Dementia Diagnostic Criteria in People with Down's Syndrome:

Back to the Future?

Multi-Disciplinary LD Academic Seminar
Ortus Centre
Maudsley Hospital
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The Puzzle (Dementia in LD) ……...

RESEARCH ARTICLE

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Dementia diagnostic criteria in Down syndrome

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Objective: Dementia is a common clinical presentation among older adults with Down syndrome. The presentation of dementia in Down syndrome differs compared with typical Alzheimer's disease. The performance of manualised dementia criteria in the International Classification of Diseases (ICD)-10 and Diagnostic and Statistical Manual of Mental Disorders-IV-Text Revision (DSM-IV-TR) is uncertain in this population.

We aimed to determine the concurrent validity and reliability of clinicians' diagnoses of dementia against ICD-10 and DSM-IV-TR diagnoses. Validity of clinical diagnoses were also explored by establishing the stability of diagnoses over time.

Content

- History.
- Background Facts.
- Aims.
- Methodology.
- Results.
- Conclusions.
- Strengths & Limitations of Study.

History

History

- DID-SIG = Dementia in Intellectual Disabilities Special Interest Group (originally pan-London).
- Led by Dr Andre Strydom (UCL).
- Problems with small case examples in local areas.
- Problems with small nos. when developing an evidence-base.
- ADSID = Aging with Down Syndrome and Intellectual Disabilities Research Database.
- Collaborative Multi-Centre research.

Research Group

- Dr Andre Strydom (Principal Investigator) / Dr Rory Sheehan / Dr Amanda Sinai / Dr Angela Hassiotis [UCL].
- Dr Pippa Blatchford.
- Dr Ingrid Bohnen [CNWL NHS Foundation Trust].
- Dr Simon Bonnell.
- Dr Ken Courtenay [Barnet Enfield Haringey Mental Health NHS Trust].
- Dr Jane McCarthy [SLAM NHS Foundation Trust].
- Dr Kamalika Mukherjee.
- Dr Asim Naeem [SWLStG Mental Health NHS Trust].
- Dr Dimitrios Paschos.
- Dr Natalia Perez-Achiaga.
- Dr Vijaya Sharma [Watford].
- Dr David Thomas (East London Foundation NHS Trust].
- Dr Zusana Walker [UCL].

Acknowledgement / Thanks

- Hannah Boardman / Sharon Jakobowitz / Camini Fernandez [Research Assistants, UCL].
- Khadija Rantell [Statistician, UCL].
- The Bailey Thomas Charitable Fund.

Background Facts

Dementia in People with Down's Syndrome

- Neuropathological changes typical of Alzheimer's disease (AD) almost universal in people with Down's Syndrome (DS) > 40 yrs age.

- Mean age of onset of AD in DS 50 – 55 yrs age.

- By 60 yrs age, 30-40 % people with DS have AD (Coppus et al, 2006; Tyrell et al, 2001; Holland et al, 1998).

- Presentation of AD in DS is different to generic population

  - Prominent BPSD*.
  - ? Influence of frontal lobe deterioration.

*is this an artefact – due to diagnosis taking longer in this patient group due to pre-existing cognitive impairment?

