Understanding dementia in people with an intellectual disability:
A model to diagnose dementia

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OUTLINE

• Ageing and Intellectual Disability
• The genetic link between Down syndrome and Alzheimer's disease
• Prevalence of dementia in people with Down syndrome
• Careful attention to differential diagnosis
• Brain Health
• The newly established National Intellectual Disability Memory Service
• Future directions
Ageing with Down syndrome

THIS IS A SUCCESS STORY

Opportunities to:

➢ Promote lifelong health and wellbeing
➢ Maintain independence
➢ Reorient services

High rates of morbidity and mortality and we need to address health inequities
➢ The incidence of dementia could be up to **five times higher** than in people without ID (Strydom *et al*, 2013)

➢ **Much higher rates** in people with Down syndrome (McCarron *et al*, 2014, 2016; Strydom *et al*, 2010)
Dementia in people with Down syndrome under the age of 40 years is very uncommon and rarely seen.
Why is there an association between Down syndrome and Alzheimer’s?
Neuropathology of Dementia in People with Down syndrome

➢ The gene coding for Amyloid Precursor Protein (APP) is on chromosome 21

➢ Individuals with DS have 3 copies of this gene and produce excess APP

➢ Over many years, this excess APP leads to β- amyloid plaque formation and eventually AD
Diagnosing Dementia in People with Down syndrome is Highly Complex

- Assessment tools for dementia in the general population are not appropriate for people with learning disabilities.
- For example, widely-used tools such as the Mini-Mental State Examination (MMSE; Folstein & Folstein, 2001) assume the pre-morbid level of functioning to have been within the average range.
- There is no single battery of assessments universally used by Intellectual Disability teams, but some useful and validated tools are available.
- Critical need for the standardization of validated assessment tools to diagnose and stage dementia in people with DS, considering pre-existing level of ID.
- Alzheimer’s Biomarker Consortium Down syndrome (ABC-DS) and the European Horizon 21 Consortium are validating various batteries of screening and cognitive tests for use in clinic settings.
Diagnosing Dementia in People with Down syndrome is **Highly Complex**

- The clinical presentation of dementia in persons with ID can differ.
- Personality and behavioural changes seem to occur earlier.
- Standardized tests often prove difficult and inaccessible.
- There may be communication difficulties for all involved.
- Improvised care environments undermine patient-centred planning.
- There may be a lack of base line data (personally and historically).
- High staff turnover limits symptom recognition.
Importance of a Brain Health Check

People with Down syndrome >40 years

Number of tools available

• National Task Group-Early Detection Screen for Dementia (NTG-EDSD) (Moran JA, et al 2013)

  Not a diagnostic instrument – early AD type changes and/or potentially reversible conditions
  - Cognition, memory, and executive functioning, communication, behavior and personality etc.

• Dementia Screening Questionnaire for Individuals with Intellectual Disabilities (Deb S, et al 2007)
Consider other physical or mental health problems and ensure the proper management of existing health problems such as:

- Depression or other mental illness
- Sensory impairment (vision and hearing)
- Thyroid impairment
- Sleep apnoea
- B12 & folate deficiency
- Medical problems (drug interaction, infection, pain, epilepsy)
- Major life events (separation, bereavement, moving)
- Catatonic Regression
Understanding the Process of Change: Early Stage

At this stage, the person is showing signs of decline from their usual level of functioning in the following areas:

- Subtle changes in behaviour and mood.
- Performance at day placements deteriorate.
- Memory problems, particularly for recent events.
- Ability to learn new information is affected
- Language and word finding problems.
- Decline in social, community and daily living skills.
- Disorientation.
- Difficulties with steps, stairs and kerbs due to depth perception problems.
Diagnostic Work-up: Some components

**Physical**
- Vital Signs
- Urinalysis
- Full Physical Examination
- Vision & Hearing Tests
- Blood Work

**Neuro-Imaging**
- CT Scan/MRI

**Neuro-Psychological Testing**
- Informant & Objective Measures
Correlating cognitive decline with new and innovative biomarkers

