Introducing genetic testing into routine psychiatric practice

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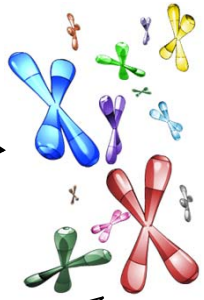
Why is Genetic Testing Important?



Explain physical/mental health illness

Clearer prognosis

Recurrence risks – impacts whole family

Pro-active screening

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What are we testing?

Copy Number Variant: Segment of DNA>1 kilobase

Compare with reference genome

→ Higher (duplication) = Microarray

→ Lower (deletion)

e.g. 22q11.2 (Velo-cardio-facial syndrome, schizophrenia)

Molecular Genetic Test:

Individual thought to be affected

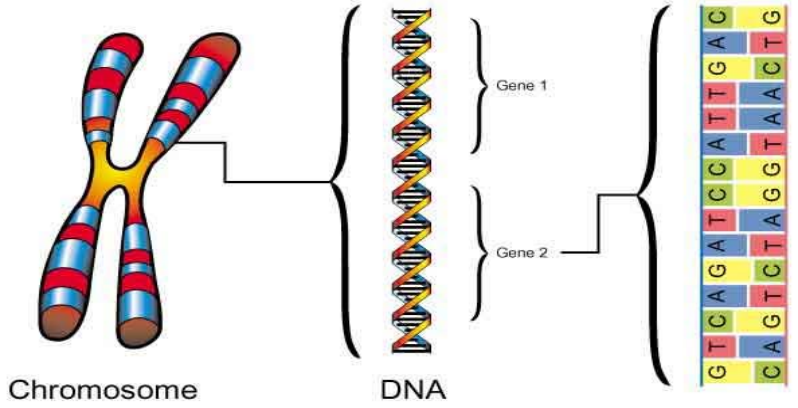
Testing to confirm clinical impression

Fragile X (autism), Cystic Fibrosis

Karyotyping:

Translocations

Down Syndrome



•http://www.rarechromo.co.uk

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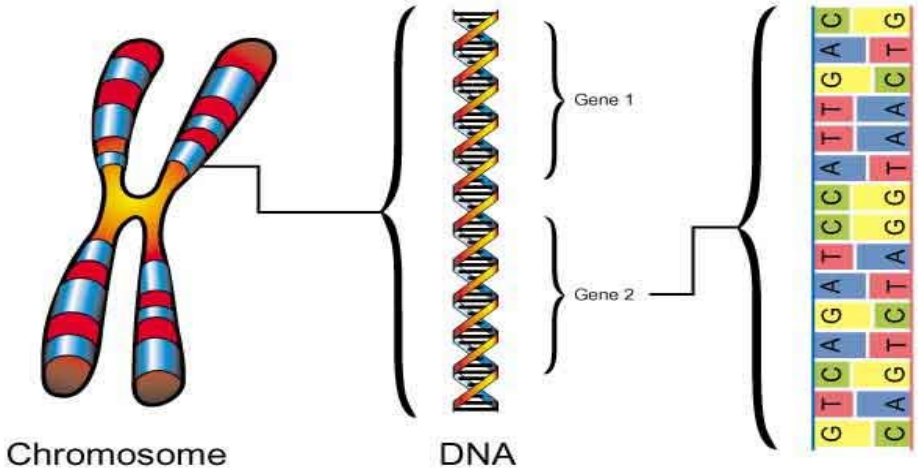
Genetic testing - How



- Karotyping
- FISH
- Microarrays
- Single gene
- Exome sequencing
- Whole Genome sequencing

- DDD and100,000 genome studies

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BJPsych The British Journal of Psychiatry (2018)
212, 287–294. doi: 10.1192/bjp.2017.65

Neurodevelopmental risk copy number variants in adults with intellectual disabilities and comorbid psychiatric disorders*