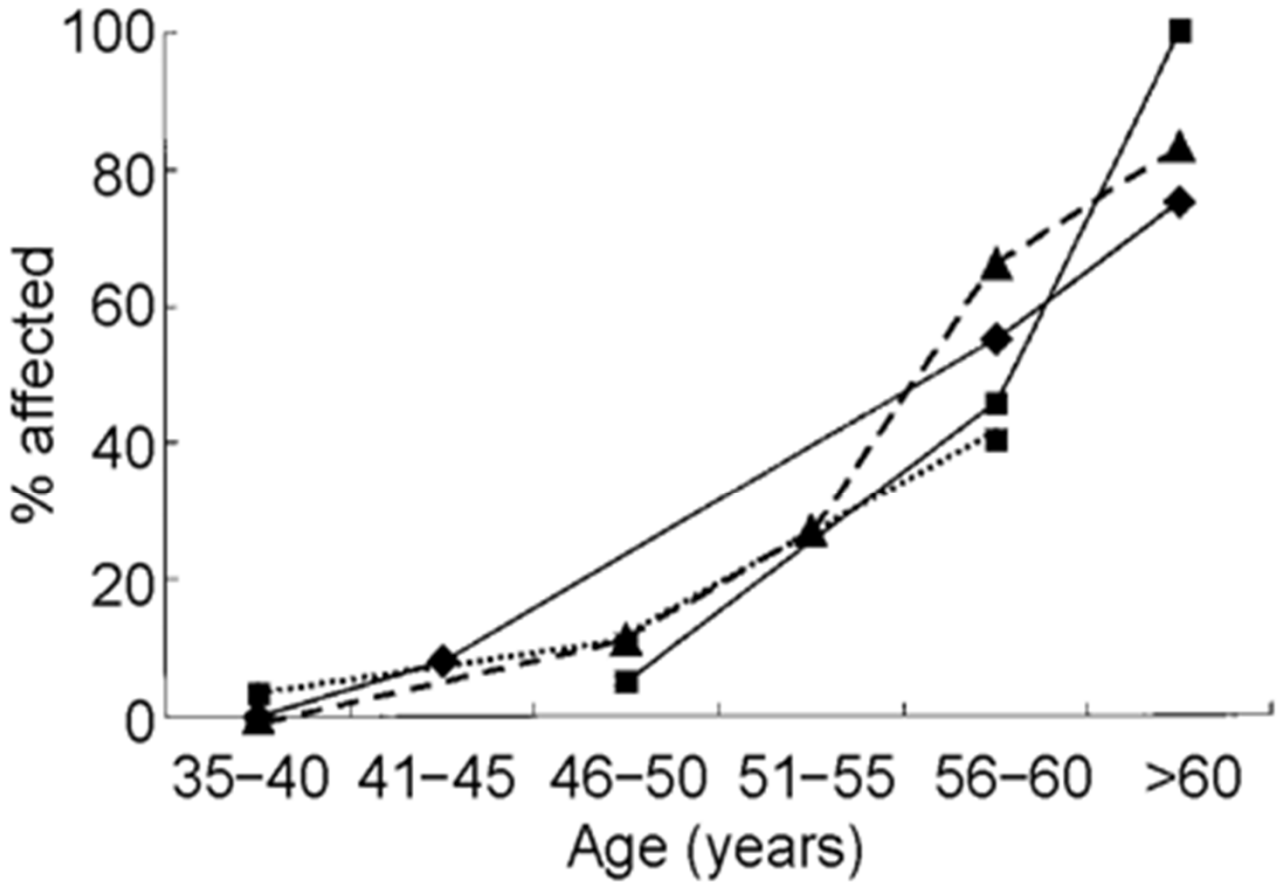
Dementia in People with Down's Syndrome

- Subtle cognitive decline difficult to elicit – depends on informant history.

- Dementia will become a more common presentation in people with DS as their life expectancy increases (Bittles et al, 2007).

- Early diagnosis important.
  - Antidementia medications.
  - Appropriate psychosocial interventions.

- Standardised assessments have been developed based on informant interviews +/- direct cognitive testing.
  - Which is better? (Strydom & Hassiotis, 2003).
  - Using physician's own 'clinical judgement' was once a 'gold standard'.


100
80
60
40
20
0
% affected
35–40
41–45
46–50
51–55
56–60
>60
Age (years)

Prevalence rates for dementia subtypes in older people with LD without DS (Strydom et al, 2007).

Dementia sub-type	**Prevalence rate in > 65 yrs age (number - % in brackets) (total n = 142)**
Alzheimer's dementia	17 (12 %)
Lewy Body Dementia (DLB)	11 (7.7 %)
Frontotemporal dementia	6 (4.2 %)
Vascular dementia	5 (3.5 %)

Clinical Assessment of Alzheimer's Dementia in Down's syndrome:

Clinical Domains of Dementia

Memory	❑Progressive forgetfulness of recent events eg, meals / day activities / planned outings [episodic memory impairment]. ❑Geographical disorientation eg, getting muddled in familiar environments. ❑Forgetting names of / failing to recognise familiar people [semantic memory impairment]. ❑Loss of previously-learnt skills eg, making cup of tea [procedural memory impairment]
Abstract reasoning (judgement / planning / organisation)	❑Selecting inappropriate clothing for activities / putting on clothes back-to-front. ❑Difficulty dressing / feeding self / brushing teeth [apraxia]. ❑Difficulty following > 1 instruction.

