What GP's need to know about intellectual disability

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Introduction

- There are multiple avenues available for a GP to help families with intellectual disability
- Is the genetic testing revolution relevant to GP's?

Aims

- Quick Cook's tour of the genetic testing revolution as it relates to intellectual disability
- Causes of intellectual disability
- Warning signs and early detection of developmental disability
- Red flags and when to investigate
- When to refer
- Role of the GP in ongoing management of intellectual disability
- National disability insurance scheme: what is the GP's role?

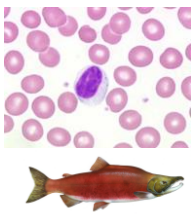
Is it intellectual disability or is it mental retardation?

- "Mental retardation" no longer widely used
- "Developmental disability" commonly used
- "Intellectual disability" widely accepted term

- Simple definition is IQ < 70 on an individually administered IQ test, onset < 18 years.

- 1-2.5% of the population have an IQ < 70
- 0.5% of the population have an IQ < 50
- M:F ratio 1.3:1

Friedrich Miescher (1869)



"Nuclein"

1869

Watson and Crick (1953)

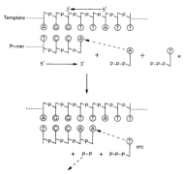
1869 1953

Joe Hin Tjio (1956)

THE CHROMOSOME NUMBER OF MAN

1869 1953 1956

Fred Sanger (1977)



1869 1953 1956 1977

Francis Collins (1993)

Public human genome project

1869 1953 1956 1977 1993

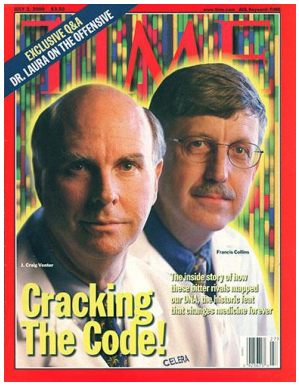
J. Craig Venter (1997)

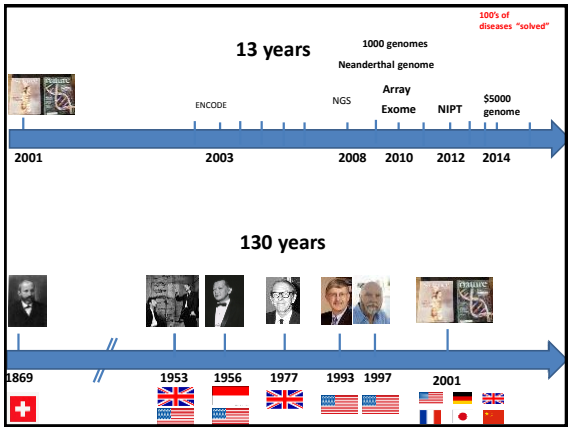
Private human genome project

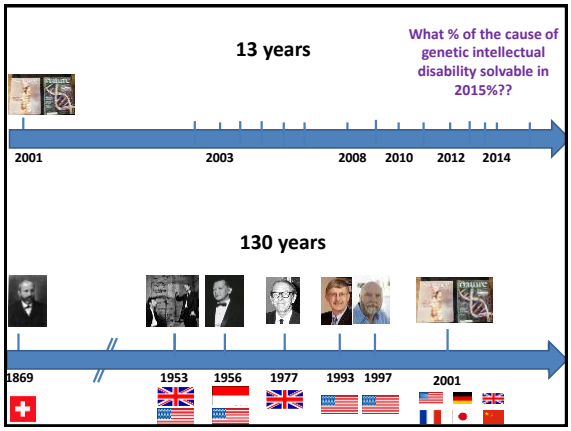
1869 1953 1956 1977 1993 1997

Human Genome published (2001)

1869 1953 1956 1977 1993 1997 2001

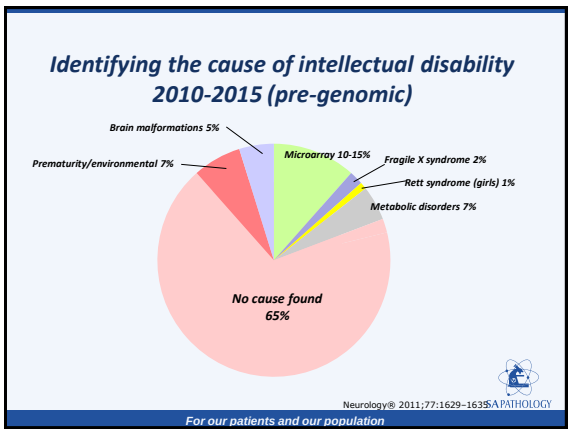




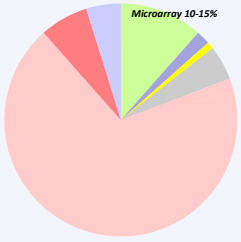


Why investigate?

- Understanding the condition and its prognosis guides optimal management
- Enables targeted evaluation for known associations
- Enables targeted surveillance for known complications
- Advice about recurrence or risk to the extended family
- Increasing use of prenatal diagnosis and PGD
- Support organisations
- Establishing a specific cause allays concerns about other possible causes such as events during pregnancy



Identifying the cause of intellectual disability 2010-2015 (pre-genomic)



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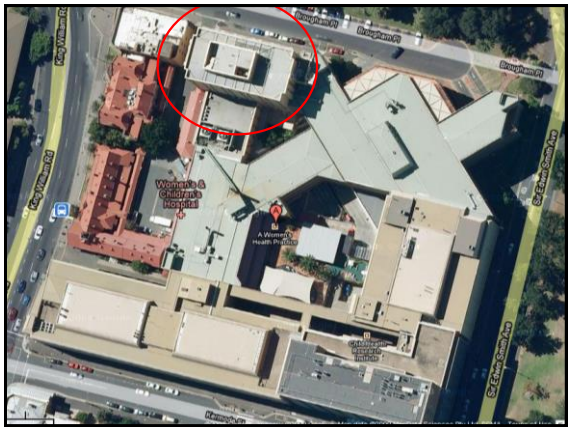
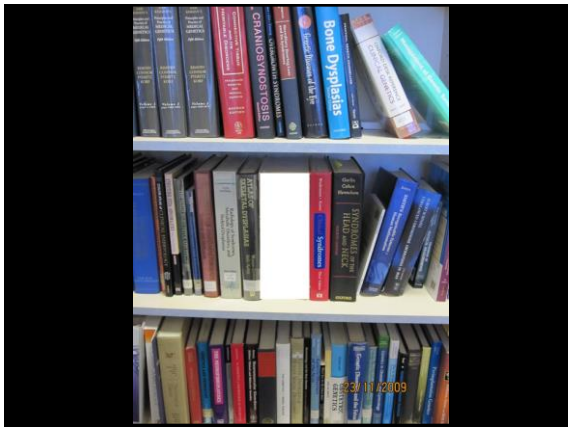