Johan H. Thygesen**, Kate Wolfe**, Andrew McQuillin, Marina Viñas-Jornet, Neus Baena, Nathalie Brison, Greet D'Haenens, Susanna Esteba-Castillo, Elisabeth Gabau, Núria Ribas-Vidal, Anna Ruiz, Joris Vermeesch, Eddy Weyts, Ramon Novell, Griet Van Buggenhout, André Strydom, Nick Bass***, Miriam Guitart*** and Annick Vogels***

High yield of pathogenic copy number variants (13%)

Rate percentage:

Participants with developmental disorder CNV = 10%
Schizophrenia = 3.1%*
Healthy control = 1.2%*

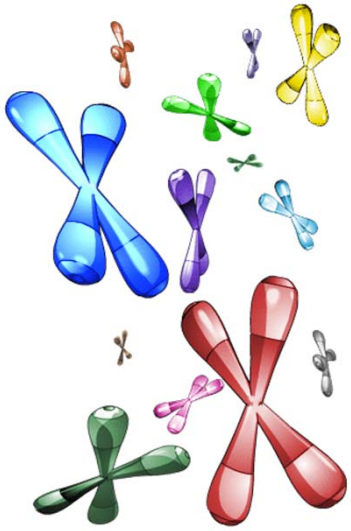
*Rees et al.

Genetic Testing in Schizophrenia

Br J Psychiatry. 2014 Feb;204(2):108-14. doi: 10.1192/bjp.bp.113.131052. Epub 2013 Dec 5.

Analysis of copy number variations at 15 schizophrenia-associated loci.

Rees E[1], Walters JT, Georgieva L, Isles AR, Chambert KD, Richards AL, Mahoney-Davies G, Legge SE, Moran JL, McCarroll SA, O'Donovan MC, Owen MJ, Kirov G.



- 2.5% of case group vs 0.9% control group

  →carry one or more copy number variants

- Increase in risk for other disorders

  →epilepsy, congenital heart disease, ADHD, obesity

- 2.5% individuals with schizophrenia carry at least one known pathogenic copy number variant

  → Odds ratios between 2 and >50

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100,000 Genome Project

→ Whole Genome Sequencing

Schizophrenia and additional features

1) age of onset below 18
2) schizophrenia in a first or second degree relative
3) neurological signs or MRI abnormalities
4) congenital disorders/dimorphisms suggesting a genomic disorder

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So let’s do it!

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QUALITY IMPROVEMENT

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Quality Improvement

- Institute of Healthcare Improvement methodology
- Multidisciplinary
  - Psychiatry, Foundation doctors
    - James Smith, Claire Smith
  - Clinical genetics
    - Elisabeth Rosser
  - Speech therapy, nursing, psychology
  - QI coach
- Ideas from the coalface

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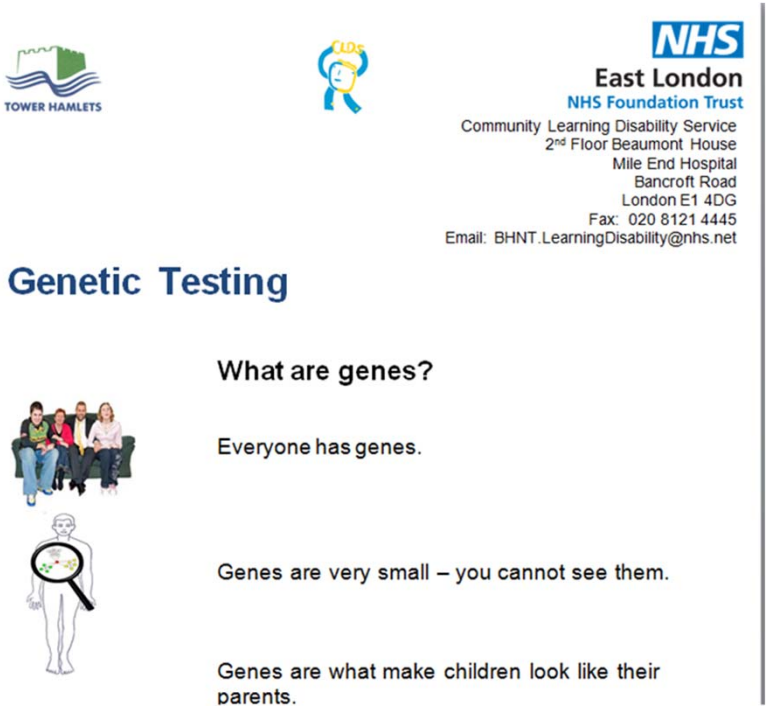
Background