Clinical Assessment of Alzheimer's Dementia in Down's syndrome:

Clinical Domains of Dementia

Abstract reasoning (judgement / planning / organisation) [contd.]	❑Inappropriate use of common objects eg, trying to write with a spoon [agnosia]. ❑Unable to distinguish between night & day. ❑Difficulty with reading [alexia], writing [agraphia] or language [aphasia].
Mood	❑Low mood / loss of interest / apathy. ❑Emotional lability eg, unexplained tearfulness. ❑Restlessness / irritability / altered sleep.
Social behaviours	❑Increased dependence on others. ❑Personality change eg, aggresssion / pervasive or obsessional slowness. ❑Fear of stairs / curbs / uneven surfaces. ❑'Covering up' memory loss eg, by saying 'sorry'.

Clinical Assessment of Alzheimer's Dementia in Down's syndrome:

Clinical Domains of Dementia

Perceptions	❑Auditory, visual or tactile hallucinations.
Neurological	❑Altered gait / falls. ❑Bradykinesia-like slowness in movements. ❑Seizures (occur early in AD & DS). ❑Dystonia / myoclonus. ❑Urinary incontinence.

Aims

Aims

1) Determine the concurrent validity and reliability of clinicians' diagnoses of AD in DS against ICD-10 & DSM-IV diagnoses.

2) Explore the validity of the clinical diagnoses by establishing their stability over time.

3) Establish the inter-rater reliability of dementia diagnoses.

Methodology

Methodology

- Data from ‘dementia assessments’ conducted since 1996 by different clinicians across several sites in London and the surrounding area.

- Clinical data (anonymised) from adults with Down syndrome only. Excluded participants for whom insufficient data was available.

- Retrospective data collected from medical / health records using a structured data collection form, and entered into ADSID database.
  - basic demographic information.
  - cognitive, behavioural and emotional symptoms from each initial + F/U assessments.
  - results of any screening tests.
  - recent physical and mental health problems / physical investigations.
  - diagnosis outcomes (dementia – poss. dementia – no dementia)

Ethics Approval

- ADSID study was approved by the Newcastle and North Tyneside 1 Research Ethics Committee.

- Approval for collecting anonymised data from medical records was obtained from the National Information Governance Board.

Clinical Vignettes

Structured data collection form
[incl. free text description of symptoms recorded in notes]

Anonymised ‘clinical vignette’ (by research assistants)
[items removed: reference to diagnosis / antidementia drug Tx / etc.].

Vignettes rated (next slide)

Rating of Clinical Vignettes

- Each vignette rated by 2 independent raters.
- Raters – clinicians (mainly psychiatrists + some psychologists) working in LD Psychiatry or Old Age Psychiatry.
- Raters ‘blind’ to pt’s true clinical diagnosis / Tx received.
- If disagreement in ratings, consensus rating derived after discussion between raters.
- Outcome of each individual rater recorded prior to consensus rating to determine inter-rater reliability.

‘Diagnostic Rating’ of Clinical Vignettes

1) ICD-10

- ❑ No dementia.
- ❑ Dementia.
- ❑ Tentative dementia.

2) DSM-IV

- ❑ Dementia.
- ❑ No dementia.

3) Rater’s ‘clinical judgement’

- ❑ Dementia.
- ❑ Possible dementia (likely dementia – sig. decline over ≥ 6/12 – but incomplete evidence from vignette to be more certain of diagnosis).
- ❑ Cognitive concern (deterioration in cognitive function but unable to exclude other cause).
- ❑ No dementia.