ARTICLE

Consensus Statement: Chromosomal Microarray Is a First-Tier Clinical Diagnostic Test for Individuals with Developmental Disabilities or Congenital Anomalies

David T. Miller,[1,*] Margaret P. Adam,[2,3] Swaroop Aradhya,[4] Leslie G. Biesecker,[5] Arthur R. Brothman,[6] Nigel P. Carter,[7] Deanna M. Church,[8] John A. Crolla,[9] Evan E. Eichler,[10] Charles J. Epstein,[11] W. Andrew Faucett,[2] Lars Feuk,[12] Jan M. Friedman,[13] Ada Hamosh,[14] Laird Jackson,[15] Erin B. Kaminsky,[2] Klaas Kok,[16] Ian D. Krantz,[17] Robert M. Kuhn,[18] Charles Lee,[19] James M. Ostell,[8] Carla Rosenberg,[20] Stephen W. Scherer,[21] Nancy B. Spinner,[17] Dimitri J. Stavropoulos,[22] James H. Tepperberg,[23] Erik C. Thorland,[24] Joris R. Vermeesch,[25] Darrel J. Waggoner,[26] Michael S. Watson,[27] Christa Lese Martin,[2] and David H. Ledbetter[2,*]

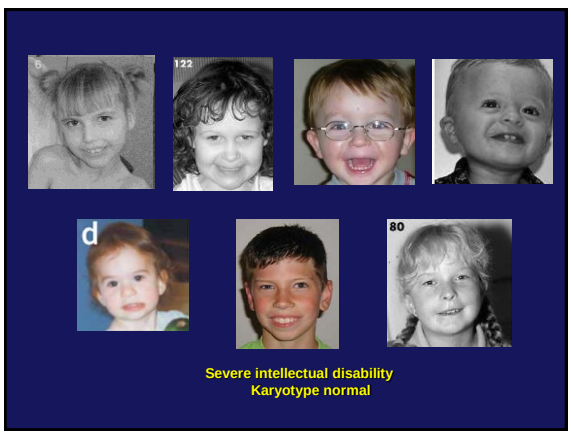
Am J Hum Genet 2010;86:749-64

MBS item 73292

One or more of: intellectual disability, developmental delay, autism

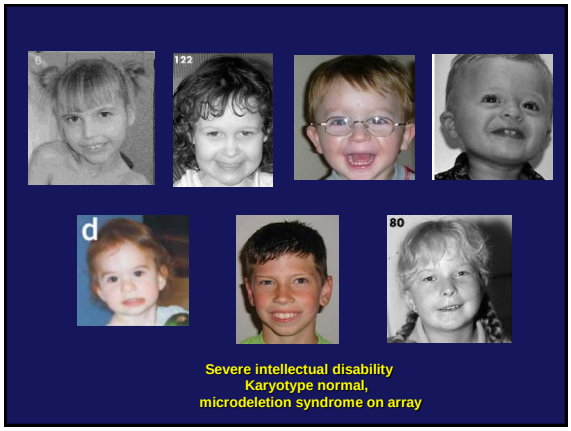
or at least 2 congenital abnormalities

Severe intellectual disability
Karyotype normal



Severe intellectual disability
Karyotype normal

Severe intellectual disability
Karyotype normal
microdeletion syndrome on array

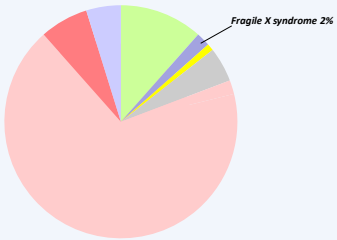


Severe intellectual disability
Karyotype normal,
microdeletion syndrome on array

Common array abnormalities

- 16p11.2 deletion
- 16p11.2 duplication
- 1q21.1 deletion
- 1q21.1 duplication
- 22q11.2 duplication
- 2p16 deletion ("NRXN1 deletion")
- 15q11.2 deletion
- Many more

Identifying the cause of intellectual disability 2010-2015



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Fragile X syndrome

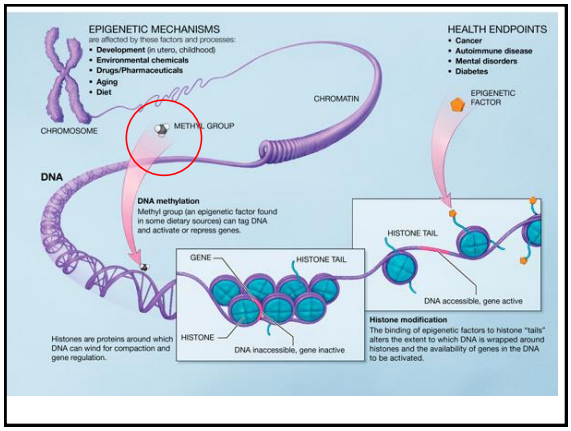
- 2% of intellectual disability
- 1 in 3600 males
- Usually no early dysmorphic features
- With time, long face, protuberant ears and enlarged testes
- Autistic features common
- Carrier mothers at risk of premature ovarian failure and FXTAS (fragile X tremor ataxia syndrome)
- Risk of FXTAS (e.g. maternal grandfather might be misdiagnosed as Parkinson's disease)

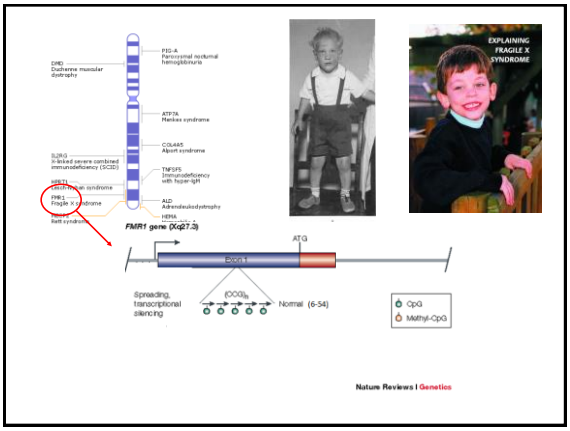
Fragile X syndrome as an example of methylation

