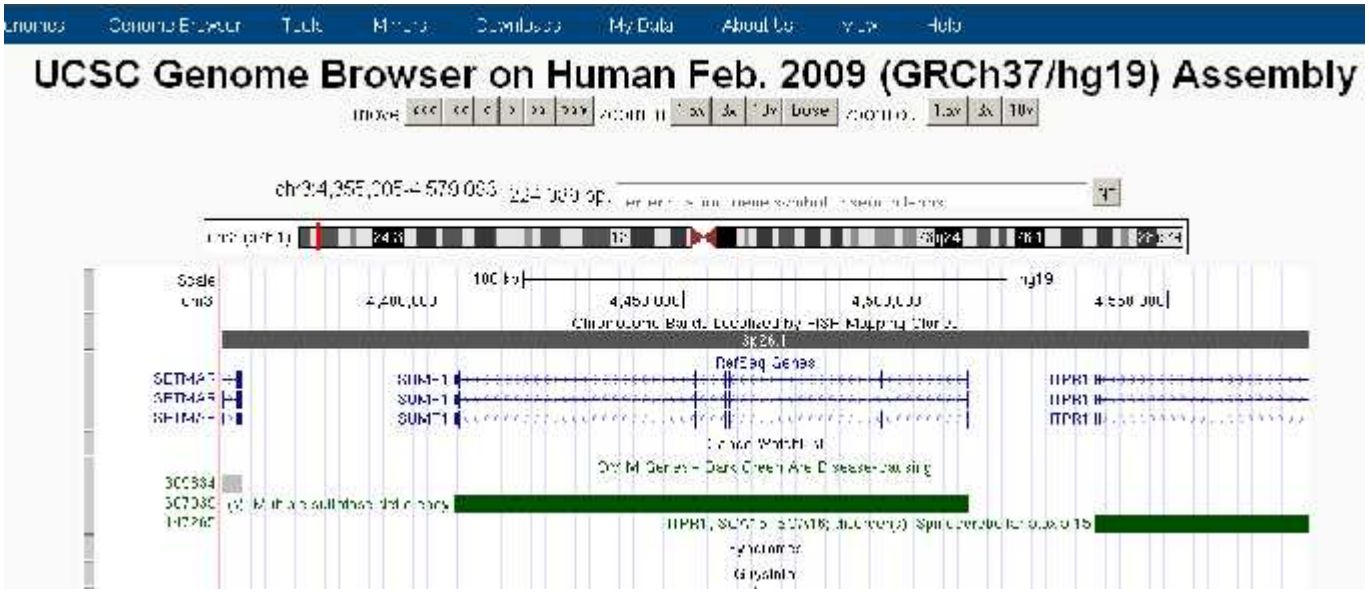
We understand that this family is attending the Genetics Clinic, Guy's Hospital.

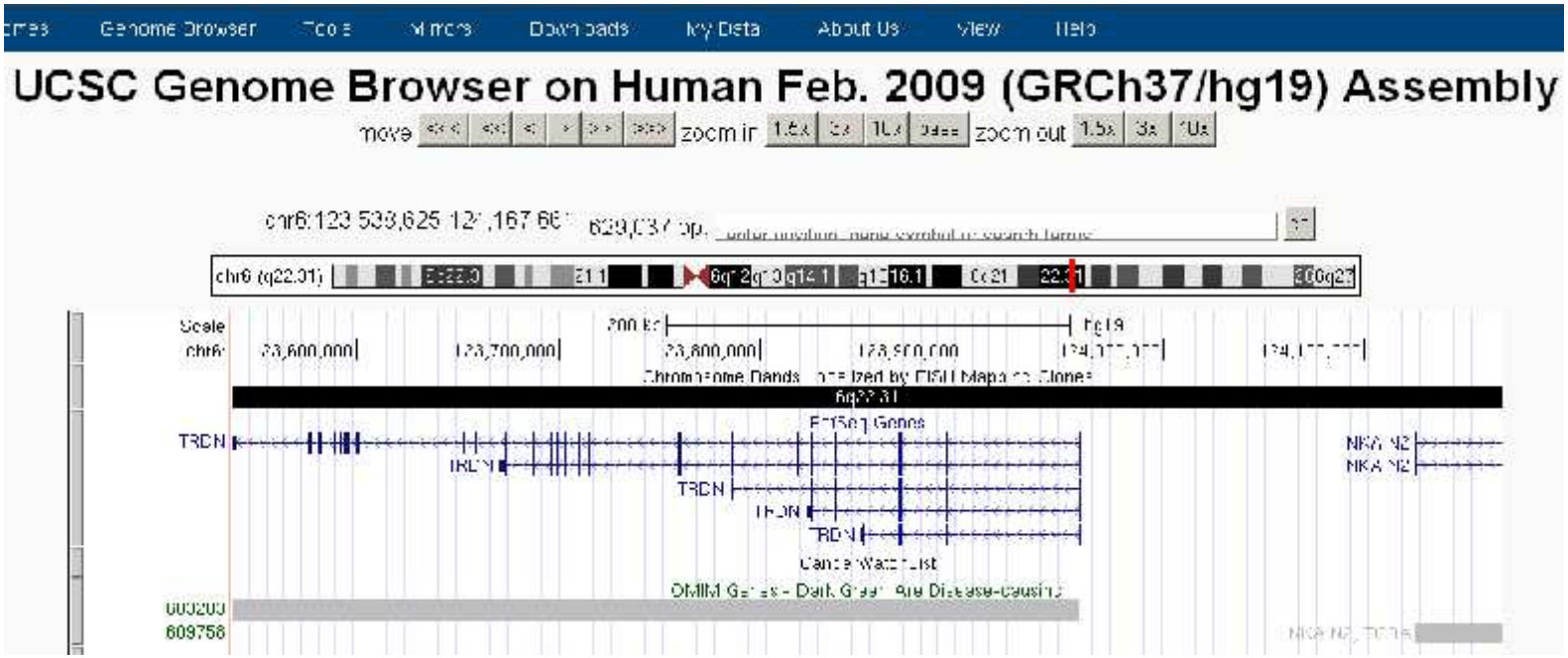
[Custom MLPA probes: 3 [redacted] 6 [redacted]]

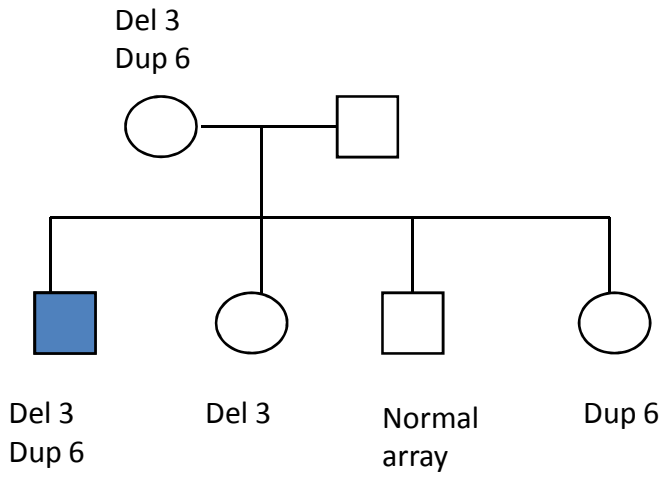
Array CGH is a technique for detecting gains and losses of genetic copy number across the genome at high resolution and is capable of detecting imbalances too small to be detected by analysis of G-banded chromosomes. This technique does not detect balanced chromosome rearrangements or point mutations such as [redacted].

Array platform: Agilent 44B ID 014951. Data analysis: Agilent DNA Analytics. Positional information: NCBI Human Genome build 36.

Analysed by :	AB	Report Date :	02/03/2009
Checked by :	CO	Page 1 of 1	Authorised by :


UCSC Genome Browser on Human Feb. 2009 (GRCh37/hg19) Assembly
RefSeq Genes
OMIM Genes - Dark Green Are Disease-causing


Genome Browser
UCSC Genome Browser on Human Feb. 2009 (GRCh37/hg19) Assembly
move
zoom in
zoom out
RefSeq Genes
TRDN
Cancer Watch List
OMIM Genes - Dark Green Are Disease-causing



Array findings probably unrelated to phenotypes in family

- Challenges
  - Variable Phenotype eg 16p 11.2 dup

ARRAY CGH REPORT **DNA**

NAME : [redacted]

DOB . [redacted] Age 5 Sex M

SPECIMEN NO [redacted]
PRU No
Date Taken
Date Rec'd
Hospital No

Referring Physician [redacted]
Hospital

INHERITED CHROMOSOME IMBALANCE DETECTED

arr 16p11.2(29,581,457-30,106,101)x3 mat

Follow-up report

Array CGH analysis of DNA from [redacted] been carried out using oligonucleotide arrays with ~44,000 probes across the genome