Table 1 Summary of ICD-10 and DSM-IV-TR diagnostic criteria for Alzheimer's dementia

Criterion	ICD-10	DSM-IV-TR
Memory impairment	X	X
Disturbance in higher cortical function[a]		
Executive functioning	X	X
Aphasia		X
Apraxia		X
Agnosia		X
Decline in behavioural or emotional function		
Emotional lability	X	
Irritability	X	
Apathy	X	
Coarsening of social behaviour	X	
Deficits cause significant impairment in functioning		X
Gradual onset and progression		X
Duration at least 6 months	X	
Exclusions		
Delirium	X	X
Other CNS, systemic or substance-induced conditions	X	X
Other mental illness		X

[a]Only one of these symptoms need be present for DSM-IV-TR diagnosis

Stability of Diagnoses over Time

- Comparison of outcomes of raters' assessments from time of clinical diagnosis (t) and at the first (t +1) and second (t +2) assessments following a clinical diagnosis.

Inter-Rater Reliability

- Recorded the raters' diagnoses before they agreed the diagnosis in a sub-set of 23 cases.

1) ICD-10
- No dementia.
- Dementia*.
- Tentative dementia*.

2) DSM-IV
- Dementia*.
- No dementia.

3) Rater's 'clinical judgement'
- Dementia*.
- Possible dementia* (likely dementia – sig. decline over ≥ 6/12 – but incomplete evidence from vignette to be more certain of diagnosis).
- Cognitive concern (deterioration in cognitive function but unable to exclude other cause).
- No dementia.

Statistical Analysis

- Data entered onto SPSS.
- Analysed using SPSS – 21.
- Cohen’s Kappa.

Results

Demographics

- 85 people with Down's syndrome.
- Male = 40 (47.1 %), Female = 45 (52.9 %).
- Dementia, n = 64 (75.3 %); No dementia, n = 21 (24.7 %).
- Mild LD, n = 21 (24.7 %).
  Moderate LD, n = 40 (47.1 %)
  Severe / profound LD, n = 12 (14.1 %)
  Unknown level of LD, n = 12 (14.1 %)
- Age range (for diagnosis of dementia, where relevant): 35.5 – 70.9 yrs.
- Mean (+/- SD) age of diagnosis of dementia (where relevant): 55.4 +/- 6.6. yrs.

‘Diagnostic Rating’ of Clinical Vignettes

1) ICD-10

- ❑ No dementia.
- ❑ Dementia.
- ❑ Tentative dementia.

2) DSM-IV

- ❑ Dementia.
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- ❑ Dementia.
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- ❑ Cognitive concern (deterioration in cognitive function but unable to exclude other cause).
- ❑ No dementia.

Clinical Diagnosis
vs.
Raters' ICD-10 outcomes

	Raters' ICD-10 outcome: Dementia	No dementia	**TOTAL**
Clinical Diagnosis:			
Dementia			64
No dementia			21
TOTAL			85

Clinical Diagnosis
vs.
Raters' ICD-10 outcomes

	Raters' ICD-10 outcome:		**TOTAL**
	Dementia	No dementia	
Clinical Diagnosis:			
Dementia			64
No dementia			21
TOTAL	45	40	85

Clinical Diagnosis
vs.
Raters' ICD-10 outcomes

	Raters' ICD-10 outcome:		**TOTAL**
	Dementia	No dementia	
Clinical Diagnosis:			
Dementia	40	24	64
No dementia	5	16	21
TOTAL	45	40	85

Clinical Diagnosis
vs.
Raters' DSM-IV outcomes

	Raters' DSM-IV outcome: Dementia	No dementia	**TOTAL**
Clinical Diagnosis:			
Dementia			64
No dementia			21
TOTAL			85

Clinical Diagnosis
vs.
Raters' DSM-IV outcomes

	Raters' DSM-IV outcome:		**TOTAL**
	Dementia	No dementia	
Clinical Diagnosis:			
Dementia			64
No dementia			21
TOTAL	36	49	85

Clinical Diagnosis
vs.
Raters' DSM-IV outcomes

	Raters' DSM-IV outcome:		**TOTAL**
	Dementia	No dementia	
Clinical Diagnosis:			
Dementia	33	31	64
No dementia	3	18	21
TOTAL	36	49	85

Clinical Diagnosis
vs.
Raters' 'Clinical Impression'

	Raters' 'Clinical Impression': Dementia	No dementia	**TOTAL**
Clinical Diagnosis:			
Dementia			64
No dementia			21
TOTAL			85