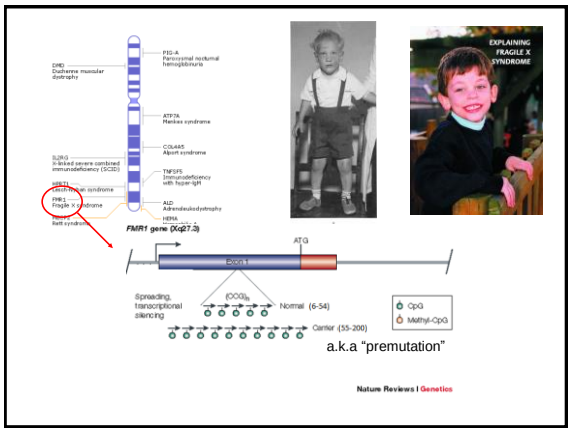
- Methylation switches off FMR1 gene, a key brain development gene (epigenetics)

Epigenetics

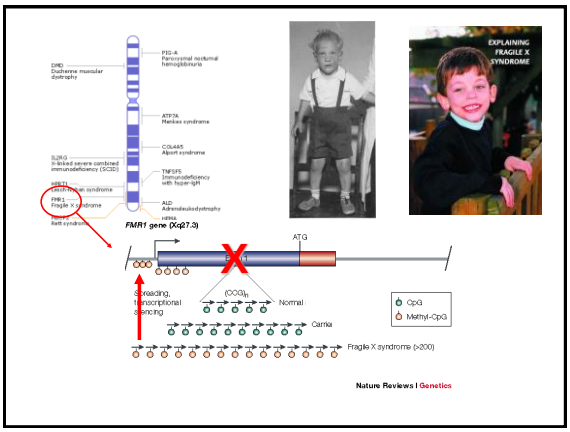
- Epigenetics means gene expression is affected (e.g. a gene is switched off, on, up or down) by DNA changes that do NOT involve DNA sequence changes
- Commonest mechanisms are methylation and histone de-acetylation





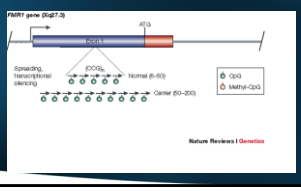


a.k.a "premutation"



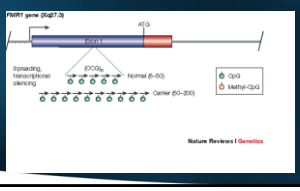
Fragile X syndrome: premutation carrier females

- 56-200 CCG repeats
- 20% risk of premature ovarian failure
- 10-15 % chance of FXTAS (tremor, ataxia)
- Risk of passing on a fully expanded CCG repeat (>200) increases with length of premutation



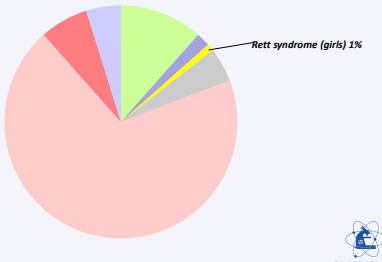
Fragile X syndrome: premutation carrier males

- 55-200 CCG repeats
- 38% risk of FXTAS by age 60
- Emerging literature on increased risk of neurocognitive problems in premutation males



- Fragile X testing remains a stand-alone test
- Microarray does not diagnose Fragile X syndrome

Identifying the cause of intellectual disability 2010-2015 (pre-genomic)



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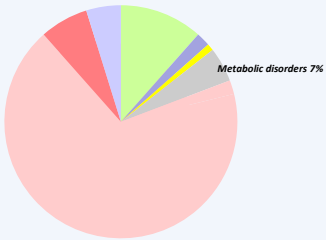
Rett syndrome

- Occurs almost exclusively in girls
- 6-18 months of apparently normal development before developing severe problems with language, communication, learning
- Hand wringing and washing a hallmark.
- Milder atypical forms
- Microarray normal
- Testing of MECP2 gene via a clinical geneticist

Identifying the cause of intellectual disability 2010-2015 (pre-genomic)



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Metabolic disorders

- Many but all individually rare
- Regression a common theme
- Blood and urine usually required
- Many will be diagnosed on newborn screen
- Notable exceptions are creatine transport disorders (1% of I.D) and congenital disorders of glycosylation (2% of I.D)

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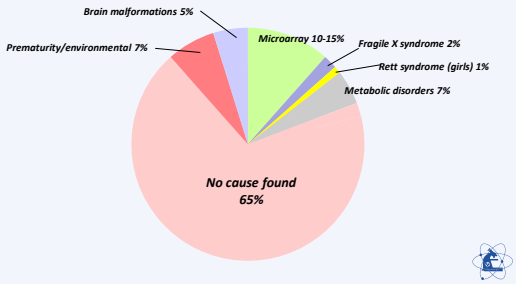

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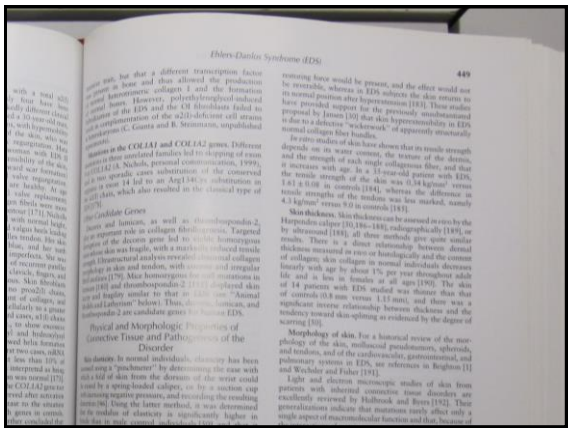


Ehlers-Danlos Syndrome (EDS) 449

restoring force would be present, and the effect would not be reversible, whereas in EDS subjects the skin returns to its normal position after hyperextension [183]. These studies have provided support for the previously unsubstantiated proposal by Jansen [30] that skin hyperextensibility in EDS is due to a defective "wickerwork" of apparently structurally normal collagen fiber bundles.