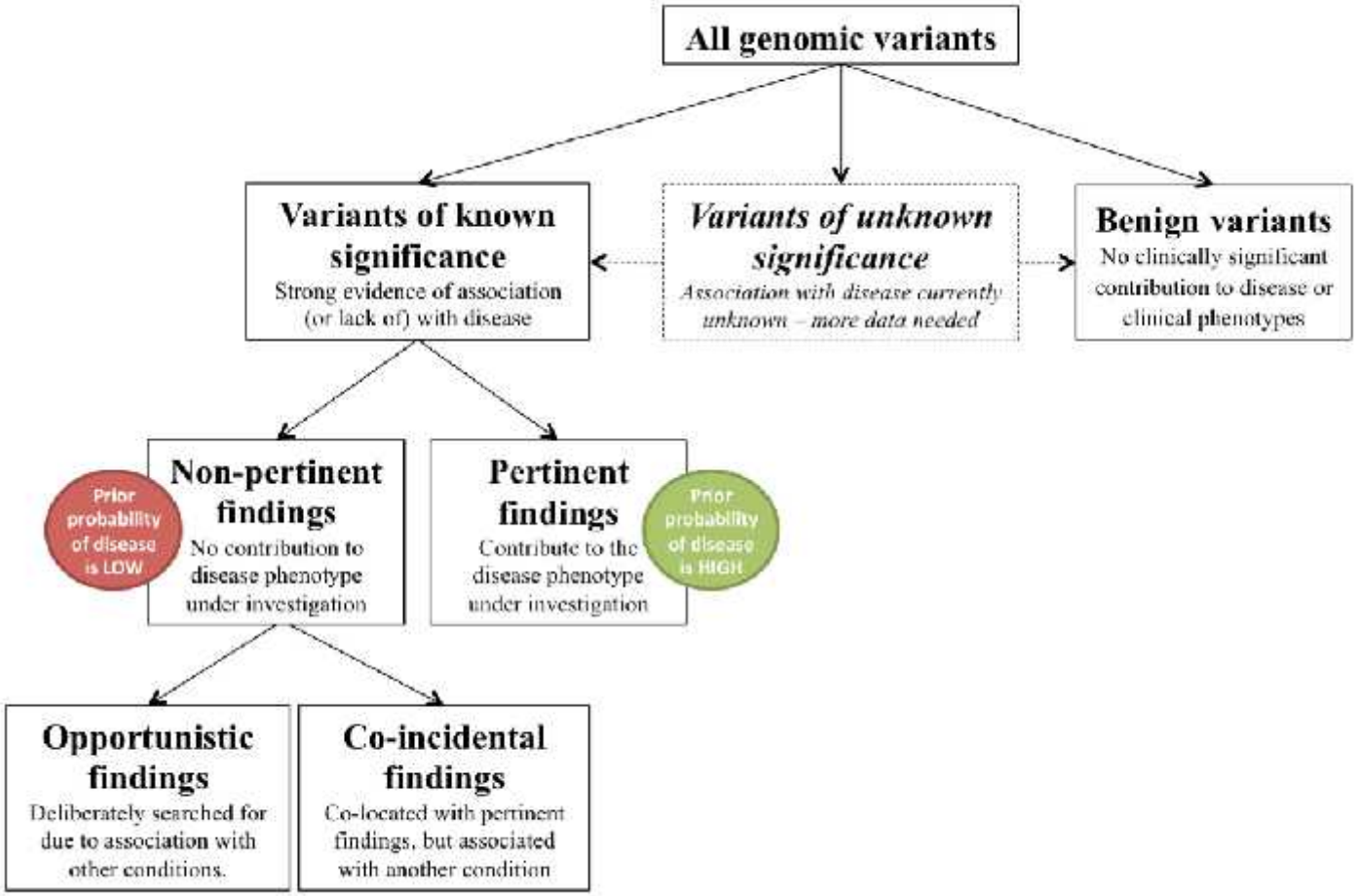
This test identified a duplication of approximately 0.525Mb of maternal from the short arm of chromosome 16 the duplicated region is from band p11.2, between base pair coordinates 29,581,457 and 30,106,101. This region represents the 16p11.2 autism susceptibility locus (OMIM %611913)

No other imbalance was detected (excluding previously published polymorphisms).

This finding has now been confirmed using an MLPA probe specific for a locus within the duplicated region. DNA from [redacted]s parents [redacted] has been tested with the same MLPA probe; the tests have shown that [redacted]s mother also carries the duplication. Variable penetrance and genetic backgrounds are likely to cause differences in phenotypic expression between carriers of this duplication. This imbalance is likely to be

‘Incidental findings’

Caroline Wright pertinent and non-pertinent findings



- Who should explain results
- Who should complete inheritance/validation/confirmation of pathogenicity studies
- New skills needed by genetic counsellor
- Close partnership working between genetic counsellor and medical consultant

Whole genome analysis

It is our view that using whole genome data in clinical diagnostic services within the NHS without first addressing these fundamental issues of diagnostic quality poses potentially unacceptable risks to patient safety, and quality of care. These risks include:

•Incorrect diagnosis (false positive or negative), leading to inappropriate patient care and decision making and threatening patient safety.

•Failure to provide a conclusive diagnosis for the patient and a continuation of their diagnostic odyssey.

•Inappropriate use of NHS resources.

- New Technologies
  - Impact on knowledge base of genetic counsellors/nurses
- Increasing impact of genomics to health
  - New ways of working, networking and multidisciplinary teams
- Strained financial resources
  - Constant evaluation of practice and services
  - Evidence of value

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http://www.eurogentest.org/professionals/info/public/unit3/final_recommendations_genetic_counselling.xhtml

Attitudes towards returning data to participants in sequencing research

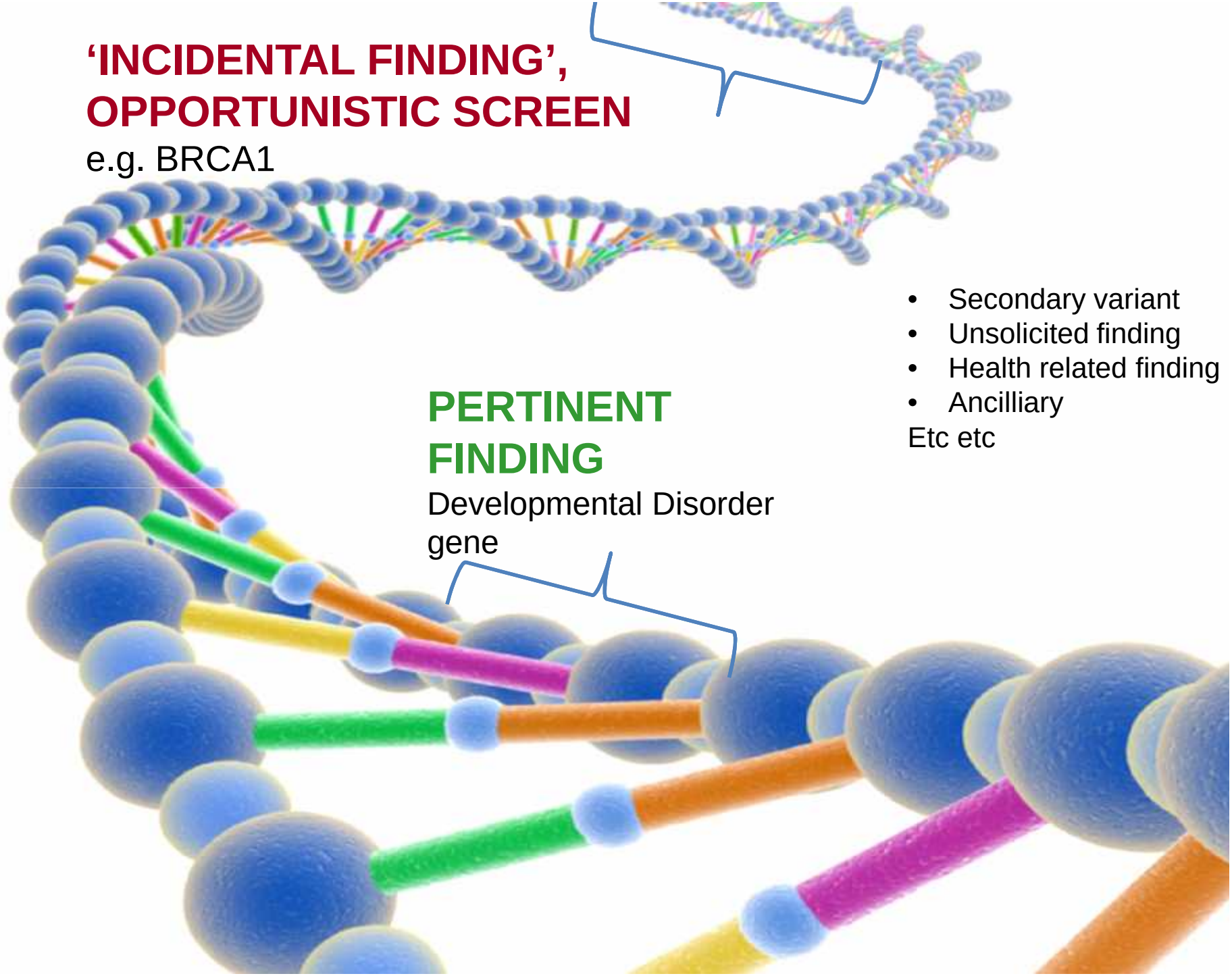
Dr Anna Middleton

Principal Social Scientist
Registered Genetic Counsellor

wellcome trust sanger institute

Sarah

- Undiagnosed developmental disorder
- Current targeted testing – no answer
- Exome sequence as part of the Deciphering Developmental Disorders (DDD) project



‘INCIDENTAL FINDING’, OPPORTUNISTIC SCREEN

e.g. BRCA1

- Secondary variant
- Unsolicited finding
- Health related finding
- Ancilliary

Etc etc

PERTINENT FINDING

Developmental Disorder gene

Objectives: to explore

Attitudes towards return of different types of genomic data

Attitudes towards the return of raw sequence data

Ethics and Genomics Survey

reset & start again

- ✔ Questions about you
- ➡ Sharing of Pertinent Findings
- Sharing of Incidental Findings
- Categorizing Incidental Findings
- Relations with Risk
- Raw data
- Duty of Genomic Researchers
- Filter of Genomic Information
- Consent for genomic research
- Last few questions about you

Sharing of Pertinent Findings

- **Should Pertinent Findings from genome studies be made available to research participants?**
  - Research participants should be able to receive pertinent findings if they want them
  - I don't think pertinent findings from research projects should be available
  - I don't know

« Previous Next »

Questionnaire designed by Dr Anna Middleton; Software developed by Eugene Bragin; Films by NeonOtter.com. www.ddduk.org, Wellcome Trust Sanger Institute, Cambridge UK

This site is hosted by the Wellcome Trust Sanger Institute.

