New Horizons for Alzheimer's Disease

The Role of Biomarkers in Assessment of Cognitive Decline

Dementia Training Australia is supported by funding from the Australian Government under the Dementia Training Program.

University of Wollongong Australia · Dementia Australia · La Trobe University · QUT · The University of Western Australia · Western Australian Centre for Health & Ageing · University of Tasmania Wicking Dementia Research and Education Centre

Dementia Training Australia

DTA would like to show our respect and acknowledge the traditional custodians of these lands. We extend this respect to elders' past, present and emerging, and to all Aboriginal and Torres Strait Islander peoples. We also pay respect to Aboriginal and Torres Strait Islander peoples living with dementia and their carers.

Dementia Training Australia

Topics

- Part 1: Understanding Mild Cognitive Impairment
- Part 2: The Role of Biomarkers in the Assessment of Cognitive Decline
- Part 3: The Role of Anti-Amyloid Therapies in Alzheimer's Disease

True or False

1. Alzheimer's disease pathology occurs 10 – 20 years before clinical symptoms
2. In Mild Cognitive Impairment a person's function is significantly impaired
3. Approximately 60% of Mild Cognitive Impairment does not progress
4. Alzheimer's disease can be present without dementia
5. The gold-standard investigation for Alzheimer's disease is a blood test called ptau 181

Understanding Mild Cognitive Impairment

Part 1

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Learning Outcomes Part 1

By the end of this session, participants will be able to:

- Describe the characteristics of Mild Cognitive Impairment (MCI)
- Apply a framework to diagnose Mild Cognitive Impairment
- Implement management strategies for people living with Mild Cognitive Impairment

Take Home Messages

To Begin With the End in Mind

- 10-15% of people with MCI will progress to dementia each year
- Many people living with MCI will improve or stay the same
- Lifestyle changes may slow progression
- People with MCI require regular monitoring

Case Study: Sue

Sue is worried about her memory and thinking

- 67-year-old retired teacher
- Complaining of forgetting people's names
- Sometimes has trouble finding the right words
- Not sure if this is normal ageing
- Her partner also agrees that she seems more forgetful and easily flustered

Sue comes to you for advice

The Spectrum of Cognitive Change

Normal Ageing	Slight slowing of processing, function intact
Subjective Cognitive Decline	Changes in cognition noticed by the individual but not objectively seen, function intact
Mild Cognitive Impairment	Objective and subjective changes in memory and thinking, and may need compensatory measures to keep function intact
Dementia	Both cognition and function are impaired

Smid J , Studart-Neto A, Cesar-Freitas K, et al (2022), Subjective Cognitive Impairment, mild cognitive impairment and dementia syndromic approach – recommendations of the Scientific Department of Cognitive Neurology, Dementia Neuropsychologica

Mild Cognitive Impairment

- Mild cognitive impairment (MCI) describes a condition of noticeable decline in memory or other cognitive (thinking) abilities
- Preserved ability to perform normal daily function
- The changes to memory and thinking are greater than usually expected from someone at a similar age

1. Adapted from DSM V - Major neurocognitive disorder

Inclusion Criteria

A new diagnosis of Mild Cognitive Impairment requires all the Inclusion Criteria to be present

- [ ] 1. Mild decline in cognition noticed by person, or others
- [ ] 2. Evidence of objective cognitive impairment (preferably on cognitive assessment)
- [ ] 3. Not interfering with activities of daily living, but compensatory strategies may be required
- [ ] 4. Absence of any exclusion criteria

Adapted from DSM V – Mild neurocognitive disorder

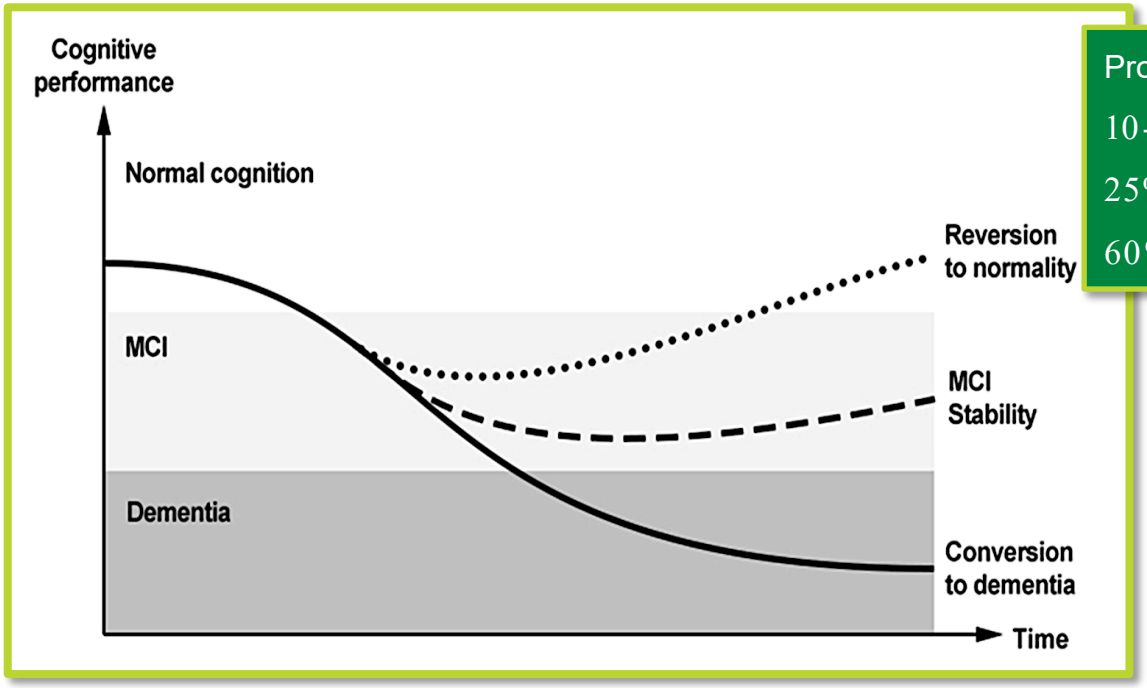
Exclusion Criteria

A new diagnosis of Mild Cognitive Impairment cannot be made during an acute episode of:

- [ ] 1. Delirium
- [ ] 2. Severe mental health disorders (psychosis and severe depression)

Adapted from DSM V – Mild neurocognitive disorder

MCI Increases Dementia Risk



Progression from all -cause MCI to Dementia:

10-15% - per year

25% - within 5 years

60% - same or better with management

Canevelli M et al. Front Med (Lausanne) 2017;4:184.