In vitro studies of skin have shown that its tensile strength depends on its water content, the texture of the dermis, and the strength of each single collagenous fiber, and that it increases with age. In a 35-year-old patient with EDS, the tensile strength of the skin was 0.34 kg/mm² versus 1.61 ± 0.08 in controls [184], whereas the difference in tensile strengths of the tendons was less marked, namely 4.3 kg/mm² versus 9.0 in controls [185].

Skin thickness. Skin thickness can be assessed *in vivo* by the Harpenden caliper [30,186–188], radiographically [189], or by ultrasound [188]; all three methods give quite similar results. There is a direct relationship between dermal thickness measured *in vivo* or histologically and the content of collagen; skin collagen in normal individuals decreases linearly with age by about 1% per year throughout adult life and is less in females at all ages [190]. The skin of 14 patients with EDS studied was thinner than that of controls (0.8 mm versus 1.15 mm), and there was a significant inverse relationship between thickness and the tendency toward skin-splitting as evidenced by the degree of scarring [30].

Morphology of skin. For a historical review of the morphology of the skin, mollusoid pseudotumors, spheroids, and tendinea, and of the cardiovascular, gastrointestinal, and pulmonary systems in EDS, see references in Beighton [1] and Wechsler and Fisher [191].

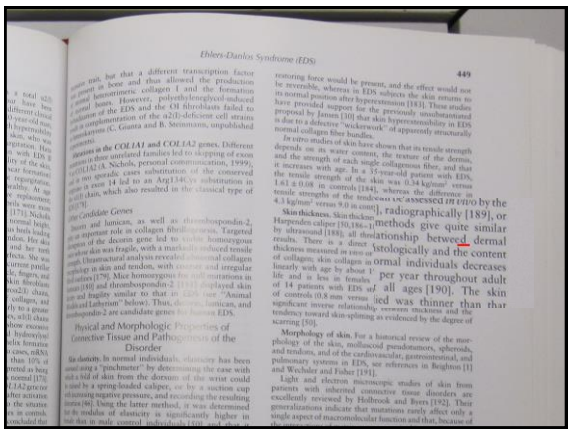
Light and electron microscopic studies of skin from patients with inherited connective tissue disorders are excellently reviewed by Holbrook and Byers [192]. Their generalizations indicate that mutations rarely affect only a single aspect of macromolecular function and that, because of

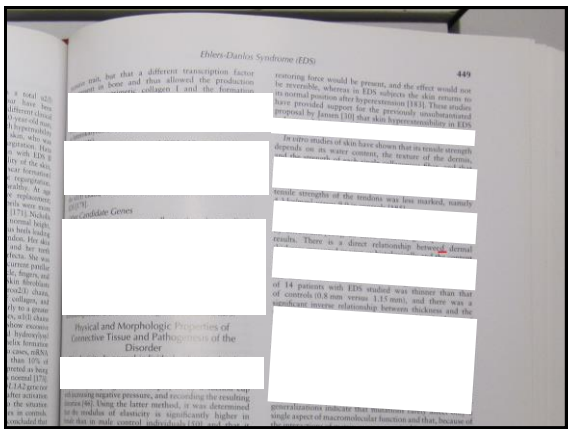
Candidate Genes

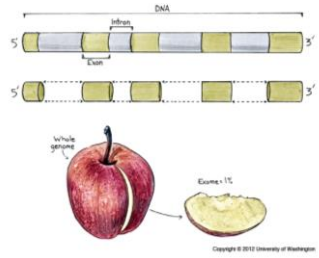
Joints and lumican, as well as thrombospondin-2, play an important role in collagen fibrillogenesis. Targeted mutation of the decorin gene led to viable homozygous offspring skin was fragile, with a markedly reduced tensile strength. Ultrastructural analysis revealed abnormal collagen fibrillogenesis in skin and tendon, with irregular and irregular diameters [179]. Mice homozygous for null mutations in the COL12A1 gene [180] and thrombospondin-2 [181] displayed skin fragility and fragility similar to that in EDS, type "Animal Models and Lethorism" below). Thus, decorin, lumican, and thrombospondin-2 are candidate genes for human EDS.

Physical and Morphologic Properties of Connective Tissue and Pathogenesis of the Disorder

In clinico. In normal individuals, elasticity has been assessed using a "pinchmeter" by determining the ease with which a fold of skin from the dorsum of the wrist could be raised by a spring-loaded caliper, or by a suction cup measuring negative pressure, and recording the resulting vertex [98]. Using the latter method, it was determined that the modulus of elasticity is significantly higher in







Identifying the cause of intellectual disability: genomic era (2015+)

Gilissen et al. *Nature* 2014; 511, 344

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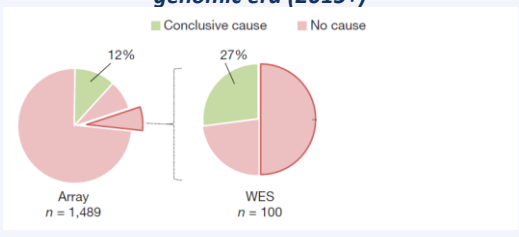
Identifying the cause of intellectual disability: genomic era (2015+)



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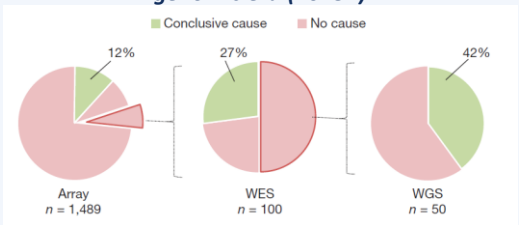

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- Inherited disease panel (550 genes): $1500
- TruSight One panel/Clinical exome (4813 genes): $1900
- Referral to a multi-D intake meeting

What investigations should a GP order?