Recruitment

10% Traditional Media

15% Direct Invitation

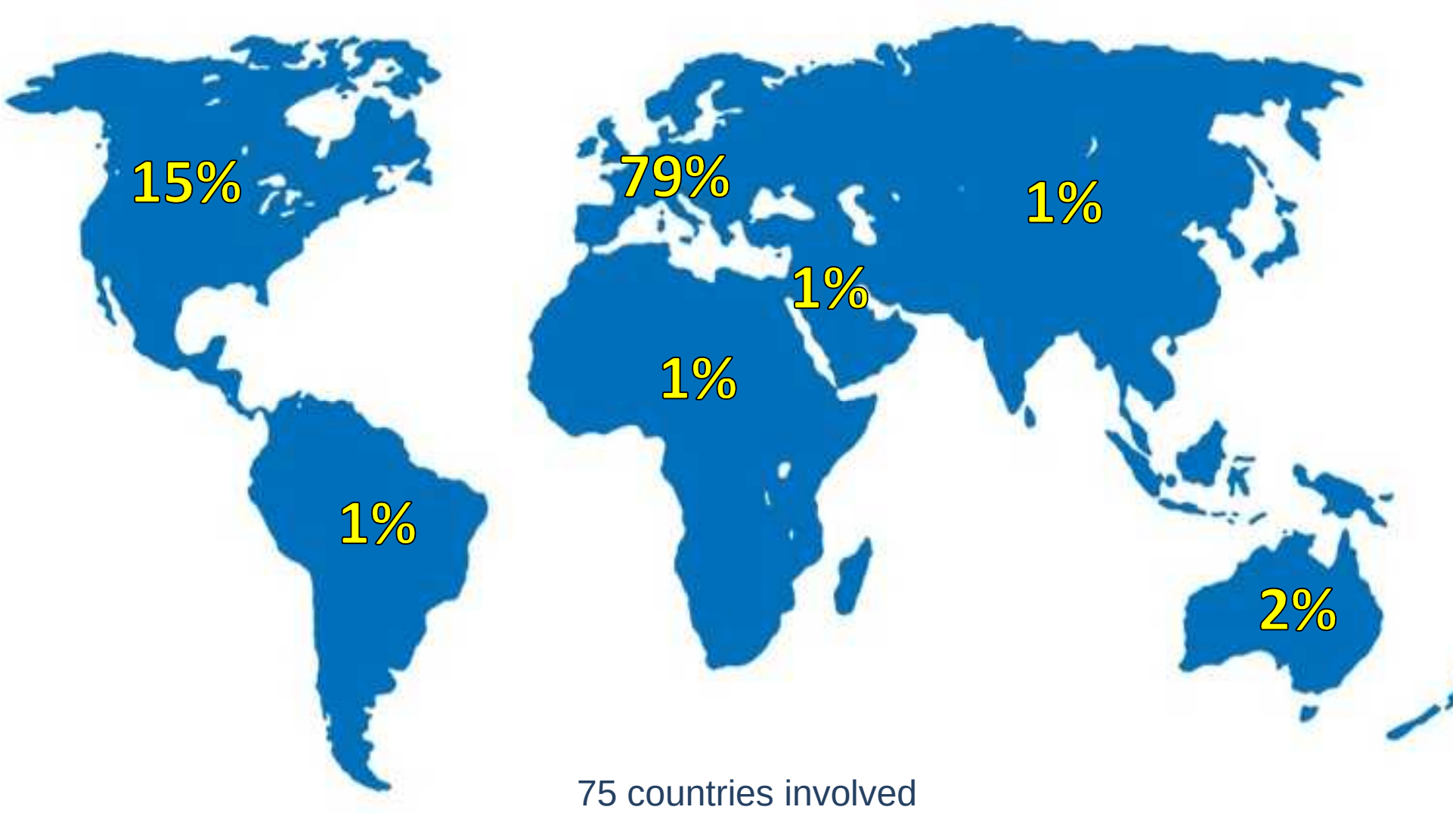
75% Social Media

Public = 4961

Genomic researchers = 607

Genetic health professionals = 533

Other health professionals = 843



75 countries involved

Q: What influences attitudes the most?

A: Our professional background rather than the country we are from

Genetic Health Professionals

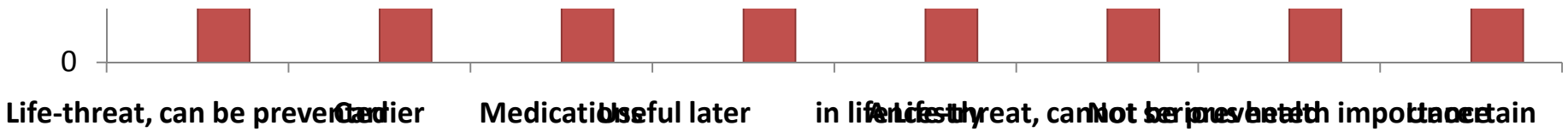
Other Health Professionals

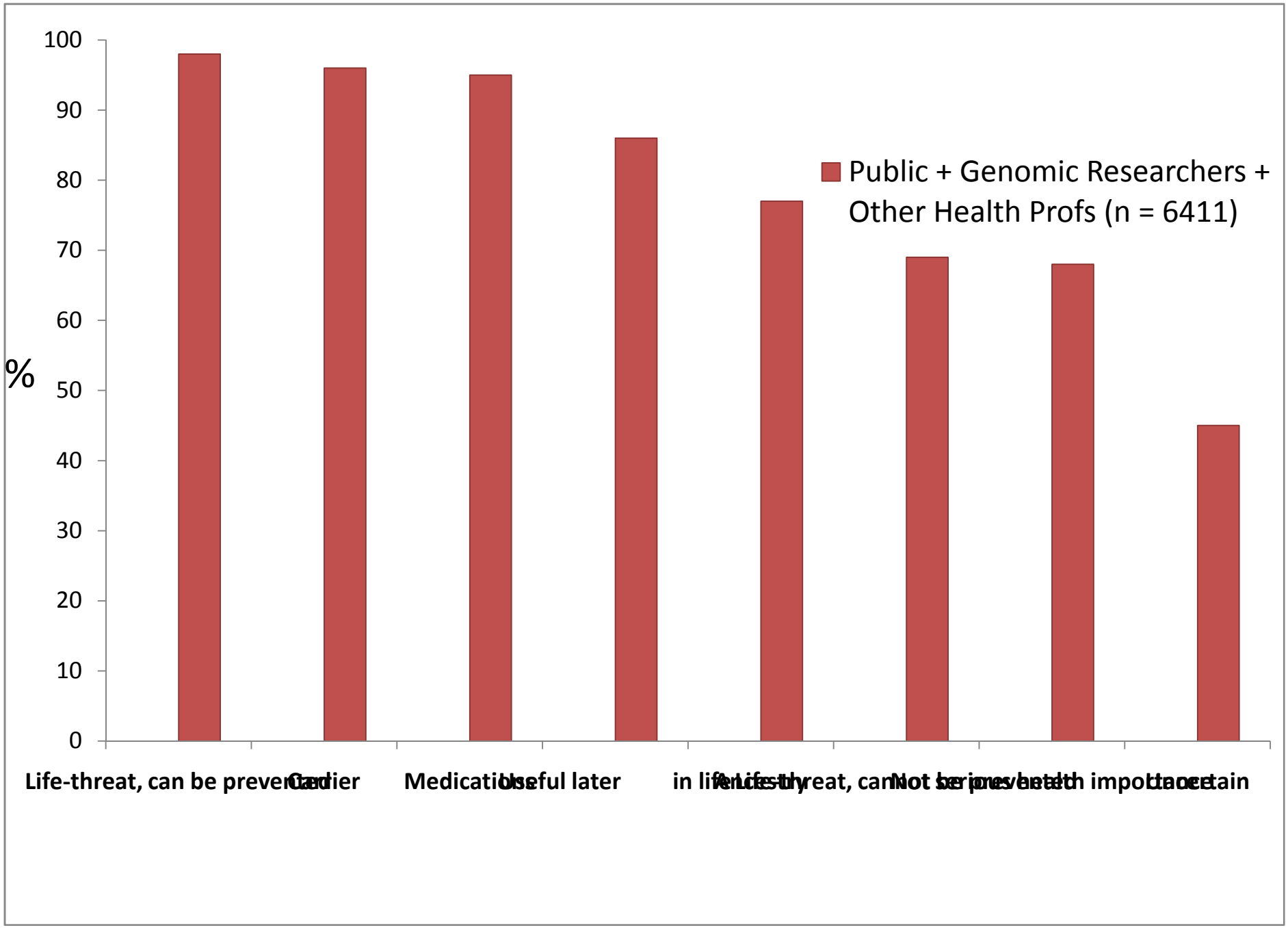
Genomic Researchers

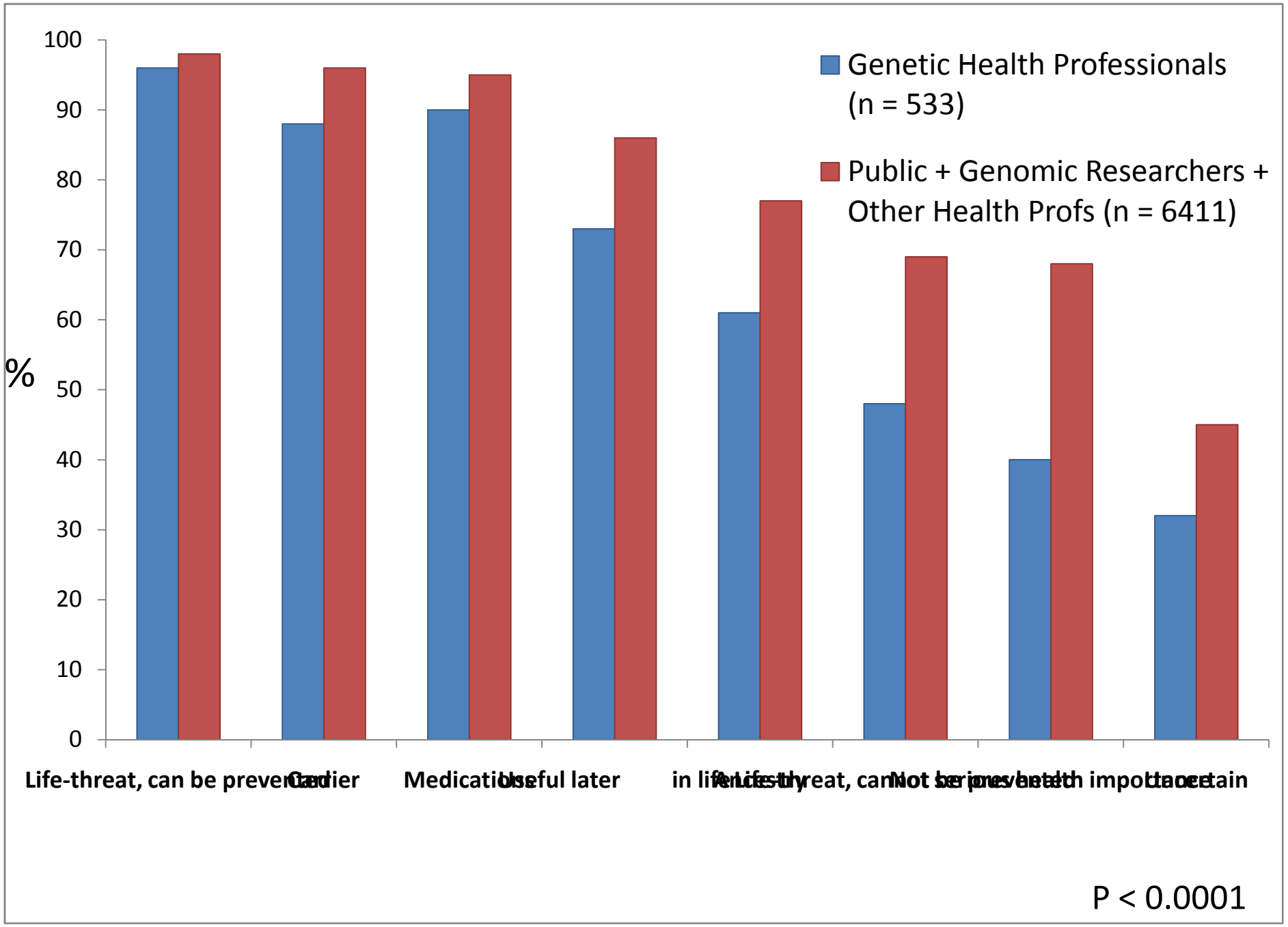
Public

Q: If Incidental Findings were categorized in the following ways
(⬇ below)

what would you want to know?