Some Causes of Mild Cognitive Impairment

- Prodromal Dementia
  - Alzheimer's disease
  - Non-Alzheimer's Disease pathology – e.g. Frontotemporal Dementia, Vascular, Lewy Body disease
- Mental health conditions
- Medications
  - Anti-cholinergic loading
- Alcohol and other recreational drugs
- Other organic pathology
  - Usually discovered on investigations e.g. B12 def, OSA

Yates M, Daly S, Long M, Pond D, Gibson C, Low L - Mild cognitive impairment and dementia – detection and diagnosis – Medicine Today 2024.

Medication That May Affect Cognition

- Sedatives
- Anticholinergic medication
- Parkinson's disease medication
- Corticosteroids
- Narcotics
- Alcohol
- Seizure medications

How to Start the Conversation

Have you noticed any issues with your memory and thinking?

- How long has this been happening?
- How has it been affecting you?
- Have other people commented?
  What did they say?
- Keep it broad
- Acknowledgement of change
- Conversation could be over multiple visits

V-REALMS of Cognition

V isuospatial
R ecall/Memory
E xecutive Function
A ttention
L anguage
M otor Function
S ocial

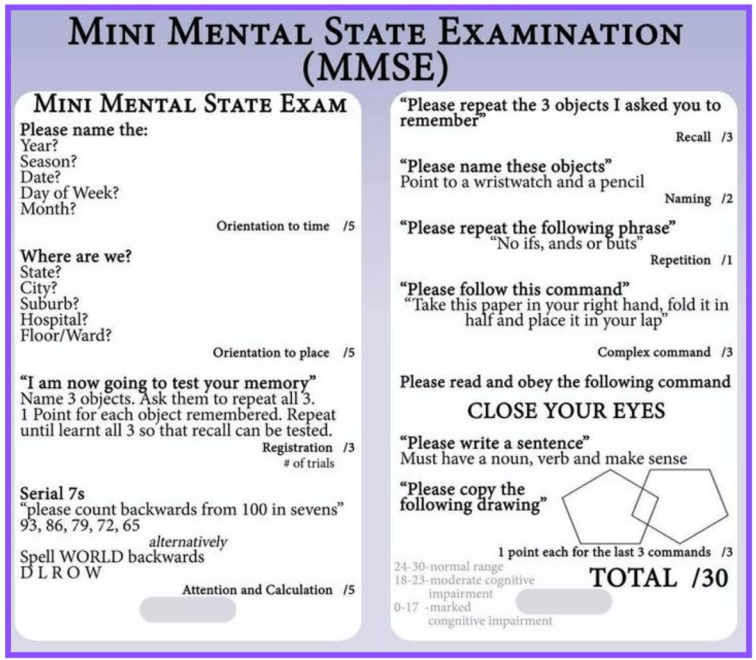
Adapted from DSM V - Major Neurocognitive Disorder

Function

Physical Examination

- Weight
- Temperature
- BP/ Pulse
- Focused neurological examination

Cognitive Assessment Tools



Mini Mental State Examination (MMSE)

Mini Mental State Exam

Please name the:
Year?
Season?
Date?
Day of Week?
Month?

Orientation to time /5

Where are we?
State?
City?
Suburb?
Hospital?
Floor/Ward?

Orientation to place /5

"I am now going to test your memory"
Name 3 objects. Ask them to repeat all 3.
1 Point for each object remembered. Repeat until learnt all 3 so that recall can be tested.

Registration /3
# of trials

Serial 7s
"please count backwards from 100 in sevens"
93, 86, 79, 72, 65
alternatively
Spell WORLD backwards
D L R O W

Attention and Calculation /5

"Please repeat the 3 objects I asked you to remember"

Recall /3

"Please name these objects"
Point to a wristwatch and a pencil

Naming /2

"Please repeat the following phrase"
"No ifs, ands or buts"

Repetition /1

"Please follow this command"
"Take this paper in your right hand, fold it in half and place it in your lap"

Complex command /3

Please read and obey the following command

CLOSE YOUR EYES

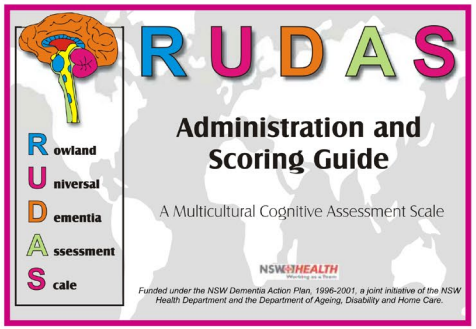
"Please write a sentence"
Must have a noun, verb and make sense

"Please copy the following drawing"

1 point each for the last 3 commands /3

24-30-normal range
18-23-moderate cognitive impairment
0-17 -marked cognitive impairment

TOTAL /30



RUDAS

Rowland Universal Dementia Assessment Scale

Administration and Scoring Guide

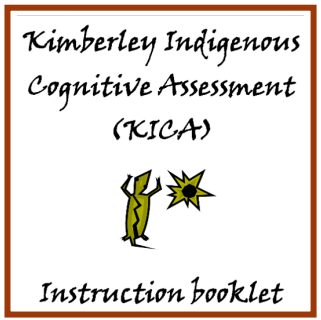
A Multicultural Cognitive Assessment Scale

NSW HEALTH

Funded under the NSW Dementia Action Plan, 1996-2001, a joint initiative of the NSW Health Department and the Department of Ageing, Disability and Home Care.