Table 3.8.1 Investigations and indications for mental retardation

Test	Indication
Chromosome microarray (CMA)	Identifies submicroscopic deletions and duplications Different types of arrays available. Because of normal copy number variation between individuals, interpretation may be difficult and require geneticist
Chromosomes (G banded karyotype)	Recognized chromosomal syndrome, a family history of chromosomal rearrangement (balanced translocation)
Fragile X	Consider in all children with intellectual impairment, especially male children, those with a family history of X-linked intellectual impairment or children with other clinical features of the syndrome
Fluorescent in situ hybridization (FISH)	Quicker than CMA and may be useful for specific clinically identified syndromes e.g. Williams
Thyroid function	Short stature, constipation, dry skin or hair, goitre or no neonatal screen
(CPK)	If muscle weakness or prominent calves are present. Duchenne dystrophy is associated with developmental disorders
Metabolic screen	Hypoglycaemia, acidosis, altered consciousness level, unusual odour or multiple body systems affected. Low yield if neonatal screening program
Ca, PO_4	Short fourth metacarpal, short stature in pseudohypoparathyroidism
Electroencephalography (EEG)	If clinical seizures or history of sleep-related seizures
Magnetic resonance imaging (MRI) or computed tomography	If abnormal neurological signs, possible regression or moderate-severe intellectual impairment of unknown cause. MRI also for developmental disorders of brain
Lead	Exposure history, at-risk environment
Ferritin	Iron deficiency anaemia associated with delayed development
Other tests	For specific rare clinical indications

Practical Paediatrics, 7th Ed, Page 109, 2012

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Warning signs and early detection of developmental disability

Perinatal History

- Quick history with emphasis on ultrasound results (NT and morphology), maternal complications (PE, diabetes, bleeding) and delivery details
- Growth restricted?
- Any nursery time?
- Did baby go home from hospital on time?
- Early feeding prowess?

Warning signs and early detection of developmental disability

Know your milestones

- **Sitting by 6 months**
- **Passing objects hand to hand by 6 months**
- **Crawling by 9 months**
- **Pulling to stand by 12 months**
- **Walking by 14-16 months**
- **20 words and at least one 2-word sentence by age 2**
- **Draw a circle by age 2**
- **Stand on one leg by age 3**
- **Hop on 1 leg by age 4**
- **Draw a square by age 5**
- **Teachers are very helpful after that**

Warning signs and early detection of developmental disability

Know your milestones

- **20 words and at least one 2-word sentence by age 2**

Red flags and when to investigate

- Regression
- Family considering more children
- Diagnosis = funding
- Intellectual disability and any congenital abnormality
- Intellectual disability and disturbance of growth
- Intellectual disability and abnormal skin
- Family history of intellectual disability

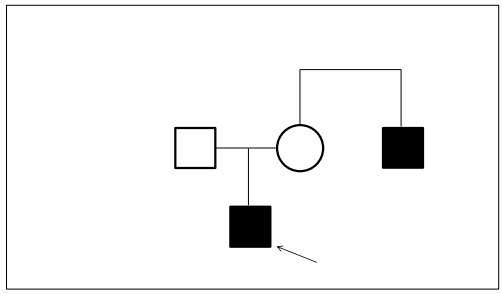
When to refer and to whom?

General Paediatrician

- Regression
- Consistent inability to meet milestones
- Intellectual disability and any congenital abnormality
- Intellectual disability and disturbance of growth
- Intellectual disability and abnormal skin
- Diagnosis = funding

Clinical Geneticist

- Seen by General Paediatrician already and family considering more children
- Family history of intellectual disability
- Anyone with fragile X syndrome or FH of
- No answers, family want second opinion



Role of the GP in ongoing management of developmental disability

Summary of important points

- Loss of function–Is it organic, dementia or depression?
- Look for pain/physical causes.
- Check that new medications have not made things worse.
- Always ask about sleep and appetite changes when checking for depression. Anhedonia is a particularly important and useful clue to depression.
- Look for specific psychiatric diagnoses.
- Refer early to a psychologist
- Refer/telephone a psychiatrist for advice regarding drugs.
- Judicious use of PRN medications can be helpful in specific situations.

Aust Fam Phys 2011;40

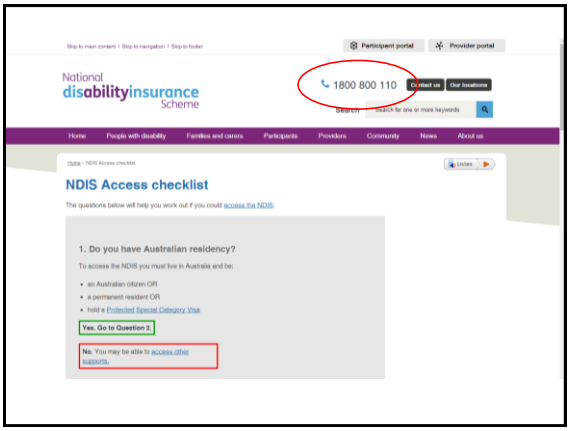
National disability insurance scheme: what is the GP's role?

Background

The NDIS commenced in South Australia on 1 July 2013 for children aged 5 and under.

Once individual plans are completed for children in this age group, the NDIS will start for older children.

From 1 July 2016, the NDIS will progressively roll out in South Australia and by July 2018, all eligible residents will be covered.



2. Are you under 65 years old?

To access the NDIS you must be aged under 65 years.

In some locations, you need to be a certain age to access the NDIS during the trial period.

Yes. Go to Question 3.

No. You may be able to access other supports.

3. Do you live in one of these areas?

To access the NDIS right now, you must live in one of these areas. In some of these areas, you also need to be a certain age to access the Scheme.

NDIS locations in Australia:

1. Hunter area, New South Wales
2. Nepean Blue Mountains area, New South Wales (for children and young people aged under 18 on 1 July 2015)
3. Australian Capital Territory
4. Tasmania (for people aged 15-24)
5. Barwon area, Victoria
6. South Australia (for children aged 13 and under on 1 July 2014)
7. Perth Hills area, Western Australia
8. Barkly area, Northern Territory

Rollout information for New South Wales has been announced. See the NSW page for further details.

Rollout information for Victoria has been announced. See the Victoria page for further details.

Yes. Go to Question 4.

No. You will need to wait for full scheme roll-out when the NDIS will be available in your area.

4. Do you usually need support from a person or equipment to do everyday things for yourself because of an impairment or condition that is likely to be permanent?

To meet the NDIS disability rules you need to have an impairment or condition that is likely to be permanent (lifelong) and that stops you from doing everyday things by yourself.

The following questions may help you decide if your answer is 'yes'.

Do you usually need support from a person or assistive equipment so you can:

- understand and be understood by other people?
- make and keep friends and cope with feelings and emotions?
- understand, remember and learn new things?
- get out of bed and move around the home and outside the home?
- take a bath or shower, dress and eat?
- do daily jobs, handle money and make decisions?

Yes. Call the NDIS on 1800 800 110 if you have any questions or to ask for an access request form.