QUALITY IMPROVEMENT

Challenging Behaviour: Improving Care and Quality

1. Reducing use of antipsychotic medications
2. Improving physical health
3. Implement Positive Behavioural Support
4. Access to genetic testing



TOWER HAMLETS

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Community Learning Disability Service
2nd Floor Beaumont House
Mile End Hospital
Bancroft Road
London E1 4DG
Fax: 020 8121 4445
Email: BHNT.LearningDisability@nhs.net

Genetic Testing

What are genes?

Everyone has genes.

Genes are very small – you cannot see them.

Genes are what make children look like their parents.

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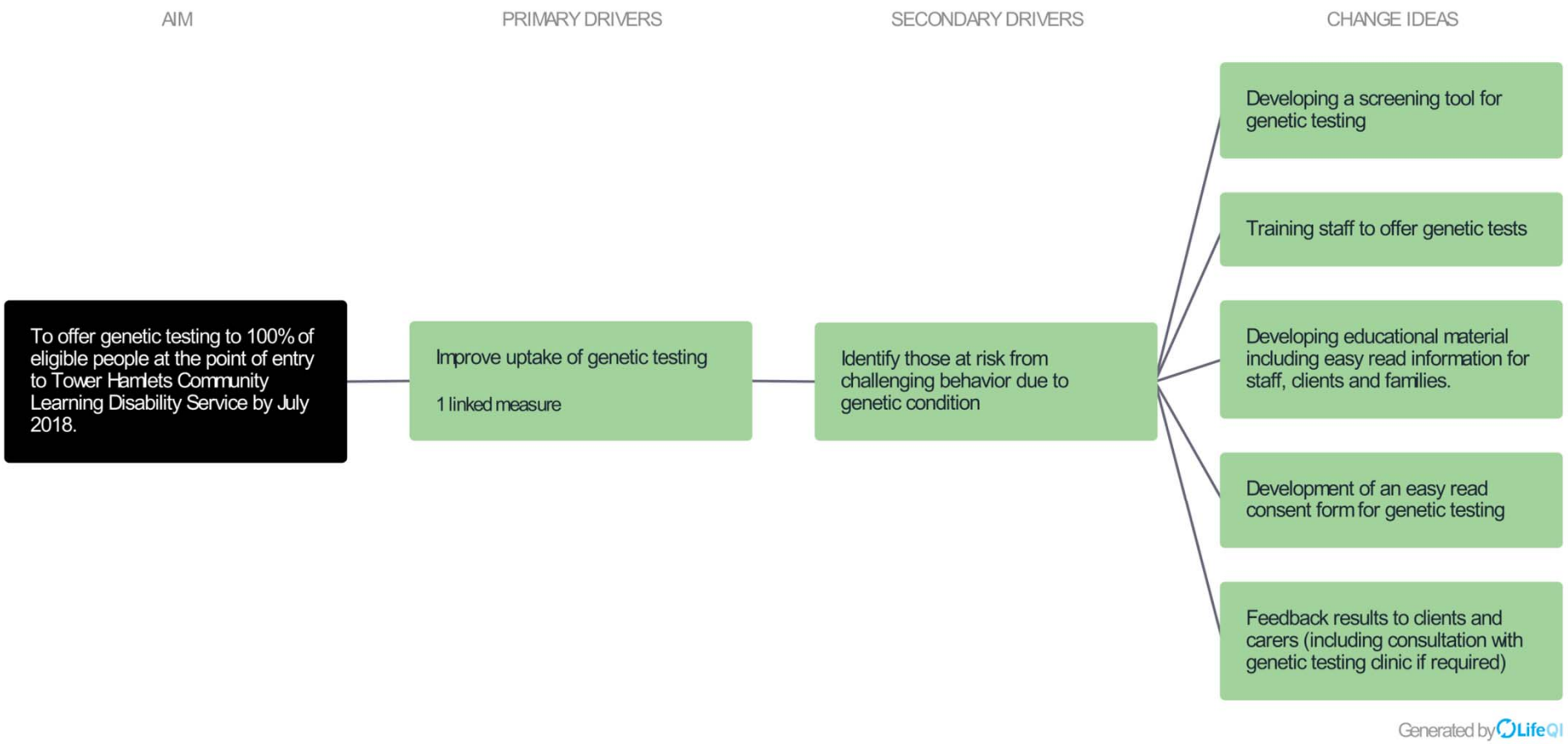
Driver diagram