MoCA COGNITION

GPCOG



Kimberley Indigenous Cognitive Assessment (KICA)

Instruction booklet

Investigations

Routine Investigations

Haematology – FBC/ESR/CRP

Biochemistry - EUC, LFT, Glucose, Calcium

TFT

Vit B12, folate

CT Brain Without Contrast

If Indicated

Fasting lipids

Urine MCS

ECG

CXR

Syphilis

HIV

Sue's History in More Detail

- Sue and her partner both agree that she is not "as sharp" as she was 12 months ago
- This includes remembering family and friend's names and word finding problems
- Struggling to remember plot lines in movies
- No changes in visuo -spatial or motor function
- Still socially active but less enthusiastic e.g. not initiating engagements
- Still able to perform her daily functions but easily flustered by simple mistakes e.g. mobile and computer use

Sue's Examination Findings

- BP 163/87, HR 78
- Weight 80kg, Height 168cm, BMI 28.4
- Examination otherwise unremarkable

Sue: Review in Two Weeks

- Geriatric depression scale = 3/15 (<5 suggests depression unlikely)
- MOCA 25/30 (Sue lost points in recall and language fluency)
- Pathology and imaging r esults are all normal

The Spectrum of Cognitive Change

Normal Ageing	Slight slowing of processing, function intact
Subjective Cognitive Decline	Changes in cognition noticed by the individual but not objectively seen, function intact
Mild Cognitive Impairment	Objective and subjective changes in memory and thinking, and may need compensatory measures to keep function intact
Dementia	Both cognition and function are impaired

Smid J , Studart-Neto A, Cesar-Freitas K, et al (2022), Subjective Cognitive Impairment, mild cognitive impairment and dementia syndromic approach – recommendations of the Scientific Department of Cognitive Neurology, Dementia Neuropsychologica

Case Study Activity: Sue

What is your assessment of her cognitive concerns?

You Diagnose Sue With Mild Cognitive Impairment

What Now?

Management of MCI

Cognition/Mental Health

- Education
- Brain health
- Medications

Function

- Legal
- Safety
- Driving

Changed Behaviour

Physical

- GPCCMP

- ☐ **Goals for care*** – consider person with MCI as well as family/care partners
- ☐ **Education*** – answer questions about MCI, prognosis and risk reduction
  - ○ Refer to Dementia Australia: Thinking Ahead small group program for MCI
- ☐ **Brain health*** – discuss exercise, staying cognitively and socially active, limit alcohol and drugs, stop smoking, healthy diet
  - ○ Ask patients to complete CogDRisk – will give them personalised recommendations for reducing risk
  - ○ BrainHQ or Cognifit – evidence based computerised training (payment required)
- ☐ **Medications** – review current medications, especially those with anti-cholinergic load
- ☐ **Legal planning*** – will, enduring powers of attorney (legal/financial, lifestyle, medical), advance care directive
- ☐ **GP chronic condition management plan*** - update or develop

(Adapted from Facing Dementia Together checklist) https://facingdementiatogether.au/en/wp-content/uploads/sites/2/2024/04/Face-Dementia-MCI-review-checklist.pdf

Resources

Forward with dementia

A guide to living with dementia

Dementia Training Australia®

dta.com.au

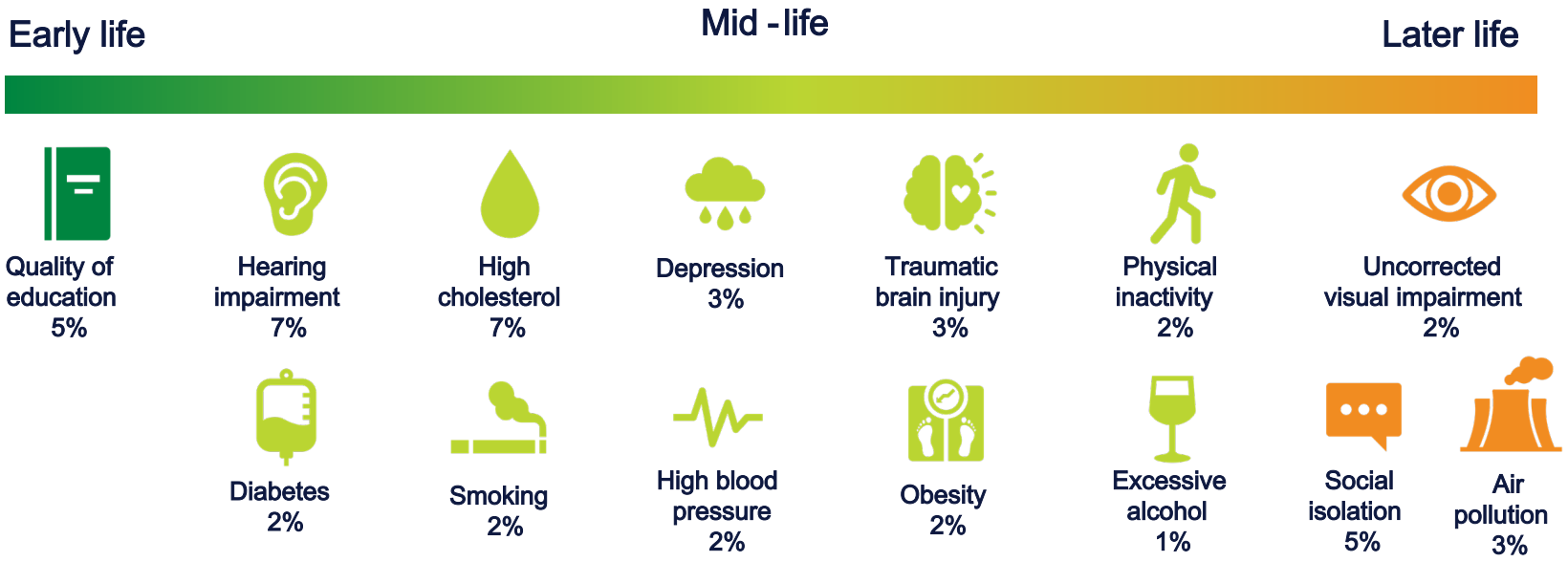
Dementia Australia®

Mild Cognitive Impairment: Thinking Ahead

Mitigating Dementia Risk

Sue wants to know what she can do to stop her cognitive changes becoming worse.