No. Go to question 5.

5. Do you need some supports now to reduce your support needs in the future?

To meet the NDIS early intervention rules, you need to

- have an impairment or condition that is likely to be permanent (lifelong); or
- be a child under 6 years of age with a developmental delay and the delay means you usually need more help with your self-care, communication, learning or motor skills than another child of the same age.

Early intervention supports provided by the NDIS are those not provided by any other services such as health and education.

The following questions may help you decide if your answer is 'yes'.

Would early intervention supports:

- reduce the impact of your impairment or condition or developmental delay?
- stop the impact of your impairment or condition from getting worse?
- strengthen your informal supports, such as helping a carer to keep supporting you?

Yes. Call the NDIA on 1800 800 110 if you have any questions or to ask for an access request form.

No. You may be able to access other supports.

National disabilityinsurance Agency

Access Request Form

Complete this form to request to become a participant in the National Disability Insurance Scheme (NDIS). You must provide proof of age and residence (including citizenship or visa status) with this Access Request Form. We cannot make a decision on your access request without this information.

If you have questions about this form, need help to complete it or would like more information about the NDIS, please contact us:

Phone: 1800 800 110 | TTY: 1800 555 677 | Speak and Listen: 1800 555 727

Internet Relay: Visit http://relayservice.gov.au and ask for 1800 800 110

Email: nationalaccessteam@ndis.gov.au

Part A: Your details (the person wishing to become an NDIS participant)

Full name	
Date of birth (DD/MM/YYYY)	___/___/____
Gender	☐ Male ☐ Female ☐ Unspecified (X)
Are you of Aboriginal or Torres Strait Islander origin?	☐ No ☐ Yes – Aboriginal ☐ Yes – Torres Strait Islander ☐ Yes – Aboriginal and Torres Strait Islander ☐ Do not wish to disclose
Country of birth	
Language spoken at home	
Are you living in Australia permanently?	☐ Yes ☐ No
Current home address	
	State: Postcode:
Is this a protected address?	☐ Yes ☐ No

Personal-to-Confidence when complete OFFICIAL DOCUMENT—DO NOT COPY

August 2016 Version 7.0

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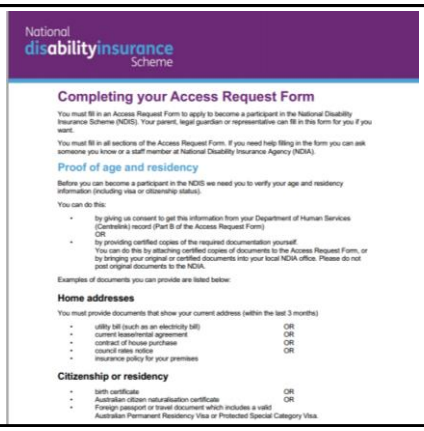
- Access team
- Request form not accessible by any other means
- Up to the 5th version of the form
- Clear documentation of patient's function is very important
- If straightforward, 21 days
- If complex, higher delegation required



National disabilityinsurance Scheme

Completing your Access Request Form

You must fill in an Access Request Form to apply to become a participant in the National Disability Insurance Scheme (NDIS). Your parent, legal guardian or representative can fill in this form for you if you want.

You must fill in all sections of the Access Request Form. If you need help filling in the form you can ask someone you know or a staff member at National Disability Insurance Agency (NDIA).

Proof of age and residency

Before you can become a participant in the NDIS we need you to verify your age and residency information (including visa or citizenship status).

You can do this:

- by giving us consent to get this information from your Department of Human Services (Centrelink) record (Part B of the Access Request Form)
  OR
- by providing certified copies of the required documentation yourself.
  You can do this by attaching certified copies of documents to the Access Request Form, or by bringing your original or certified documents into your local NDIA office. Please do not post original documents to the NDIA.

Examples of documents you can provide are listed below:

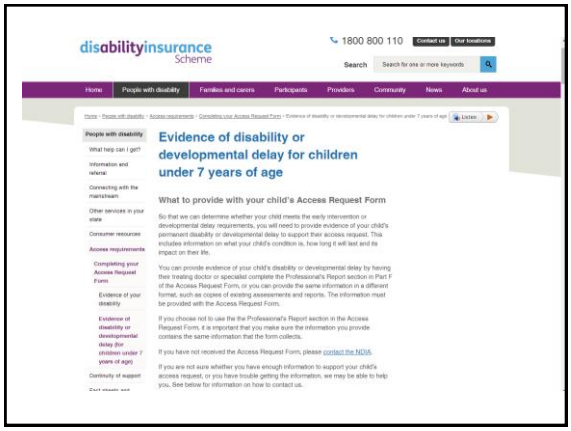
Home addresses

You must provide documents that show your current address (within the last 3 months)

- utility bill (such as an electricity bill) OR
- current lease/rental agreement OR
- contract of house purchase OR
- council rates notice OR
- insurance policy for your premises

Citizenship or residency

- birth certificate OR
- Australian citizen naturalisation certificate OR
- Foreign passport or travel document which includes a valid Australian Permanent Residency Visa or Protected Special Category Visa.



disabilityinsurance Scheme

1800 800 110 Contact us Our locations

Search Search for one or more keywords

Home | People with disability | Families and carers | Participants | Providers | Community | News | About us

People with disability
What help can I get?
Information and referral
Connecting with the mainstream
Other services in your state
Consumer resources
Access requirements
Completing your Access Request Form
Evidence of your disability
Evidence of disability or developmental delay (for children under 7 years of age)
Continuity of support

Evidence of disability or developmental delay for children under 7 years of age

What to provide with your child's Access Request Form

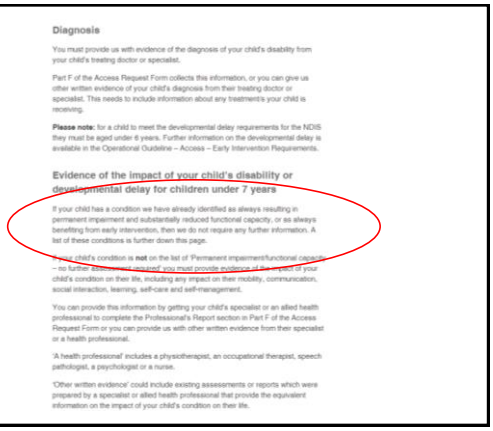
So that we can determine whether your child meets the early intervention or developmental delay requirements, you will need to provide evidence of your child's permanent disability or developmental delay to support their access request. This includes information on what your child's condition is, how long it will last and its impact on their life.