100
90
80
70
60
50
40
30
20
10
0
%
Public + Genomic Researchers + Other Health Profs (n = 6411)
Life-threat, can be prevented
Earlier
Medications
Useful later
in life-threat, cannot be prevented
Not serious health impact
Uncertain


100
90
80
70
60
50
40
30
20
10
0
%
Genetic Health Professionals (n = 533)
Public + Genomic Researchers + Other Health Profs (n = 6411)
Life-threat, can be prevented
Earlier
Medications
Useful later
Not life-threat
Not serious health impact
Uncertain
P < 0.0001

Key messages

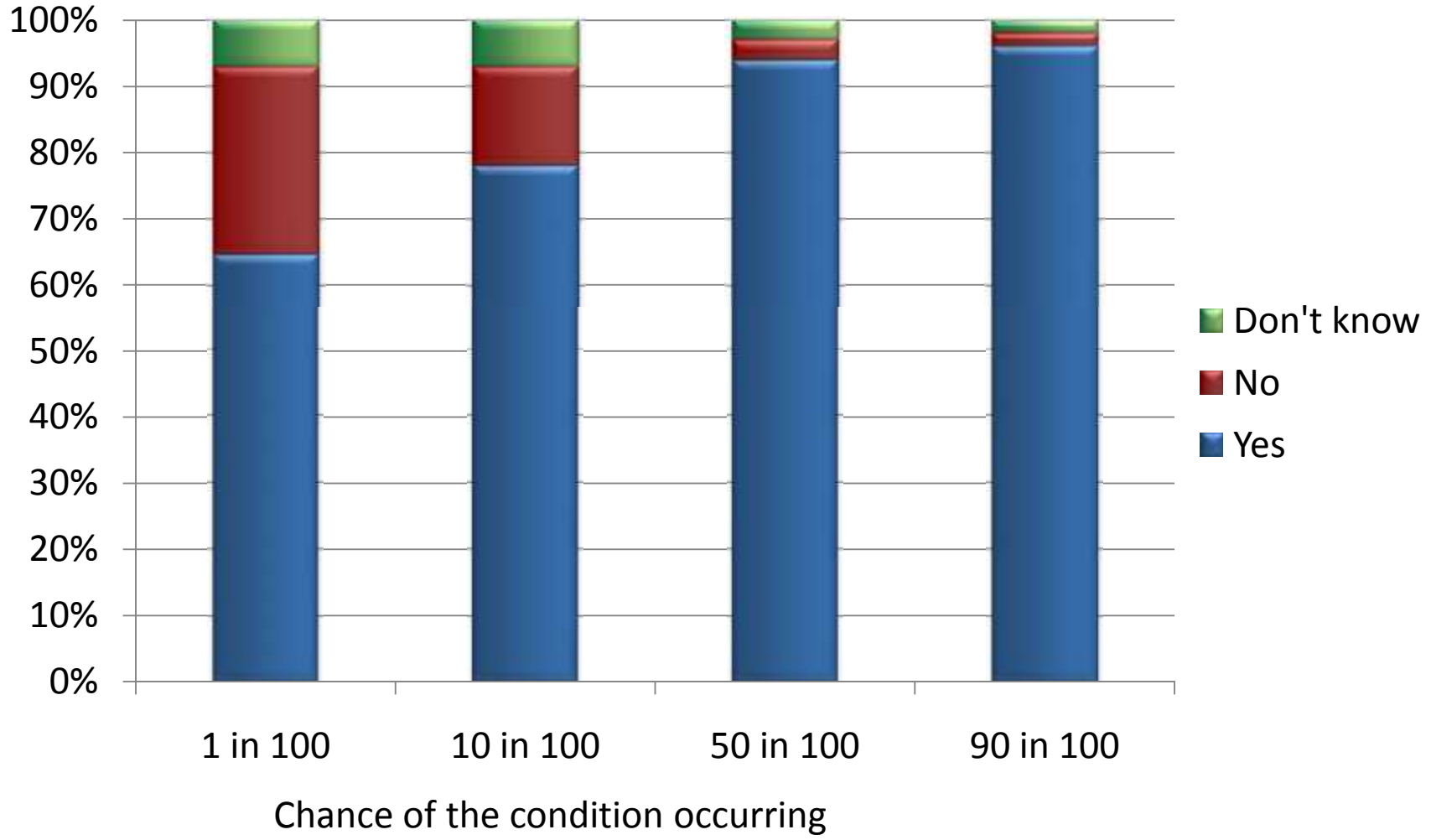
- People want data
- Treatability is important
- Genetic health professionals have more conservative views

Middleton et al (2015) Eur J Hum Genet
Middleton et al (2015) J Med Genet
Middleton et al (2014) Lancet

Q: LETS ASSUME IT IS POSSIBLE TO RETURN IFS RELATING TO A CONDITION THAT IS **SERIOUS AND PREVENTABLE**.

DOES THE **LEVEL OF RISK** AFFECT WHETHER YOU THINK THE RESULT SHOULD BE RETURNED?

‘I’d be interested in knowing about a serious, actionable condition at these levels of risk…’



Key messages

- Even at ‘low risk’ some people still want data – (if it’s usable)
- ‘If its about me, I want to know’
- ‘I’ll decide how important this data is, not you’

Is there a profile to those who want data?

I want to know EVERYTHING!

Information Seeker

I just want some things…..

Information Discriminator

- Are you an….?

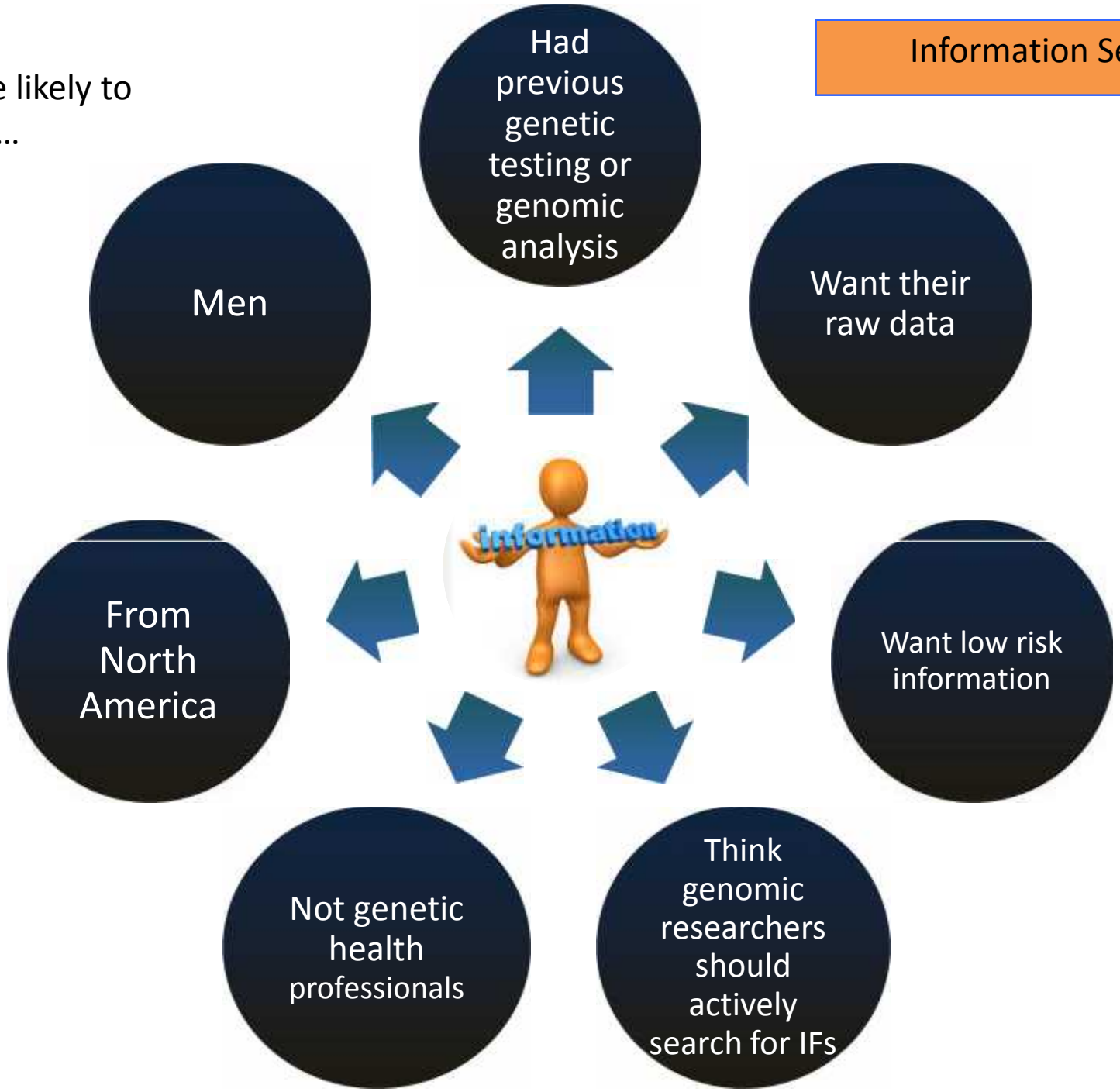
Information Seeker

Information Discriminator

- Explored the profiles of each
- Adjusted for all potential confounding effects
- Only show data relating to significant odds ratios