Modifiable Risk Factors for Dementia



The percentage figure refers to the reduction in **worldwide** cases if this risk factor were eliminated.

In Australia, a 1% reduction = 4,200 people

1. Adapted from the Lancet Standing Commission on Dementia Prevention, Intervention and Care, 2024.

Optimising Brain Health

- Address vascular risks
- Optimise diabetes management
- Cognitive stimulation
- Address hearing and vision impairment
- Optimise mental health
- Physical activity
- Social engagement
- Minimise alcohol intake
- Medication review
- Diet
- Sleep
- Vaccinations
- Consider Souvenaid

Driving and Mild Cognitive Impairment

Mild Cognitive Impairment

- MCI causes slight but measurable decline in cognitive abilities
- Cognitive changes are noticeable to the person, family or friends, but do not affect ability to perform everyday activities
- Driving studies examining effects of MCI show limited evidence of increased driving errors rates – driving is not significantly impaired
- If multiple cognitive areas (e.g. visuospatial, attention, executive function) are affected, a driving fitness assessment may be needed

Adapted from Austroads Guidelines

Recommendations for Clinical Review

- 6, 12 or (maximum of) 18 month follow up in primary care
  - Repeat cognitive assessment tool and assessment of function
- Reasons for earlier review
  - Patient or family concern
  - Recent hospital admission
  - Multi-domain amnestic MCI symptoms
  - Neurological signs
  - Mood or behavioural symptoms

Take Home Messages

To End With the Beginning in Mind

- 10-15% of people with MCI will progress to dementia each year
- Many people living with MCI will improve or stay the same
- Lifestyle changes may slow progression
- People with MCI require regular monitoring

The Role of Biomarkers in the Assessment of Cognitive Decline

Dementia Training Australia

Learning Outcomes Part 2

By the end of this session, participants will be able to:

- Recognise the presence of Alzheimer's disease pathology in Mild Cognitive Impairment predicts ongoing cognitive decline
- Identify which patients may benefit from testing with blood - based biomarkers for Alzheimer's disease
- Outline the necessary counselling when ordering Alzheimer's disease blood -based biomarkers

Take Home Messages

- The diagnosis of dementia remains a clinical diagnosis
  - There is no test that can diagnose dementia
- Alzheimer's disease is a pathological process which starts years before symptoms
- Alzheimer's disease dementia is a clinical syndrome
- Blood-based biomarker currently available in Australia is designed to "rule out" the presence of Alzheimer's disease pathology

True or False

6. AD blood-based biomarkers are an excellent screening tool for Alzheimer's disease in family members with normal cognition

7. A negative Alzheimer's disease biomarker result excludes a neurodegenerative disorder

8. The currently available Anti-Amyloid therapies improve cognition

9. The currently available Anti-Amyloid therapies show better effects if started earlier in the condition

10. Most people with Alzheimer's disease will be eligible for current Anti-Amyloid therapies

The Spectrum of Cognitive Change

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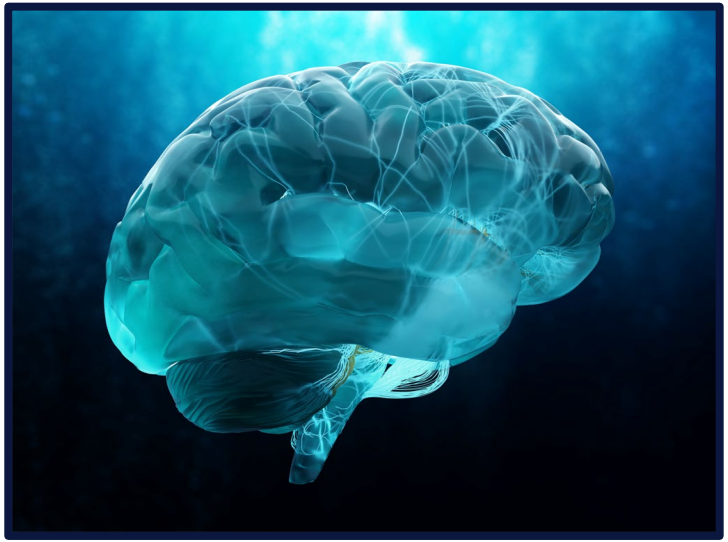
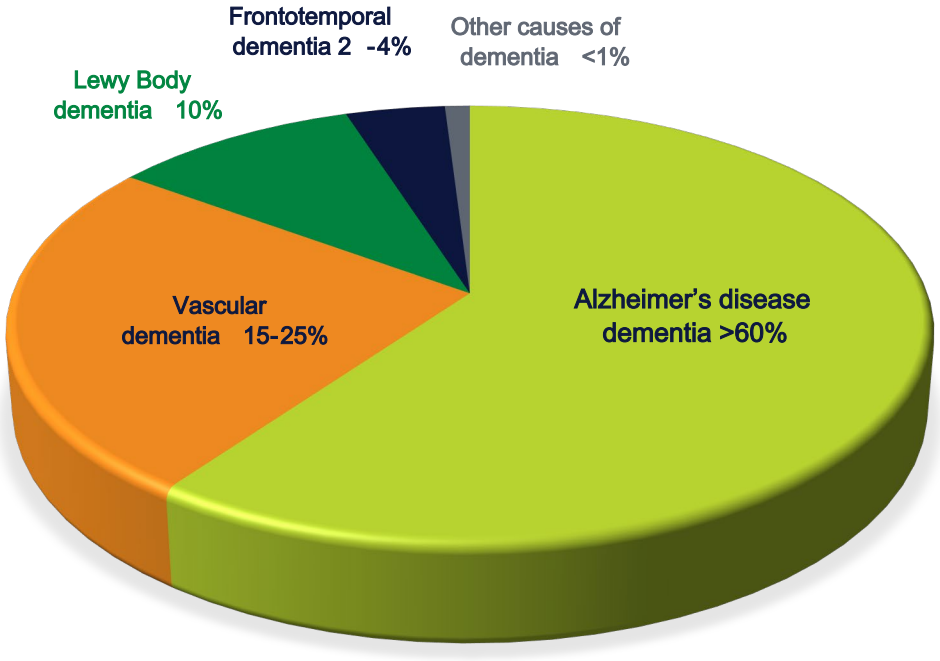
Defining Dementia