Clinical Diagnosis
vs.
Raters' 'Clinical Impression'

	Raters' 'Clinical Impression':		**TOTAL**
	Dementia	No dementia	
Clinical Diagnosis:			
Dementia			64
No dementia			21
TOTAL	54	31	85

Clinical Diagnosis
vs.
Raters' 'Clinical Impression'

	Raters' 'Clinical Impression':		**TOTAL**
	Dementia	No dementia	
Clinical Diagnosis:			
Dementia	45	19	64
No dementia	9	12	21
TOTAL	54	31	85

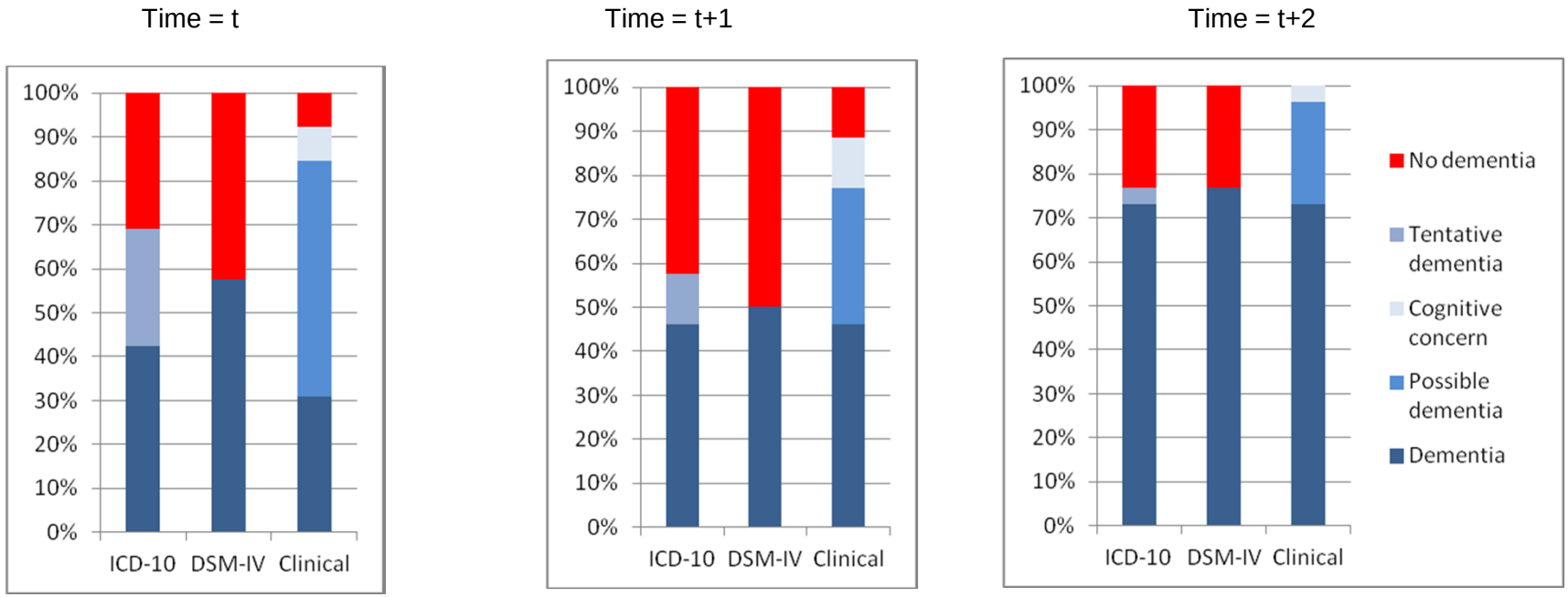
Summary of Results

	Correctly Diagnosed with dementia *(n / 64)*
ICD-10	45 / 64 (70.3 %)
DSM-IV	36 / 64 (56.3 %)
'Expert clinician's impression'	54 / 64 (84.4 %)

Summary of Results

	Correctly Diagnosed with dementia *(n / 64)*	**False positives** *(n / 21)*
ICD-10	45 / 64 (70.3 %)	5 / 21 (23.8 %)
DSM-IV	36 / 64 (56.3 %)	3 / 21 (14.3 %)
'Expert clinician's impression'	54 / 64 (84.4 %)	9 / 21 (42.9 %)

<u>Figure 1</u> – Stability of diagnoses over time – showing ratings at time of clinician's diagnosis of dementia (t), and first (t+1) and second (t+2) assessments following clinician's diagnosis of dementia (n=26)



Inter-Rater Reliability

- Sub-set of 23 initial assessments (27.1 % of overall sample).