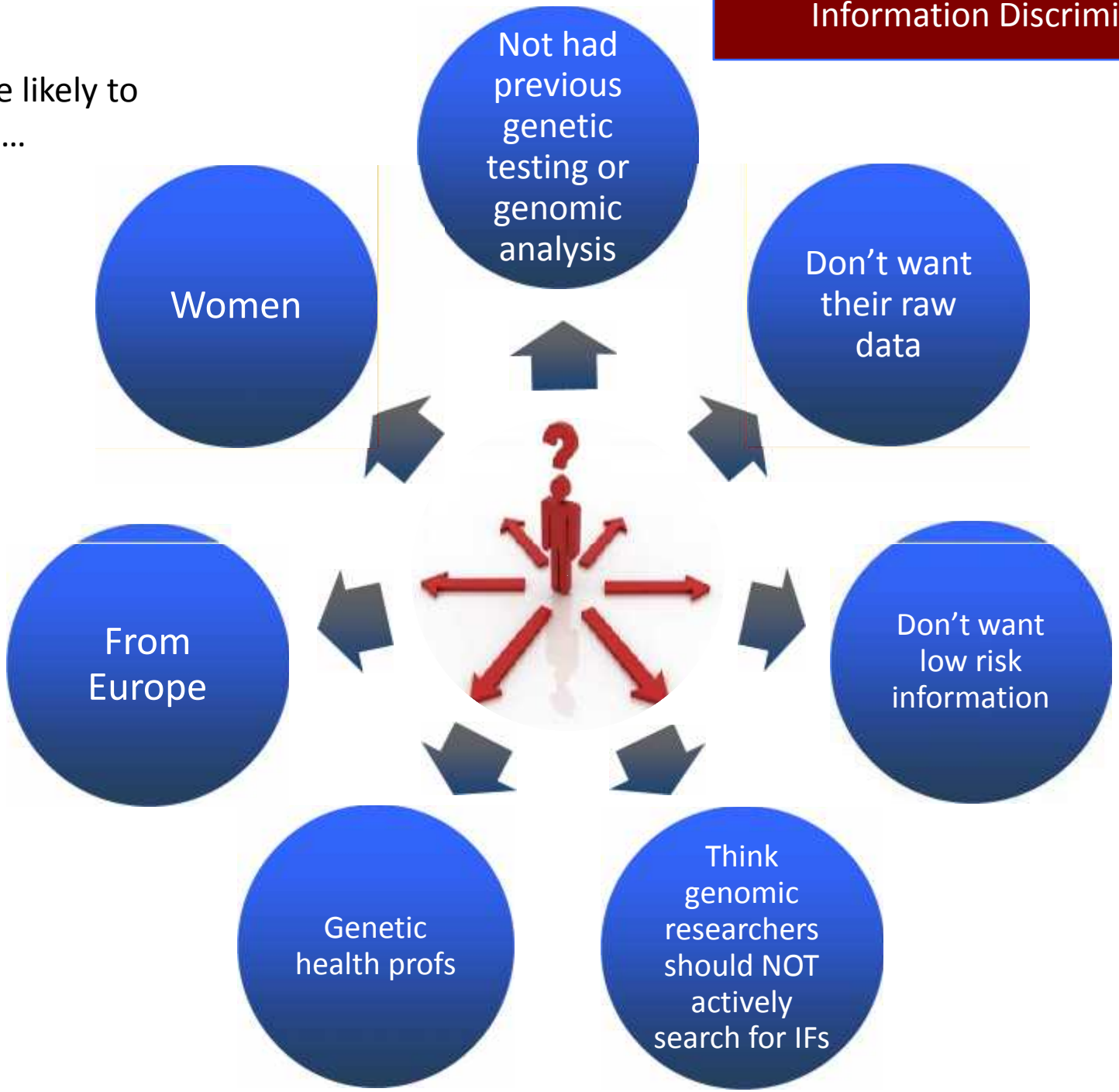
Information Seeker

Are more likely to be/want…



Information Discriminator

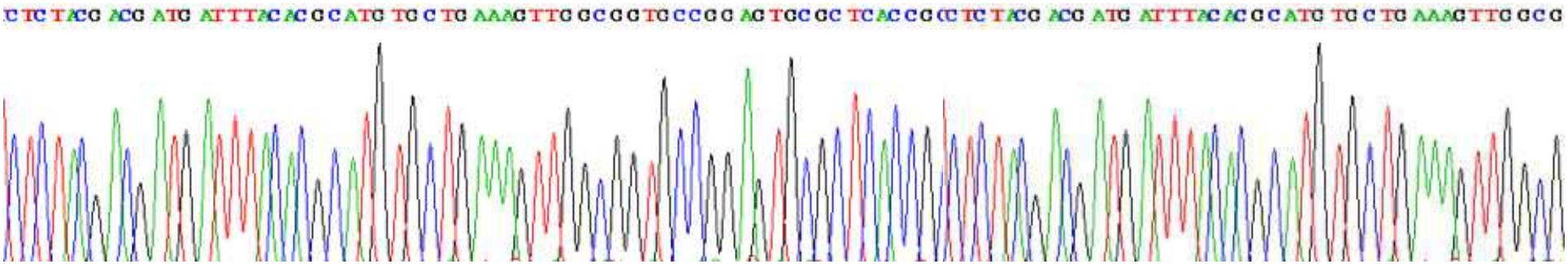
Are more likely to be/want…

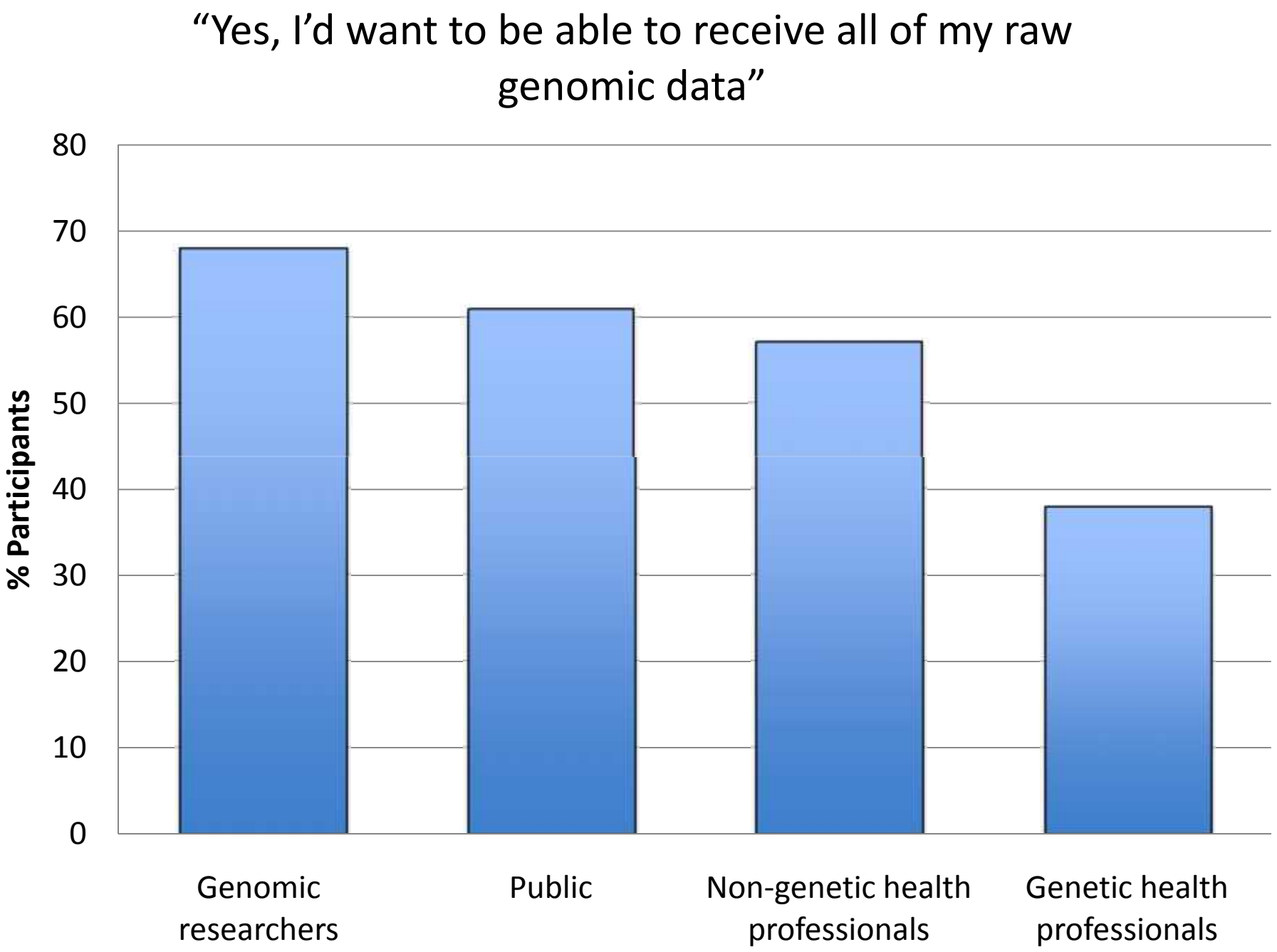


Returning raw data

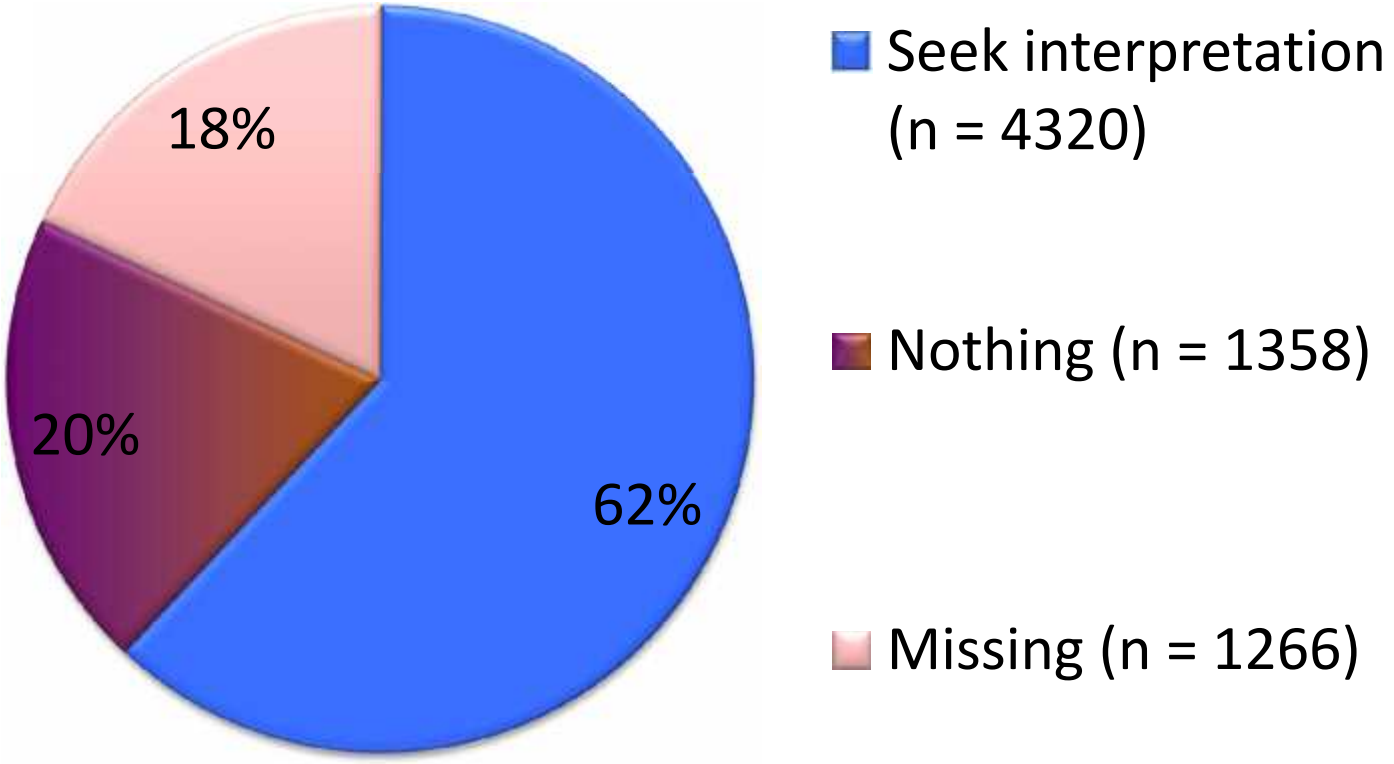
- ‘Raw genomic data’ (sequence reads or called variants) on a hard drive