Dementia is a progressive, global, life-limiting condition that involves generalised brain degeneration which affects people in different ways and has many different forms.



Dementia Australia. About Dementia. Dementia Australia, 2023

Dementia Types and Causes



Other causes of dementia include:

- Alcohol
- Parkinson's Disease
- Creutzfeldt Jakob Disease
- Huntington's Disease
- Supranuclear Palsy
- HIV
- Chronic Traumatic Encephalopathy
- Limbic-Predominant Age-Related TDP-43 Encephalopathy (LATE)

Australian Institute of Health and Welfare. Dementia in Australia. AIHW, 2023

Why Should We Aim to Subtype Dementia?

- Certain Subtypes affect specific populations
- Initial presentation and symptoms will differ between sub -types
- The trajectory is dependent on the underlying pathology
- There are different treatment options available for different subtypes
- Important for participation in trials

Enables an individual and tailored approach to the person living with dementia

Alzheimer's Disease Is a Pathological Process

- A progressive, incurable, neurodegenerative condition
- Has characteristic pathology including amyloid plaques and neurofibrillary tangles
- Pathology is present well before cognitive changes present
- The most common cause of dementia in Australia

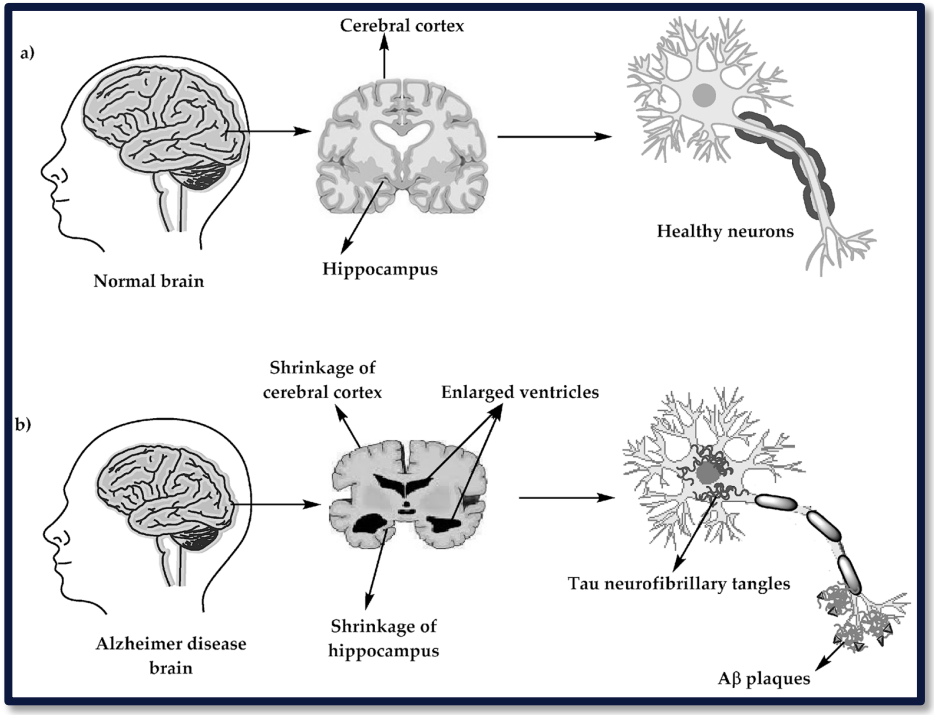
Dementia Australia – Alzheimer's Disease https:// www.dementia.org.au /about -dementia/ alzheimers -disease -everything -you -need -know

Alzheimer's Disease Is a Pathological Process

Amyloid Cascade Hypothesis
Aggregation of Aβ forming amyloid plaques.

Activation of Tau, leading to abnormal phosphorylation – leading to Neuro Fibrillary Tangles.

Both the above lead to atrophy of affected areas of the brain, loss of synapses and neurons.



Alzheimer's Disease Dementia Is a Clinical Syndrome

- Insidious, progressive, life -limiting condition caused by Alzheimer's disease pathology
- Usually, the most prominent feature is short -term memory loss
- Language areas, executive function and visuospatial function may also have prominent deficits
- 15% "atypical variants" where memory loss is not the initial presentation

Mild Cognitive Impairment due to Alzheimer's disease pathology is a prodrome to Alzheimer's disease dementia.