To understand the role of existing biomarkers and validate new biomarkers to further assist with differential diagnosis in the clinic setting

- Promising work on Amyloid PET and tau PET biomarkers in adults with Down syndrome and their relationship to clinical diagnosis (Handen BL. 2020; Strydom A, et al 2018)
- Blood based bio markers –neurofilament light (NF-L)-excellent measure of neurodegeneration and a strong correlation with brain atrophy and clinical status (Rafii MS, et al 2019)
A Prospective 20 Year Longitudinal follow-up of Dementia in Persons with Down syndrome

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Risk Trajectory By Age
Dementia in Persons with Down syndrome

Age 65 = 88% Risk
Age 55 = 45% Risk
Age 50 = 23% Risk
Dementia Co-Morbidities

- Heart disease: 29.3%
- Hypertension: 1.3%
- Epilepsy: 80%
- Hypothyroidism: 61.3%
- Cancer: 0%
- Lung: 13.3%
- Vision: 93.3%
- Hearing: 61.3%
- Diabetes: 4%
- Depression: 48%
- Hyperlipidaemia: 18.7%
Dementia and Epilepsy
In Persons with Down syndrome

Life Time Prevalence

- LTP Dementia
- LTP Epilepsy

77.9% with Dementia had Epilepsy
Dementia Mortality In Persons with Down syndrome

Survival Function

Cum Survive
0.0  0.2  0.4  0.6  0.8  1.0
0.00  5.00  10.00  15.00  20.00

Duration

Survival Function
Censored

Trinity College Dublin, The University of Dublin

@NIDMSIrl #ageingwithID
## In Summary

There is a substantial increased risk of dementia >50 years but.....

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<tbody>
<tr>
<td>1</td>
<td><strong>Survival less precipitous</strong> than previously reported</td>
</tr>
<tr>
<td>2</td>
<td><strong>The rate of progression varies</strong> among individuals</td>
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<td>3</td>
<td>Previous concerns of adults with Down syndrome ‘falling off a cliff’ are uncommon</td>
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<tr>
<td>4</td>
<td>There is a high risk of <strong>new onset epilepsy</strong></td>
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<tr>
<td>5</td>
<td>There is <strong>increased survival</strong> at advanced dementia</td>
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Address inequity in service provision for people with ID with memory concerns

A National Intellectual Disability Memory Service (NIDMS)
Background to the National ID Memory Service

‘stressed the need for systems, structures and age appropriate services specifically **to promote timely diagnosis of people experiencing early onset dementia, including people with Down Syndrome**’
Translating Findings

Working with the Federation of Voluntary Bodies’ 60 member services, initially exploring service responses to dementia
TCAID was delighted to sign a Memorandum of Understanding (MoU) between Trinity College Dublin, Tallaght University Hospital and the Daughters of Charity Disability Support Services in September.

The MoU has enabled the development of a new memory service in Ireland specifically for people with an intellectual disability.
The diagnosis of Alzheimer’s disease in persons with ID requires appropriate evaluation tools and a specialized team

- Harmonizing diagnosis procedures (diagnostic work up including clinical investigations, neuropsychology, biochemistry, blood, imaging etc)

- Defining common criteria for diagnosis of Alzheimer’s disease
## Confirming Dementia: Consensus Meetings

**Overall classification established based upon a comprehensive evaluation**

<table>
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<tr>
<th>Category</th>
<th>Description</th>
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<tr>
<td><strong>No Dementia</strong></td>
<td>• Stable or age-related changes</td>
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<tr>
<td><strong>Questionable with Complication</strong></td>
<td>• Some declines or concerns; may be due to some other underlying aetiology</td>
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<tr>
<td></td>
<td>(e.g. mental or physical health condition, environmental, major life event)</td>
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<tr>
<td><strong>Query Dementia/Red Flag</strong></td>
<td>• Substantial declines of late onset, query MCI requires further follow up</td>
</tr>
<tr>
<td><strong>Definite Dementia</strong></td>
<td>• Substantial declines of across several key areas-day to day living, memory, cognition etc &gt; than 6 months</td>
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Easy-Read Information for the Memory Service

What is dementia?