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Explaining tests

Chromosome test: You can see the whole Chromosome (Necklace) but not the individual genes (beads)

Microarray test: allows a closer look at the genes making up the chromosome. (It allows us to have a closer look at sections of 2-3 beads in the necklace)

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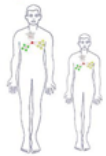
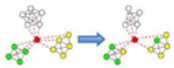


Genes are what make children look like their parents.

Genes make some of us tall and some of us short.



Sometimes, part of the genes can get lost or changed. This can cause problems.

We think that this may explain why some people have Intellectual disabilities or mental health problems.

What will happen to me?

If we know more about genes, we may be able to give people more help.

A blood test can help us find out about genes.

We can also test your Saliva.

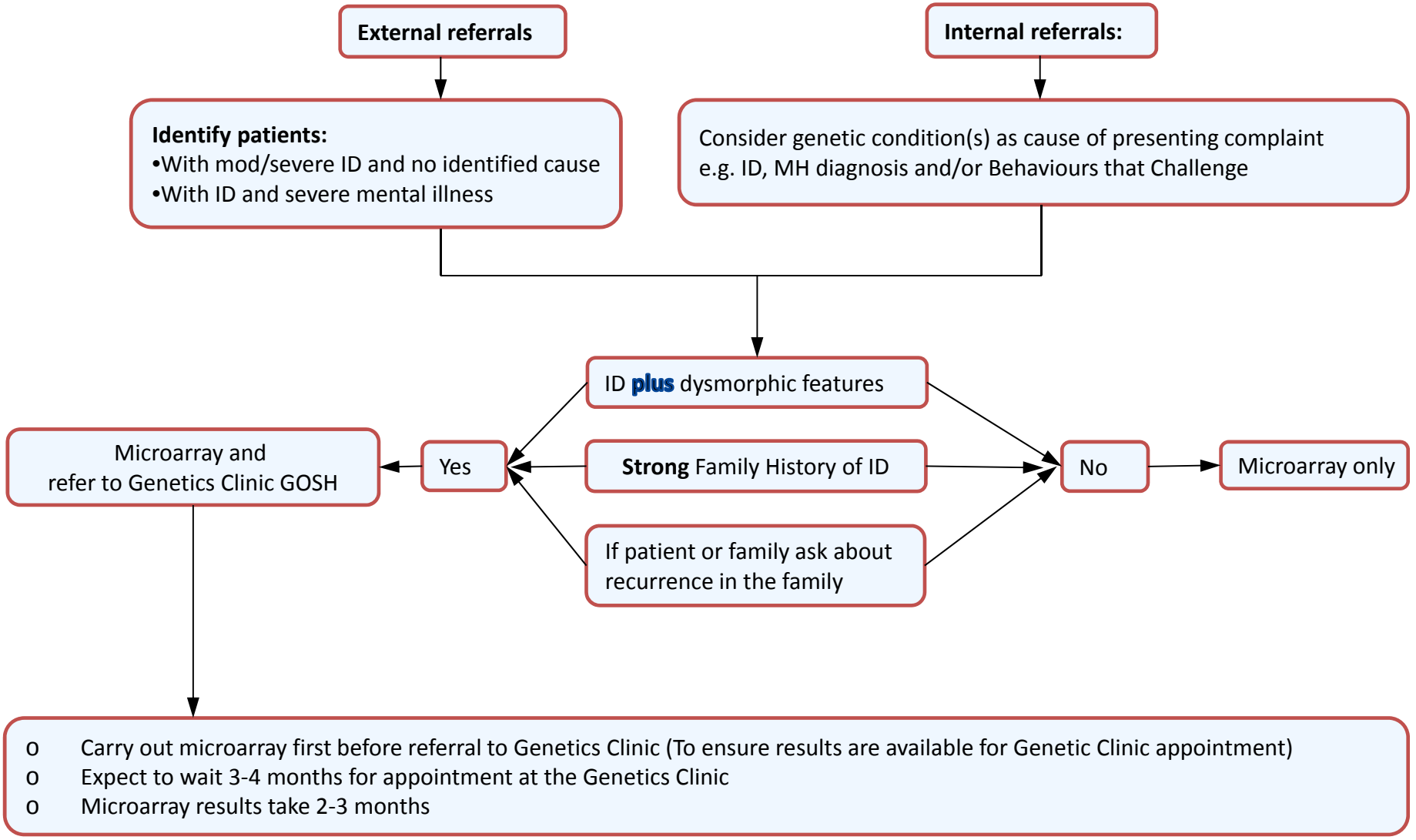
These tests are free.