Dementia Australia – Alzheimer's Disease https://www.dementia.org.au/about-dementia/alzheimers-disease-everything-you-need-know

Pre-Clinical Alzheimer's Disease May Occur Over 10 – 20 Years

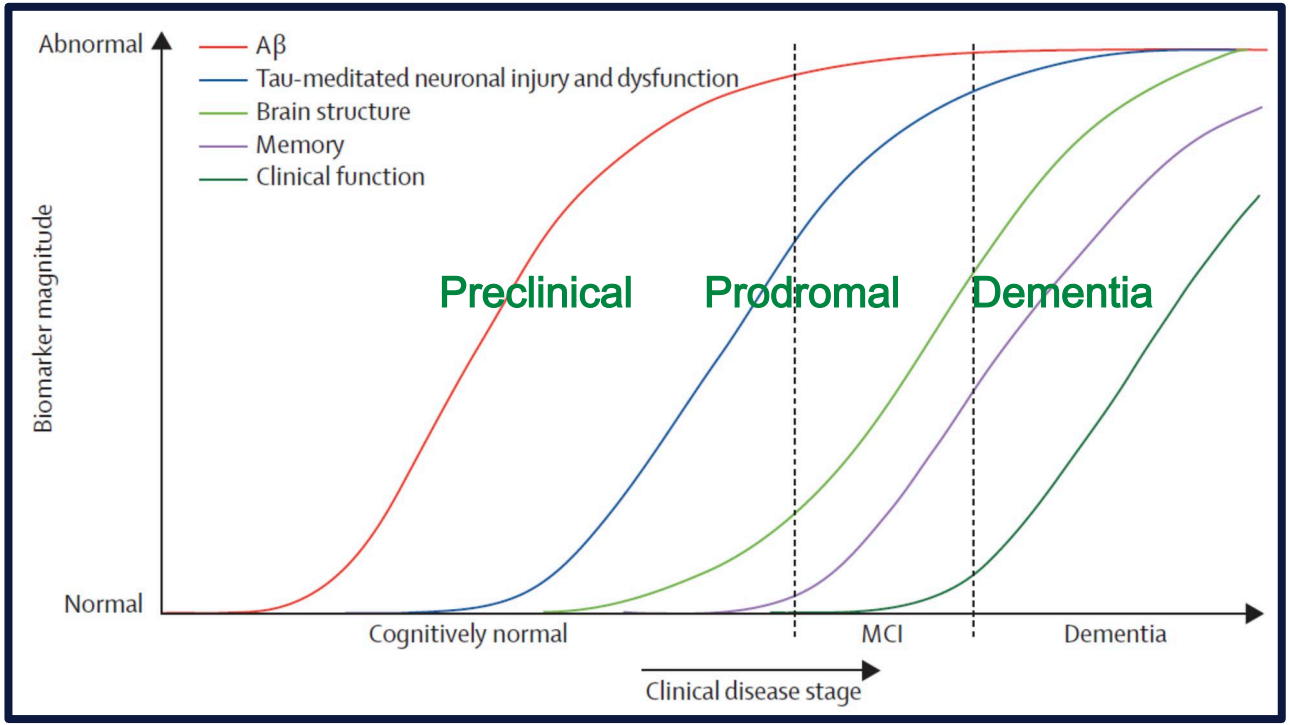
- The build -up of amyloid is slow – increasing, about 4% per year so may start in some in midlife
- The preclinical phase of Alzheimer's disease, when the amyloid is building but there are no symptoms, may last 10 -20 years

Hampel H, Blennow J, Chen C, et al 2021, The Amyloid β Pathway in Alzheimer's Disease – Molecular Psychiatry

Stages of Pathology

Stages of Alzheimer's Disease:

Amyloid accumulation starts **decades** before clinical changes are evident.



Hypothetical Model of Dynamic Biomarkers of the Alzheimer's Pathological Cascade

Figure reference: Jack, C. R. et al (2010), Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade. *The Lancet. Neurology* , *9*(1), 119–128. https://doi.org/10.1016/S1474-4422(09)70299-6

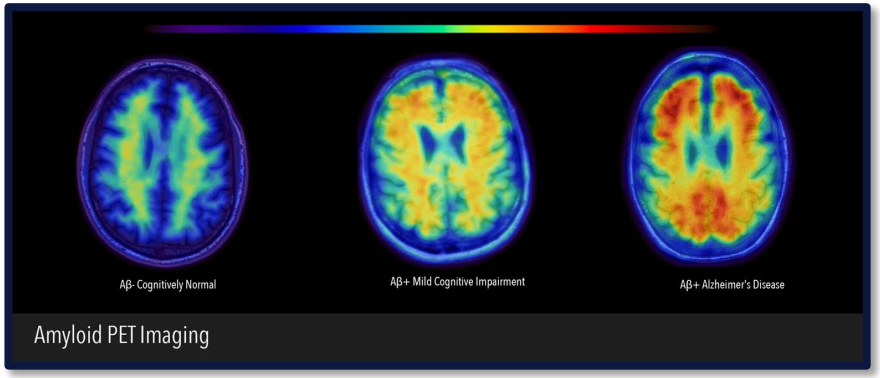
Biomarkers in Alzheimer's Disease

- Imaging
- CSF biomarkers
- Blood biomarkers

Amyloid PET in Alzheimer's Disease

- Identifies amyloid presence
- Current gold standard
- Specialist referral only
- Available in select institutions

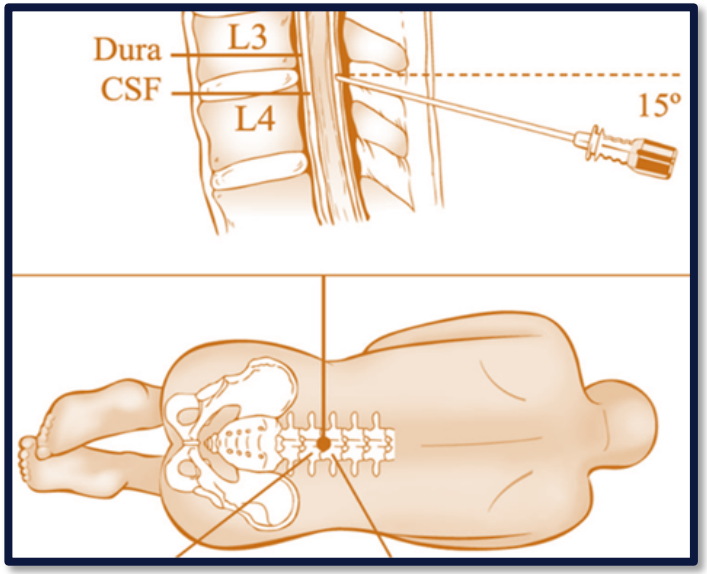
  in Australia ($1000 - $2500)