You can provide evidence of your child's disability or developmental delay by having their treating doctor or specialist complete the Professional's Report section in Part F of the Access Request Form, or you can provide the same information in a different format, such as copies of existing assessments and reports. The information must be provided with the Access Request Form.

If you choose not to use the the Professional's Report section in the Access Request Form, it is important that you make sure the information you provide contains the same information that the form collects.

If you have not received the Access Request Form, please contact the NDIA.

If you are not sure whether you have enough information to support your child's access request, or you have trouble getting the information, we may be able to help you. See below for information on how to contact us.



Diagnosis

You must provide us with evidence of the diagnosis of your child's disability from your child's treating doctor or specialist.

Part F of the Access Request Form collects this information, or you can give us other written evidence of your child's diagnosis from their treating doctor or specialist. This needs to include information about any treatment/s your child is receiving.

Please note: for a child to meet the developmental delay requirements for the NDIS they must be aged under 6 years. Further information on the developmental delay is available in the Operational Guideline – Access – Early Intervention Requirements.

Evidence of the impact of your child's disability or developmental delay for children under 7 years

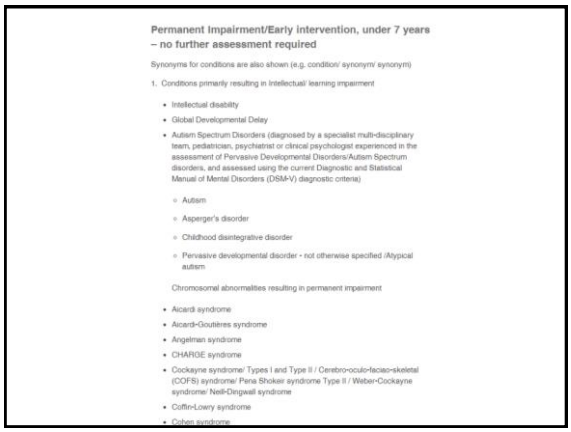
If your child has a condition we have already identified as always resulting in permanent impairment and substantially reduced functional capacity, or as always benefiting from early intervention, then we do not require any further information. A list of these conditions is further down this page.

If your child's condition is **not** on the list of 'Permanent impairment/functional capacity – no further assessment required' you must provide evidence of the impact of your child's condition on their life, including any impact on their mobility, communication, social interaction, learning, self-care and self-management.

You can provide this information by getting your child's specialist or an allied health professional to complete the Professional's Report section in Part F of the Access Request Form or you can provide us with other written evidence from their specialist or a health professional.

'A health professional' includes a physiotherapist, an occupational therapist, speech pathologist, a psychologist or a nurse.

'Other written evidence' could include existing assessments or reports which were prepared by a specialist or allied health professional that provide the equivalent information on the impact of your child's condition on their life.



Permanent Impairment/Early intervention, under 7 years – no further assessment required

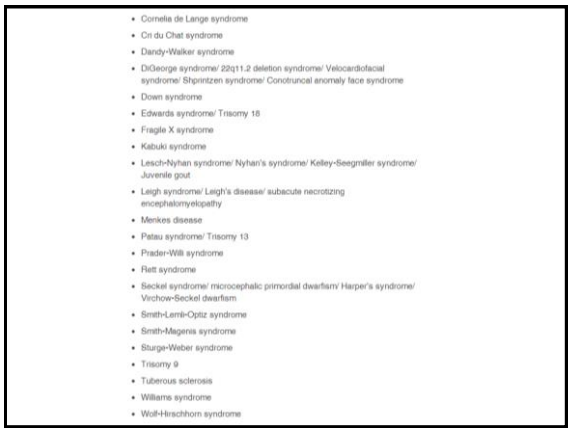
Synonyms for conditions are also shown (e.g. condition/ synonym/ synonym)

1. Conditions primarily resulting in Intellectual/ learning impairment

- Intellectual disability
- Global Developmental Delay
- Autism Spectrum Disorders (diagnosed by a specialist multi-disciplinary team, pediatrician, psychiatrist or clinical psychologist experienced in the assessment of Pervasive Developmental Disorders/Autism Spectrum disorders, and assessed using the current Diagnostic and Statistical Manual of Mental Disorders (DSM-V) diagnostic criteria)
  - Autism
  - Asperger's disorder
  - Childhood disintegrative disorder
  - Pervasive developmental disorder - not otherwise specified /Atypical autism

Chromosomal abnormalities resulting in permanent impairment

- Aicardi syndrome
- Aicardi-Goutières syndrome
- Angelman syndrome
- CHARGE syndrome
- Cockayne syndrome/ Types I and Type II / Cerebro-oculo-facio-skeletal (COFS) syndrome/ Pena Shokair syndrome Type II / Weber-Cockayne syndrome/ Neill-Dingwall syndrome
- Coffin-Lowry syndrome
- Cohen syndrome



- Cornelia de Lange syndrome
- Cri du Chat syndrome
- Dandy-Walker syndrome
- DiGeorge syndrome/ 22q11.2 deletion syndrome/ Velocardiofacial syndrome/ Shprintzen syndrome/ Conotruncal anomaly face syndrome
- Down syndrome
- Edwards syndrome/ Trisomy 18
- Fragile X syndrome
- Kabuki syndrome
- Lesch-Nyhan syndrome/ Nyhan's syndrome/ Kelley-Seegmiller syndrome/ Juvenile gout
- Leigh syndrome/ Leigh's disease/ subacute necrotizing encephalomyelopathy
- Menkes disease
- Patau syndrome/ Trisomy 13
- Prader-Willi syndrome
- Rett syndrome
- Seckel syndrome/ microcephalic primordial dwarfism/ Harper's syndrome/ Virchow-Seckel dwarfism
- Smith-Lemli-Opitz syndrome
- Smith-Magenis syndrome
- Sturge-Weber syndrome
- Trisomy 9
- Tuberous sclerosis
- Williams syndrome
- Wolf-Hirschhorn syndrome

2. Conditions primarily resulting in Neurological impairment

Systemic atrophies primarily affecting the central nervous system:

- Friedrich's ataxia
- Hereditary spastic paraplegia/ Infantile-onset ascending hereditary spastic paralysis/ L1 syndrome/ spastic paraplegias types 2 and 11
- Louis-Bar syndrome/ Ataxia-telangiectasia
- Niemann-Pick disease (Types A and C)
- Progressive bulbar palsy of childhood/ Fazio-Londe disease

The following spinal muscular atrophies:

- Spinal muscular atrophy Type I/ Werdnig Hoffmann disease/ infantile SMA
- Spinal muscular atrophy Type II/ Dubowitz disease
- Spinal muscular atrophy Type III Kugelberg-Welander disease/ juvenile SMA
- Spinal muscular atrophy lower extremity dominant/ SMA-LED
- X-linked spinal muscular atrophy

Extrapyramidal and movement disorders:

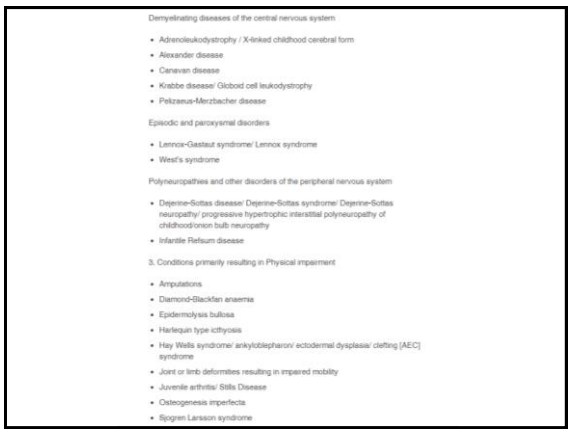
- Hallervorden-Spatz syndrome / Pantothenate kinase-associated neurodegeneration (PKAN)/ neurodegeneration with brain iron accumulation 1 (NBIA 1)

Other degenerative diseases of the nervous system:

- Alpers disease/ Alpers syndrome/ Grey-matter degeneration/ Progressive sclerosing poliodystrophy/ Progressive infantile poliodystrophy

Demyelinating diseases of the central nervous system

- Adrenoleukodystrophy / X-linked childhood cerebral form
- Alexander disease



Demyelinating diseases of the central nervous system

- Adrenoleukodystrophy / X-linked childhood cerebral form
- Alexander disease
- Canavan disease
- Krabbe disease/ Globoid cell leukodystrophy
- Pelizaeus-Merzbacher disease

Episodic and paroxysmal disorders

- Lennox-Gastaut syndrome/ Lennox syndrome
- West's syndrome

Polyneuropathies and other disorders of the peripheral nervous system

- Dejerine-Sottas disease/ Dejerine-Sottas syndrome/ Dejerine-Sottas neuropathy/ progressive hypertrophic interstitial polyneuropathy of childhood/onion bulb neuropathy
- Infantile Refsum disease

3. Conditions primarily resulting in Physical impairment

- Amputations
- Diamond-Blackfan anaemia
- Epidermolysis bullosa
- Harlequin type ichthyosis
- Hay Wells syndrome/ ankyloblepharon/ ectodermal dysplasia/ clefting [AEC] syndrome
- Joint or limb deformities resulting in impaired mobility
- Juvenile arthritis/ Stills Disease
- Osteogenesis imperfecta
- Sjogren Larsson syndrome

Diseases of myoneural junction and muscle

- Congenital muscular dystrophy
- Congenital myotonia / Thomsens disease/ Becker myotonia
- Distal muscular dystrophy
- Duchenne muscular dystrophy
- Emery-Dreifuss muscular dystrophy
- Facioscapulohumeral muscular dystrophy
- Myotubular myopathy
- Oculopharyngeal muscular dystrophy
- Paramyotonia Congenita

Cerebral palsy and other paralytic syndromes

- Cerebral palsy
- Diplegia
- Hemiplegia
- Monoplegia
- Paraplegia
- Quadriplegia
- Tetraplegia

4. Conditions resulting in Sensory and/or Speech impairment

- Permanent blindness in both eyes, diagnosed and assessed by an ophthalmologist as follows:
  1. Corrected visual acuity (extent to which an object can be brought into focus) on the Snellen Scale must be less than or equal to 6/60 in both eyes; or
  2. Constriction to within 10 degrees or less of arc of central fixation in the better eye, irrespective of corrected visual acuity (i.e. visual fields are

Evidence of the impact of your child's disability or developmental delay for children under 7 years

If your child has a condition we have already identified as always resulting in permanent impairment and substantially reduced functional capacity, or as always benefiting from early intervention, then we do not require any further information. A list of these conditions is further down this page.

If your child's condition is **not** on the list of 'Permanent impairment/functional capacity – and further assessment required' you must provide evidence of the impact of your child's condition on their life, including any impact on their mobility, communication, social interaction, learning, self-care and self-management.

You can provide this information by getting your child's specialist or an allied health professional to complete the Professional's Report section in Part F of the Access Request Form or you can provide us with other written evidence from their specialist or a health professional.

'A health professional' includes a physiotherapist, an occupational therapist, speech pathologist, a psychologist or a nurse.

'Other written evidence' could include existing assessments or reports which were prepared by a specialist or allied health professional that provide the equivalent information on the impact of your child's condition on their life.

Submitting evidence

The evidence about your child's disability or developmental delay must be submitted with their Access Request Form. Their access request will not be considered complete unless we have received all the information we need. We will use the information about your child's disability or developmental delay to help us determine whether your child can become a participant in the NDIS.

NDIS funding

- Self managed or agency managed
- Families have an "NDIS planner"
- Families attend OT/speech/physio, pay themselves then claim back from NDIS
- Most children receive a "trans disciplinary package" worth $8000-$12000 per year
- Completely separate from all other Centrelink payments
- Does not pay for transportation costs

SA Clinical Genetics Service

- Paediatric and Reproductive Genetics
- Adult Genetics
- Metabolic Genetics

- Four fulltime clinical geneticists, five part time
- 10 genetic counsellors

- 81617375

Thank you

Exome sequencing

- General principle is to capture only the coding part of the genome (<2% in total, about 30Mb) and then to use new sequencing techniques to sequence this DNA
- Massively-parallel DNA sequencing is the mainstay of “next generation sequencing”
- Repeated cycles of sequencing on a massive number of fragments allows for excellent coverage of the DNA sections in question, in this case coding exons
- Next variants in the DNA sequence are compared to reference sequence for differences (variant calling)