Dementia is a disease that affects some people as they get older.

Dementia causes some changes in the brain.

You might have trouble remembering things.

You might forget people’s names.

You might forget where you put things.

Sometimes you might be confused or sad.

You family or support staff can help you with these feelings.

Living Well with Dementia

You might need someone to help you with things like:
- getting dressed
- doing shopping
- doing work around the house

You can keep doing all of the things you enjoy!
Your family and staff will help you.

You need to keep your brain and body healthy.

Eat healthy food
Future Directions

Addressing questions that remain unanswered
There are HUGE Gaps in Knowledge

➢ All adults with DS by age 40 have key neuropathological hallmarks of AD, and yet many will not present with the clinical features of dementia until they are much older-Why?

➢ We need to urgently develop skills in dementia recognition and assessment for people with DS, as well as valid diagnostic standards

➢ Significant opportunities for boosting cognitive reserve education, exercise, cognitive stimulation and social engagement.

➢ Most critically, we need to develop responsive and humane services for the changing needs of this increasingly at risk population with dementia.

➢ Masterclasses series will address some of these issues
Into the Future ....
Questions that Remain Unanswered

• Is it excess β amyloid production ‘driving’ the risk of dementia in people with Down syndrome or are there other factors?

• What role can neuroimaging, amyloid PET scanning and biomarkers play?

• Can a simple blood test help determine the risk for developing dementia in people with Down syndrome or help with clinical diagnosis?

• What further markers could signal progression and decline in this group?
“Like everybody here, I have dreams for the future. There are things that I want to do and I know dementia might play a part of my life too.

So, when you start talking about dementia, I want to be included in that conversation. I want to be included in the conversation about my future.

I want to be empowered so that I can choose how to reduce the risk of dementia”

- Mei Lin Yap
We need a **Paradigm Shift** in health care

**DIAGNOSE & MANAGE**

**PRE-EMPT & PREVENT**

**GOOD NEWS**
- COLLABORATIVE EFFORTS
- TRIAL READY COHORTS
Future Directions
We want to ensure that people with Down syndrome have the opportunity to be involved in dementia research.

➢ Research in dementia needs to focus on dementia prevention.

➢ We need to focus research at a much younger age.
The PREVENT Dementia study aims to identify the earliest signs of dementia

Scientists believe these may occur in the brain decades before symptoms appear

Prevent Dementia is a UK and Ireland wide study for people aged 40 – 59

Includes thinking and memory assessments, clinical examinations, MRI brain imaging and genetics to track how the brain changes throughout middle age

We hope to find ways to predict who is at greatest risk of dementia, so that we can intervene and prevent the disease taking hold
PREVENT Dementia – DS

➢ Aims to complete the same protocol as in the general population
➢ This will include people with Down syndrome between the ages of 25-40

- Physical health checks
  - Blood pressure readings, an Electrocardiogram (ECG), height and weight

- Biological sample collection
  - Blood, urine, saliva

- Memory assessments
  - Memory and thinking tasks are completed which aim to identify subtle changes in cognition.

- Brain Scanning
  - Participants will undergo an MRI scan

- Lifestyle questionnaires
  - Diet, education, personality, history of brain injury, sleep quality, life events.

Dr Eimear McGlinchey
Remember we are all human

Those with dementia are still people and they still have their stories and they still have their character, and they are all individuals, and they are all unique. And they just need to be interacted with on a human level.

Carey Mulligan
The National Intellectual Disability Memory Service

The National Intellectual Disability Memory Service is a centre of excellence in proactive dementia assessment and diagnosis for people with an intellectual disability (ID), particularly supporting people with Down syndrome given their increased genetic risk for dementia.
Thank You

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