The Jagust lab (viewed 2025) Amyloid PET https:// jagustlab.neuro.berkeley.edu /

CSF Biomarkers in Alzheimer's Disease

- More extensively used overseas
- Measures:
  - Aβ42/ Aβ40
  - t tau (total)
  - p tau (phosphorylated)
- High levels of sensitivity when the three tests are combined



Engelborghs, S. et al (2017), Consensus guidelines for lumbar puncture in patients with neurological diseases. Alzheimer's & Dementia: Diagnosis, and Disease Monitoring, 8: 111-126. https://doi.org/10.1016/j.dadm.2017.04.007

Blood-Based Biomarkers in Alzheimer's Disease

There are several commercially available AD biomarker assays with different levels of positive and negative predictive value.

- Aβ42/ Aβ40
- ptau 181 & 217

TGA have approved Elecsys ptau 181 as a "rule out test".

Rowe, C (11/ 6/ 25) Symposium: Current Australian "real world" clinical impact studies of Blood Based Biomarkers for AD, 2. Adamek, J (email 12/ 9/ 25) Roche Diagnostics

Alzheimer's Disease Blood-Based Biomarkers Are Not for Screening Purposes

- **Not** for screening purposes
- Clinical assessment remains paramount
- Accuracy may be greater in those with cognitive impairment
- Less accurate in younger or very old /renally impaired
- Beware of the psychological impact of early Alzheimer's disease diagnosis

Basic dark green background could be used as divider pages.

Dementia Training Australia is supported by funding from the Australian Government under the Dementia Training Program.

Precautions When Using Alzheimer's Disease Blood-Based Biomarkers

- Significant variability in diagnostic test accuracy between testing methods
- Currently, there are no Australian guidelines
- No one test is recommended although Elecsys ptau 181 is TGA approved as a 'rule out' test
- If testing biomarkers you are recommended to seek specialist input at this stage

Blood-Based Biomarkers (BBM) in Alzheimer's Disease

The "rule-out" BBM

Elecsys ptau 181 has been approved for use in Australia as a "rule-out" BBM (Oct 2025)

- $250-$400 (not Medicare rebatable)
- 2-4 weeks for results

BBM in Alzheimer's Disease

The "confirmatory" BBM

There are several commercially available "confirmatory" BBM available internationally.

- Aβ42/ Aβ40
- ptau 217

For a "confirmatory" BBM to be reliable, a person needs to have MCI or dementia.

It is likely that "confirmatory" BBM will become available in Australia in the next 12 months.

“Rule-Out” Test – ptau 181 BBM

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“Rule-Out” Test - ptau 181 BBM Who Might Benefit….

- Aged 55 -80 years
- With cognitive symptoms, including people with SCD and MCI
- Has had assessment of cognition and its impact on functioning
- Has had treatable or reversible causes of their impaired cognition assessed and managed as best as possible
- Understands the implications of having the test, including meaning of negative or positive result
- Able to pay $250-400 for the test

"Rule-Out" Test - ptau 181 BBM Not Indicated for People....

- Aged under 55 or over 80 years
- With no cognitive symptoms
- Do not understand the implications of having the test, including meaning of negative or positive result
- Who would be psychologically at risk from a positive result
- Not willing or able to pay $250-400 for the test

Currently available BBM are not indicated as a screening test for asymptomatic people

How Can Knowing Help?

- Assist in future planning for the person and their family
- Enhance motivation for risk -factor management
- Consider Souvenaid
- Commence cholinesterase inhibitors early
- Streamline specialist access
- Consider disease -modifying medication
- Offer trial participation

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Case Study: Sue

Sue wants to know if she is going to develop dementia.

Case Study Activity: Sue

How would you counsel Sue about the use of biomarker ptau 181 for Alzheimer's disease?

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What to Do If a Person Has a Negative ptau 181 Result (AD Ruled Out)

Patient Details
Name:
DOB & Age:
Laboratory No: 24/0001P
Sample received date:

Sample Details
Referring Laboratory:
Number:
Referring doctor:
Sample type: Plasma Collection date:

Tests: Protein	Result (ng/L)*	Reference (ng/L)	Result*
1. Plasma Phospho-Tau (181P)	0.155	Negative ≤0.934 Positive: >0.934	Negative

Interpretation:
A normal (negative) plasma Phospho-Tau(181P) result is consistent with a negative (normal) brain amyloid-PET scan result, indicating a low likelihood of having neuropathological changes associated with Alzheimer's disease (see comment 1 and 2).

What to Do If a Person Has a Negative ptau 181 Result (AD Ruled Out)

For All Patients

- Explain the result – "Currently no signs of Alzheimer's disease pathology"
- Continue brain health strategies
- Consider referral

For People With Subjective Cognitive Decline (SCD)

- Remain alert for causes other than AD for their SCD
- Review cognition and function 12-24 months or sooner if concerns

For People With Mild Cognitive Impairment (MCI)

- Remain alert for causes other than AD for their (MCI)
- Review cognition and function 6-12 months or sooner if concerns

For People With Early Dementia

- Investigate for causes of dementia other than AD

What to Do if a Person Has a Positive ptau 181 BBM Result (AD Not Ruled Out)

Patient Details
Name:
DOB & Age:
Laboratory No: 24/0001P
Sample received date:

Sample Details
Referring Laboratory:
Number:
Referring doctor:
Sample type: Plasma Collection date:

Tests: Protein	Result (ng/L)*	Reference (ng/L)	Result*
1. Plasma Phospho-Tau (181P)	2.000	Negative ≤0.934 Positive: >0.934	Positive

Interpretation:
An elevated plasma Phospho-Tau(181P) result requires further investigation with either CSF bio-markers or brain amyloid PET imaging, due to low Positive Predictive Value of 46.6% (see comment 1 and 2).