- Cohen's Kappa for rater agreements:

✓ 0.9111* (ICD-10)

✓ 0.704* (DSM-IV)

✓ 0.826* (rater's clinical judgement)

*statistically significant at $p \leq 0.001$ level.

Results

- Just under half of those with a clinical diagnosis of dementia were rated as having dementia at initial assessment by all three of ICD-10, DSM-IV and rater's clinical judgement.
- The overall figure for diagnosis of dementia by any means in these subjects was 84.4%.
- Clinician's judgement corresponded best with clinically-diagnosed cases of dementia, identifying 84.4% cases of clinically-diagnosed dementia at the time of diagnosis.
- ICD-10 criteria identified 70.3% cases.
- DSM-IV criteria were the most exclusive, as their application identified only 56.3% cases at the time of clinically-diagnosed dementia.
- Over time, the proportion of cases meeting ICD-10 or DSM-IV diagnoses increased.

Conclusions

Conclusions

- ? Experienced clinicians use their clinical knowledge of dementia presentation in Down syndrome to diagnose the disorder at an earlier stage than would have been possible had they relied on the classic description contained in the diagnostic systems.
- The criteria in ICD-10 and DSM-IV seem to underdiagnose dementia in this population - ? the presentation of Alzheimer's disease is sufficiently different in people with Down syndrome to affect performance of standardised criteria in this population.
- Use of standardised criteria (ICD-10 / DSM –IV) lead to false positives similar to clinical judgement!
- High degree of agreement on inter-rater analysis - interpretation of the criteria is consistent between clinicians.
- **A clinical diagnosis of dementia in Down syndrome is valid and reliable.**

Flash Back...

The Puzzle (Dementia in LD) ……The Twist

Dementia in People with Down's Syndrome

- Subtle cognitive decline difficult to elicit – depends on informant history.

- Dementia will become a more common presentation in people with DS as their life expectancy increases (Bittles et al, 2007).

- Early diagnosis important.
  - Antidementia medications.
  - Appropriate psychosocial interventions.

- Standardised assessments have been developed based on informant interviews +/- direct cognitive testing.
  - Which is better? (Strydom & Hassiotis, 2003).
  - Using physician's own 'clinical judgement' was once a 'gold standard'.

Back to the Future……?

> “Not everything that can be counted counts, and not everything that counts can be counted.” (Albert Einstein)

Diagnosing Dementia in People with LD

- Specialist ‘Clinical Assessment’ (pt. + carer / informants + clinical Hx / Ex).
- Use of standardised criteria (incl. ICD-10 / DSM-IV).
- Specific Dementia Screening Tests eg, DSQIID, DMR, DSDS, etc.
- Specific Physical Health Tests eg, dementia blood screen, CT Brain.

Strengths & Limitations of Study

Study Strengths

- Data derived from clinical assessments conducted over a wide time period from both urban and suburban locations.
- Good sample size.
- A range of people with Down syndrome between 35 - 70 yrs age with differing baseline levels of cognitive impairment and adaptive function included.
- Data representative of clinical practice in the UK.
- Raters were blinded to the outcome of the clinical assessment and rated each case individually before reaching a consensus opinion.

Study Limitations

- Subtleties of clinical assessment that would be apparent to the treating clinician were not always available to our raters.
- Data dependent on the thoroughness and documentation of the original clinical records.
- Raters did not have the privilege of prior knowledge of the patient, as would often be the case in clinical practice -> may have been less likely to make a diagnosis of dementia than their counterparts in the clinic.
- Experienced / expert raters.
- Did not categorise the severity of dementia.

Dementia Diagnostic Criteria in People with Down's Syndrome

- History.
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- Aims.
- Methodology.
- Results.
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- Strengths & Limitations of Study.