What does it mean for my family?

Your genes came from your mum and dad

They may wish to have the test to find out if they have the same genes.

CLDS Referral for Genetic Testing



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Screening Tool

Clients name:
Dob:
Referral made by:

Information required:	Give as much information as you can in the space below
Moderate to severe Intellectual Disability (see appendix 1 on next slide)	
Small or large head	
Does not look like family members	
Very short or tall stature	
Other learning or behavioural issues: Including Autism Spectrum Disorder. • …… • ……	
Other physical or health problems eg congenital heart disease, cleft palate • …… • ……	
Family history of:	
• Other people with ID	
• Multiple miscarriages, stillbirths or childhood deaths	
• Has the referral been discussed with the client/carer/family?	

Appendix 1: Intellectual disability:

Intellectual disability severity	IQ	Typical functional description
Mild	50-69	Fluent speech Able to be part of society Has a semi-skilled job Able to develop independent social contacts Mental age of 9-12 years
Moderate	35-49	Enough language skills to communicate basic needs Needs help and support in community Can be helped to sustain a paid job role – typically manual Mental age of 6-9 years
Severe	20-34	Minimal language Needs continuous community support Mental age of 3-6 years
Profound	<20	Needs continuous community support – all self-care must be provided. Mental age under 3 years

PDSA: 3

Consent form: Genetic testing:

Patient Name:

Date of Birth:

NHS number:

Responsible health professional:

Special requirements (eg interpreter):

Please tick **no** ✗ or **yes** ✓ for each part	✗	✓
 I have read the information sheet about genetic testing.		
 I can understand the information sheet.		
 I could ask questions if I wanted to.		

Consent form: 21/02/17

Please tick **no** ✗ or **yes** ✓ for each part	
	I understand that it is my choice to have the test.
	I understand that I can change my mind and not have the test.
	I understand that it will not change the care I get.
	I am happy for you to share this information with my doctor.