- “Meaningless” (McGuire et al, 2008)
- “Non-sensical” (Bredenoord et al, 2011)




"Yes, I'd want to be able to receive all of my raw genomic data"
% Participants
80
70
60
50
40
30
20
10
0
Genomic researchers
Public
Non-genetic health professionals
Genetic health professionals

Q: If you were given all of your raw genomic data from a research study, what would you do with this? (n = 6944)



“I would seek out an interpretation”
(n = 4320)

60% ‘I’d analyse it myself’ (n = 2581)

57% ‘I would ask for referral to local clinical genetics service’ (n = 2459)

43% ‘I would ask my GP or Primary Care Physician’ (n = 1844)

41% ‘I would find a genomics researcher and ask them’ (n = 1775)

15% ‘I would pay a commercial genetics company to analyse’ (n = 658)

5% ‘Other’ (n = 237)

“I would do nothing with it” (n = 1358)

78% said ‘I wouldn’t do anything immediately with it, but would keep for future use’ (n = 926)

16% said ‘I wouldn’t know what to do with it’ (n = 194)

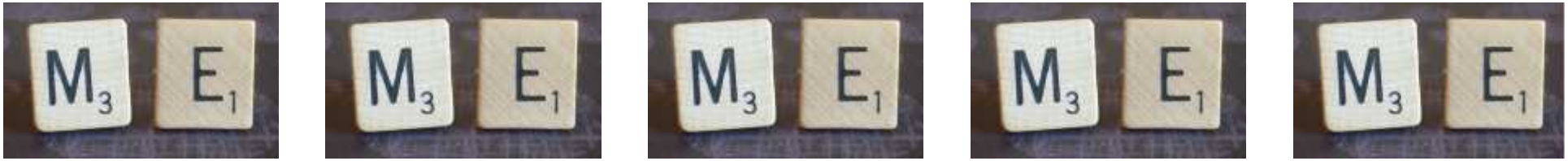
3% said ‘I would delete the data’ (n = 40)

3% ticked ‘other’ (n = 32)

Key Messages

There is an appetite for receiving raw genomic data

- For interpretation
- Just because it's about me



Conclusions

- People want:
  - to be connected to the research process
  - the option to receive data
- There is a perceived value in the data
  - need to manage expectations
  - sign post to what they can do with it

Enormous thanks to:

- Mike Parker
- Caroline Wright
- Helen Firth
- Eugene Bragin
- Matt Hurles
- Kate Morley
- DDD ‘actors’ in films
- DDD team

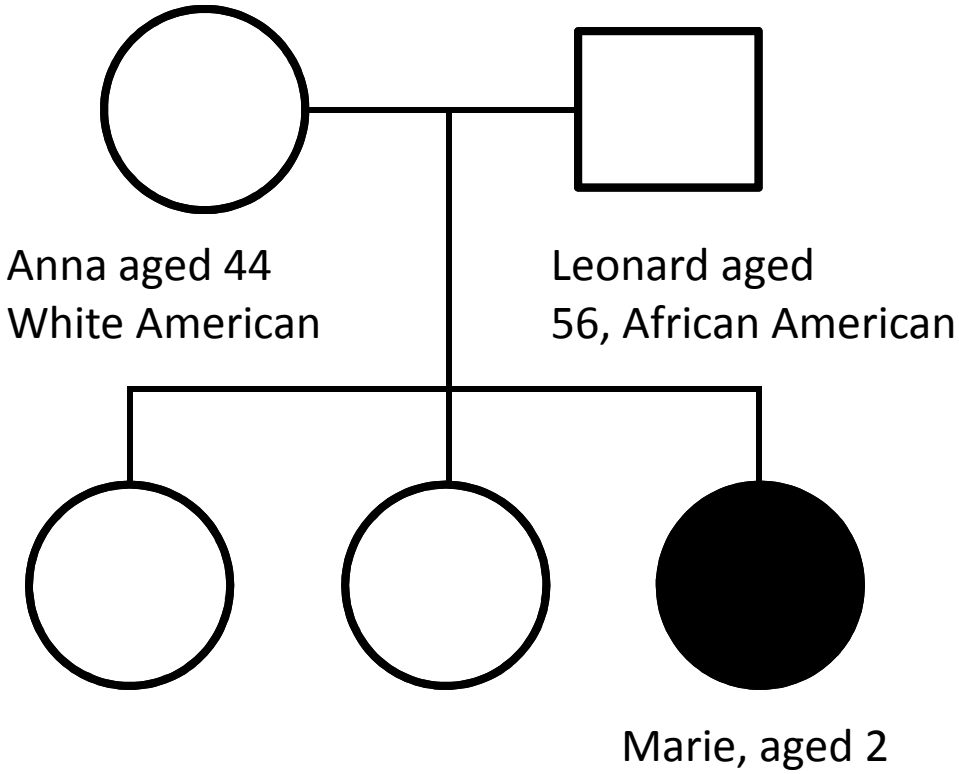
wellcome trust sanger institute

UNIVERSITY OF OXFORD

KING'S College LONDON

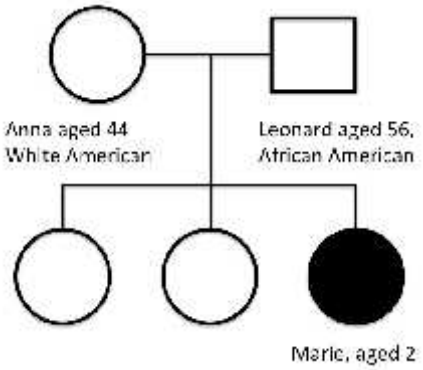
CASE 1: BENEFICENCE

USA Case

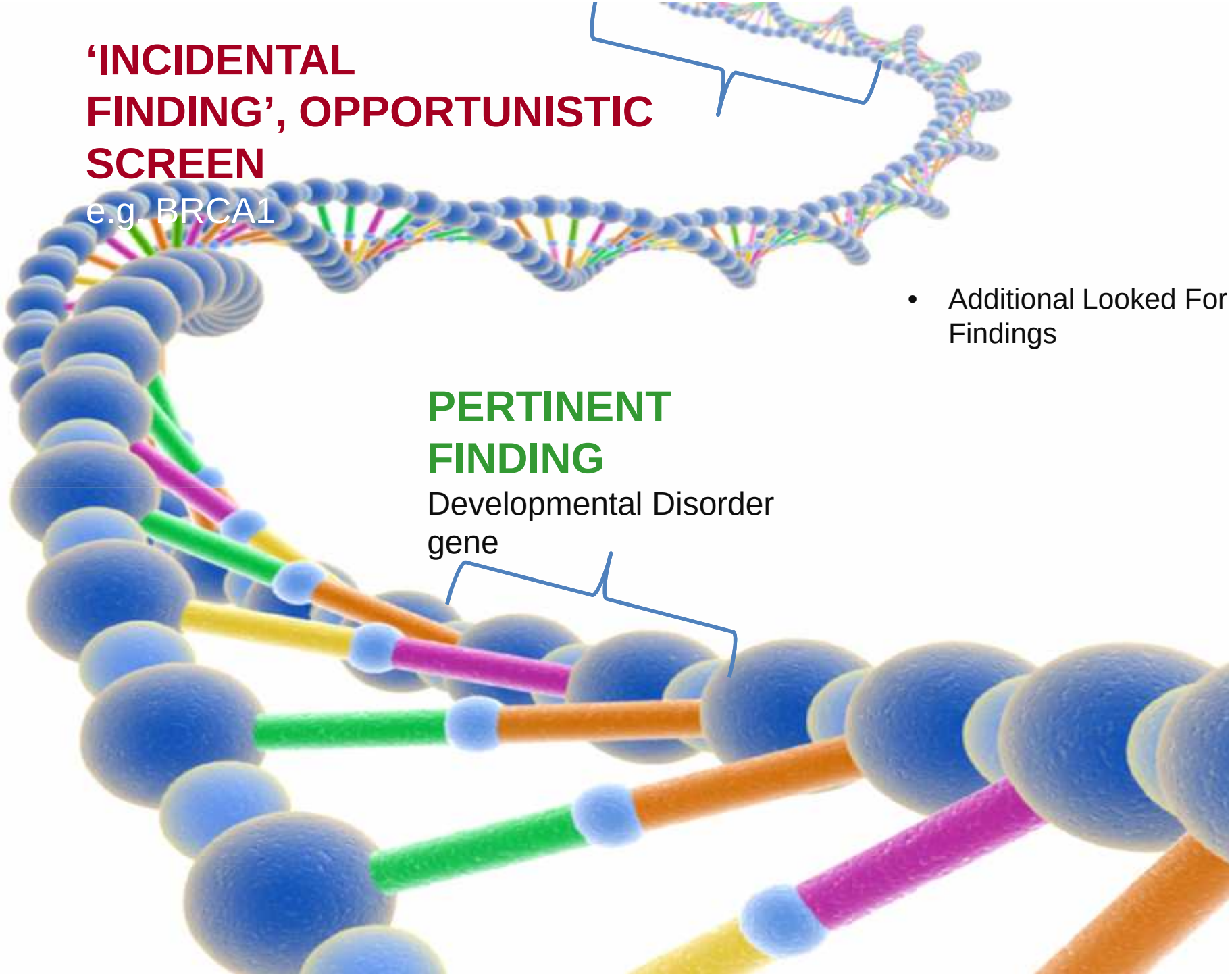


Severe developmental
delay, dysmorphic features

Pre-consultation



- No significant family history in any relatives
- Marie is severely disabled. Parents very anxious and want to know everything about Marie's possible prognosis
- WGS can be offered to find a diagnosis
- ACMG list for opportunistic screen is available
- List contains adult and child onset conditions
- Trio testing



‘INCIDENTAL FINDING’, OPPORTUNISTIC SCREEN

e.g. BRCA1

- Additional Looked For Findings

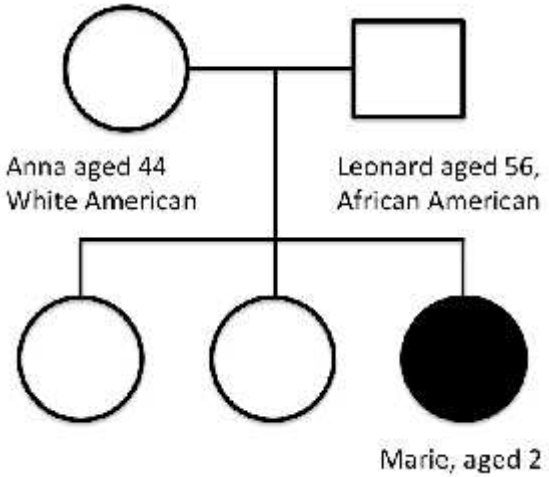
PERTINENT FINDING

Developmental Disorder gene

Broad Consent

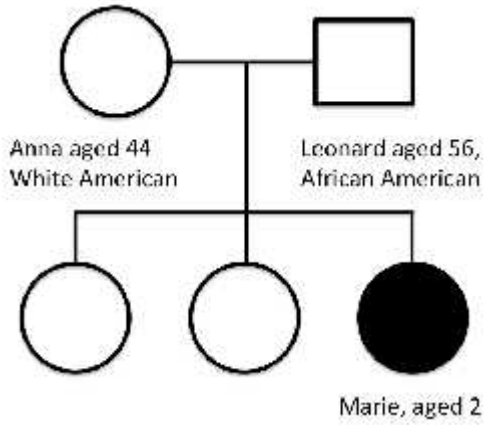
- Different to specific consent for a particular condition
- Testing for conditions not heard of and have no emotional connection to
- List of conditions may change (as per 100kGP)

Results



- Variant in P53 discovered in Leonard and Marie, “likely pathogenic” based on known research
  - (which has been done on data biased to affected people and without much ethnic diversity)
- Leonard is fit and well and has no family history of cancer (with many elderly relatives)
- How should we interpret this result?

The Ethical Dilemmas



- How to do good in the absence of strong data?
- What health screening should we offer Marie and Leonard? (Marie is severely disabled and annual MRI scanning is not feasible, would require a general anaesthetic)
- Extensive genomic data sharing is needed to confirm risks in specific ethnic groups

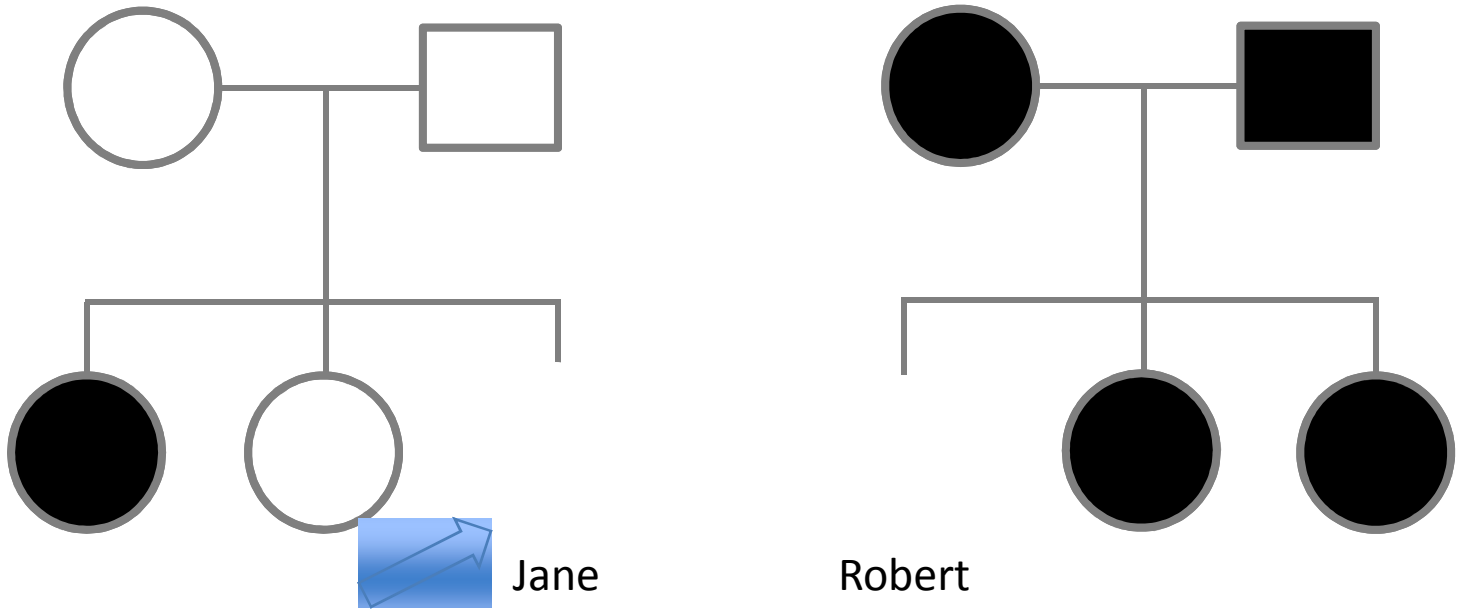
Discussion

- How would you handle this situation?
- What do the family want?
- What have we offered them?

Genomics England

"It may help to explain the degree of uncertainty which surrounds the clinical utility of these [*additional looked for findings*] at the current time: the research effort to help us understand and interpret these findings will be ongoing throughout the project, and we will not know for certain what risks patients carry for some time."

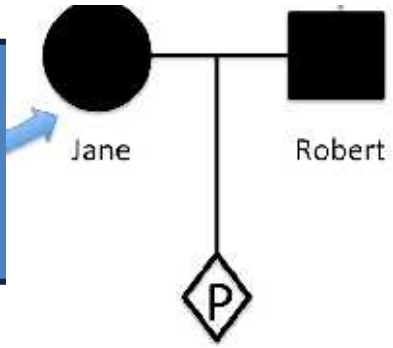
CASE 2: NON-MALEFICENCE



P

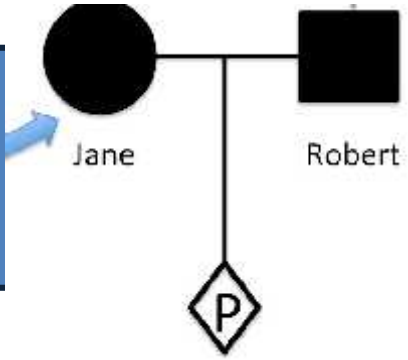
Profound deafness

Background



- Jane and Robert are both medically deaf, but also culturally Deaf
- Sign language is first language (spoken and written English is second language)
- Positive and proud to be Deaf
- Generations of deafness (i.e. genetic/inherited)

Consultation



- Jane and Robert have a preference for deaf children
- Concerned about having a hearing child
- Asked to chat through the chances of having a deaf or hearing child
- Would we offer pre-natal testing ‘just for information’ – risk of miscarriage from the amnio/CVS procedure
- Would couple ask for a termination of pregnancy, would we allow them?

The ethical dilemmas

- Balancing beneficence for the couple and family versus non-maleficence for a child that does not exist yet (although foetus exists)
- Parents right to have autonomy over pregnancy
- Hearing children might be disadvantaged in this family
- Health professionals balancing their focus between non-directiveness versus personal values

The outcome

- Jane and Robert had a deaf child
- They were relieved and delighted
- If the baby had been hearing, I would have referred them to the local social services for deaf people, to access speech therapy

Case studies HD

- Michael is 24 years old
- His mother who is a single parent is affected with HD.
- She has just gone into a residential home
- Michael is referred to talk about testing

- What issues may emerge
- What should we discuss

- Michael has a younger brother aged 14

- He says he wants to be tested what do we do?

Overview of guidelines/position papers (1991-2005)

1991 National Consultative Ethics Committee for Health and Life Sciences (France), Opinion regarding the application of genetic testing to individual studies, family studies and population studies.

1992 German Society of Human Genetics Statement on post-natal predictive genetic diagnosis

1993 Swiss Academy of Medical Sciences Genetic investigations in humans

1994 Institute of Medicine Assessing genetic risks. Implications for health and social policy

1994 Working Party of the CGS (UK) The genetic testing of children.

1995 GIG response to the CGS report**

1995 American Medical Association Testing children for genetic status

1995 ASHG and ACMG (US) Points to consider: ethical, legal and psychosocial implications of genetic testing in children and adolescents

1995 National Consultative Ethics Committee for Health and Life Sciences (France) Opinion and recommendations on Genetics and medicine: from prediction to prevention'

1995 German Society of Human Genetics Statement on genetic diagnosis in children and adolescents

1996 German Society of Human Genetics Position paper of the German Society of Human Genetics

1996 Japanese Society of Human Genetics Guidelines for genetic testing.

1997 National Human Genome Research Institute Promoting safe and effective genetic testing in the US

1998 BMA Human Genetics: choice and responsibility

1998 ACGT (UK) Report on genetic testing for late-onset disorders

1998 Australian Medical Association Human genetic issues

1999 Italian National Bioethics Committee Bioethical guidelines for genetic testing

2000 Canadian College of Medical Geneticists Position statement – genetic testing of children

2000 ESHG Provision of genetic services in Europe – current practices and issues.

2001 Danish Council of Ethics Genetic investigation of healthy subjects – report on presymptomatic gene diagnosis

2001 American Academy of Pediatrics Ethical issues with genetic testing in paediatrics

2001 Japanese Society of Human Genetics Guidelines for genetic testing

2002 Human Genetics Society of Australasia DNA presymptomatic and predictive testing for genetic disorders

2003 Canadian Paediatric Society Guidelines for genetic testing of healthy children

2003 Belgian Society of Human Genetics Guidelines for predictive genetic testing for late-onset disorders

2003 Genetics-Medicine-Related Societies (Japan) Guidelines for genetic testing

2005 Human Genetics Society of Australasia Child testing policy

Testing in adolescence

- At request of doctor
- At request of parents
- At request of young person

Types of genetic testing in children

Presymptomatic testing- untreatable late onset disorders with no effective intervention (usually AD)

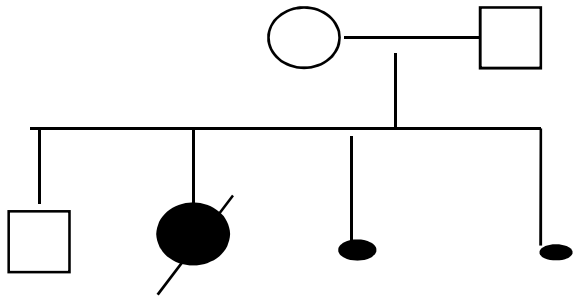
Adults requesting such testing are advised through counselling pre testing to prepare for results as can have major life impact. International guidelines followed.