Quality Improvement Measures:

- Outcome

% Offered Genetic Testing at Single Assessment	75%
% Uptake of Genetic Testing to those eligible	25%

In total, 15 people have undergone genetic testing to date

Of the 15, we have received 5 results, of which 3 have had a positive result

Exciting, innovative, but also highlighted areas for improvement with the feedback process

Example results

- 3q29 deletion syndrome
  - Intellectual Disability
  - Hearing impairment
  - Autism

- Chromosome 1 copy number gain
  → Discussion about marriage and children

- Negative result - Prader-Willi Syndrome

Qualitative Feedback

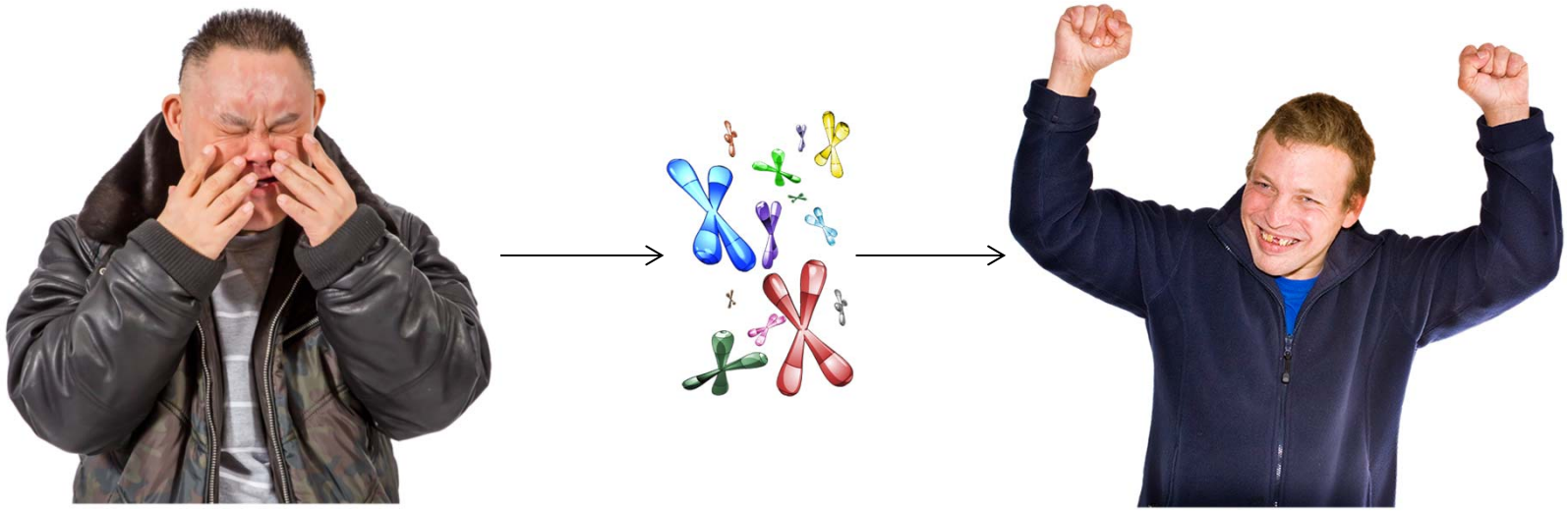
Staff views on feeding back results:

What did you like?	What did you dislike?	How could it be improved?
Being able to present information to patients	Complicated	Clear structure and knowledge on responsibilities of various clinicians involved
Helpful meeting patient face to face	Technically difficult information	Clearer plan on who gives feedback
Satisfying for patient to know	Complicated to find correct information	Clearer protocol for feedback

Impact: Where is the value?

Patient	Tangible benefits e.g. Screening
	Knowing the cause of the learning disability
Family	Blame
	Guilt
	Understanding
Clinician	Tangible benefits e.g. tailoring interventions
	Fits the medical model

Summary



- Applying innovative neuroscience to clinical practice
- Clear benefits to patients and their families
- Individualised interventions
- Achievable goal
- QI methodology engages team and delivers complex service improvement