Implications include;

Managing results, pos or neg
Limitations of prediction
Emotional impact
Social- family, friends
Practical- insurance, employment

Presumption no testing

Case study Reproductive choice



SMA Type 1

Sarah and John ‘s daughter was diagnosed with SMA1.
Sadly she died at the age of six months
Sarah has now had two early miscarriages and in her words desperately wants another child

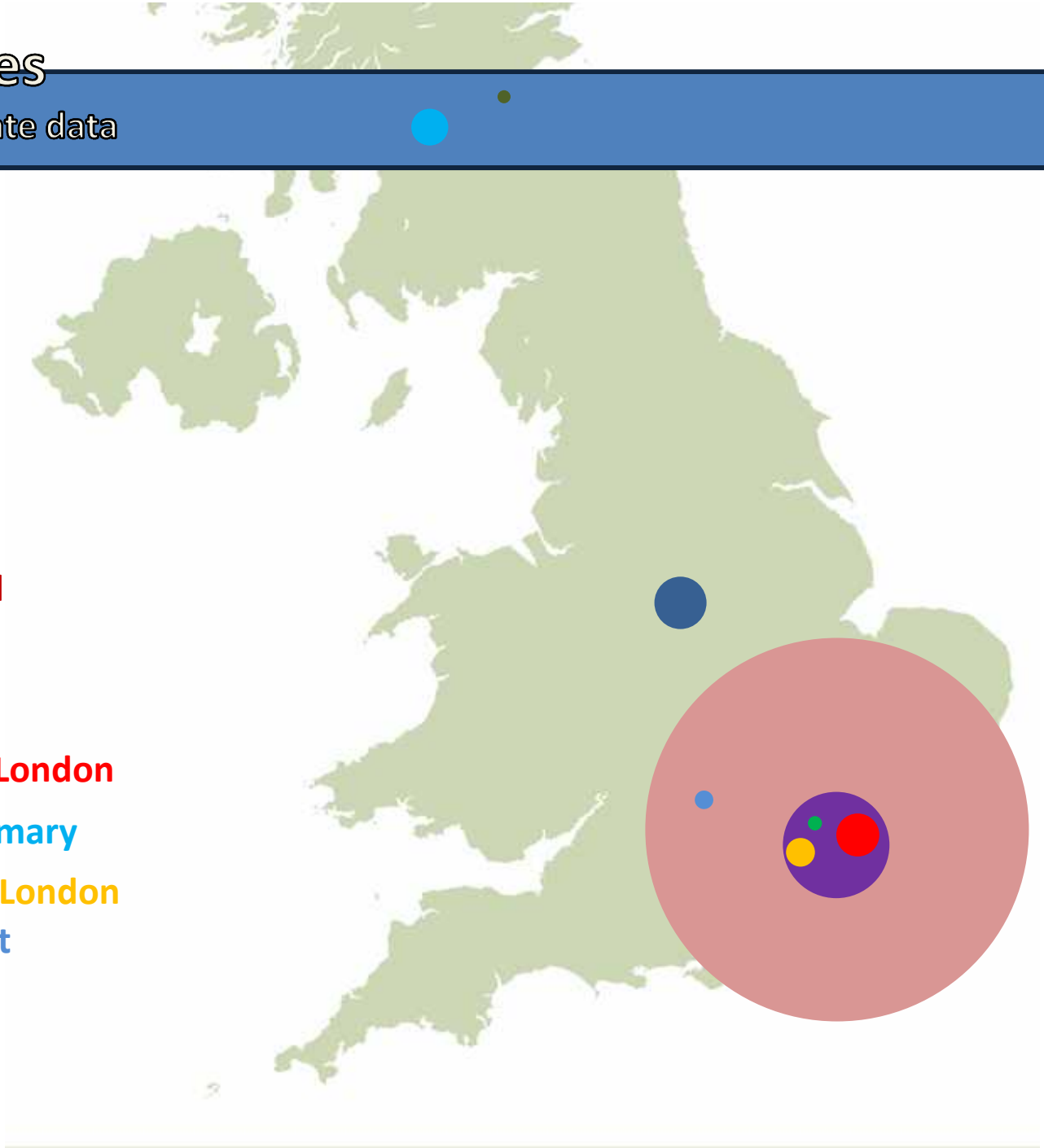
What issues may emerge

Reproductive options for those at risk of having a child with a genetic condition

- *Reproductive roulette*
- Prenatal diagnosis & TOP
- Gamete donation
- Adoption
- Remain childless
- PGD

UK PGD cycles

HFEA 3 year aggregate data



ACU, Guy's Hospital

UCH, London

CARE, Nottingham

The Bridge Centre, London

Glasgow Royal Infirmary

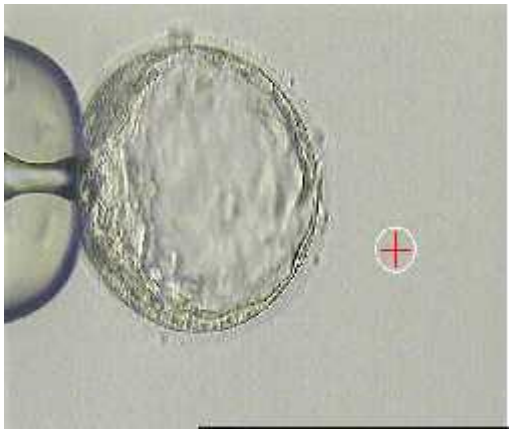
IVF Hammersmith, London

Oxford Fertility Unit

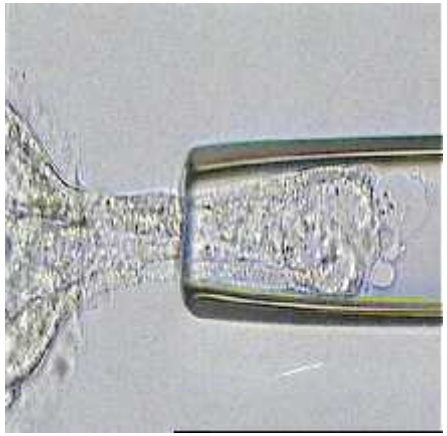
ARGC, London

Edinburgh ACU

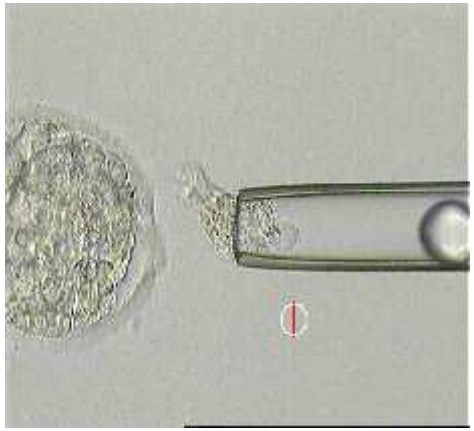
Blastocyst Biopsy Procedure



Blastocyst held in position



Trophectoderm cells extruded through small hole made in the outer coating of the embryo



Cells removed and sent for testing

FREEZE ALL EMBRYOS

Babies born (June 2013)

Total babies born = 473

Treatment cycle to embryo transfer	71%
Clinical pregnancy per egg collection	32%
Clinical pregnancy per transfer	41%

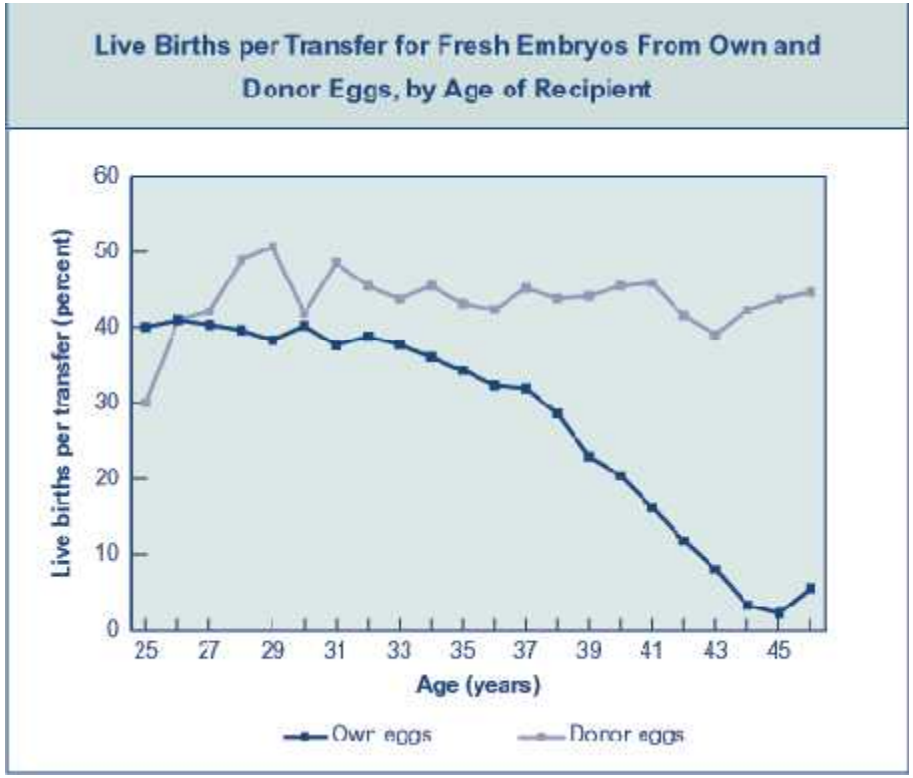
- 343 singletons
- 121 twins (x 2)
- 15 triplets (5 x 3)

- Multiple pregnancy rate = 8%

- 50 ongoing pregnancies

Success and age

- <35yr CPR = 36%
- 35-37 CPR = 19%
- 38-39 CPR = 8%
- >39 CPR = 0%



BMI

- No treatment if BMI>35
- No funding if BMI>30

Risks:

- egg collection
- decreased success
- increased chance of miscarriage
- increased risks in pregnancy

- Is PGD the solution?