What to Do If a Person Has a Positive ptau 181 BBM Result (AD Not Ruled Out)

- Explain the result

  "The test has not ruled out Alzheimer's disease as the cause of your symptoms. We need to investigate further to determine if Alzheimer's disease is present or if there are other reasons for your symptoms"

- Continue brain health strategies

- Recommend specialist referral for further assessment

Case Study: Sue

Scenario A

- She has a negative ptau 181 BBM test

Scenario B

- She has a positive ptau 181 BBM test

Dementia Training Australia

The Role of Anti-Amyloid Therapies in Alzheimer's Disease

Part 3

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Learning Outcomes Part 3

By the end of this session, participants will be able to:

- Outline the different Anti -Amyloid therapies available in Australia
- Identify which patients are eligible for Anti -Amyloid therapies
- Outline a pathway for people presenting with cognitive changes who want to access biomarkers and/or Anti -Amyloid therapies

Anti-Amyloid Therapies – Donanemab and Lecanemab

- Passive Immunisation – monoclonal antibodies bind to parts of amyloid β.
- Not yet PBS listed (capped at $40000yr not including MRI/appointments)
- Needs diagnosis of AD MCI or early AD dementia
- Confirmation required with validated AD biomarker
- Not for people with APOE4 homozygosity

Donanemab and Lecanemab – Trial Outcomes

- Very effective at removing amyloid plaque (disease modifying)
- Both slow decline by about 30% over 18 months
- Translated to functional impact of "4-7 months delay in progression" over 18 months
- Longer term studies show that benefits appear to widen over three years
- Benefits appear greater when treatment is started earlier

Treatment: Donanemab & Lecanemab

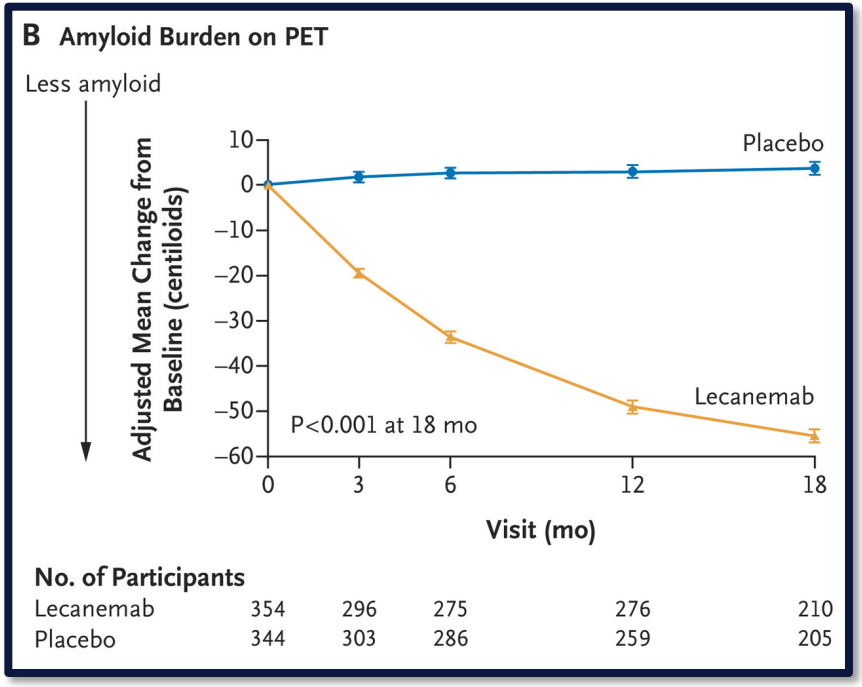
Donanemab

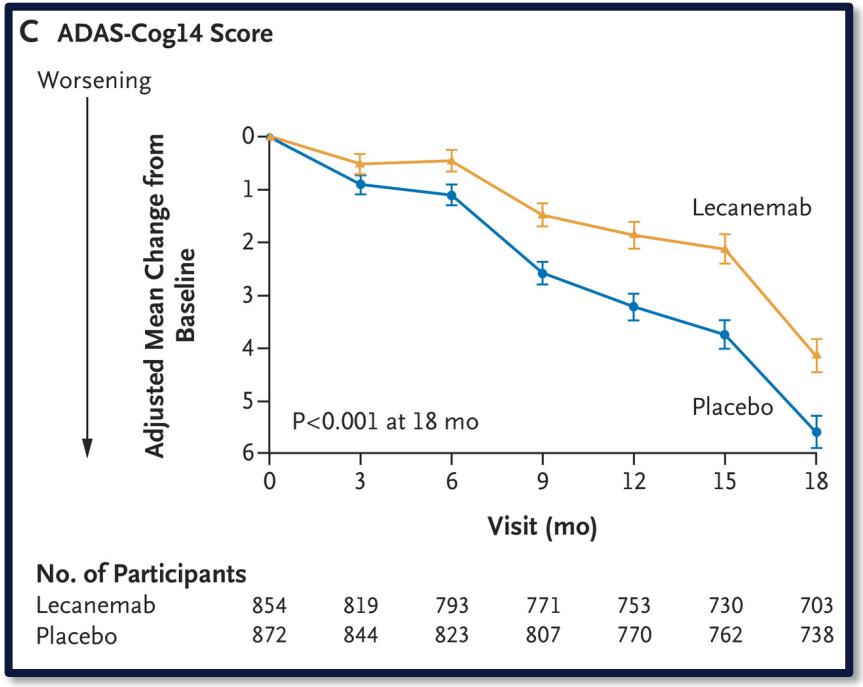
- Targets mature amyloid plaques
- 4 weekly infusion and regular MRI
- Treatment continued for 18 months or until amyloid has cleared on PET – whichever occurs first

Lecanemab

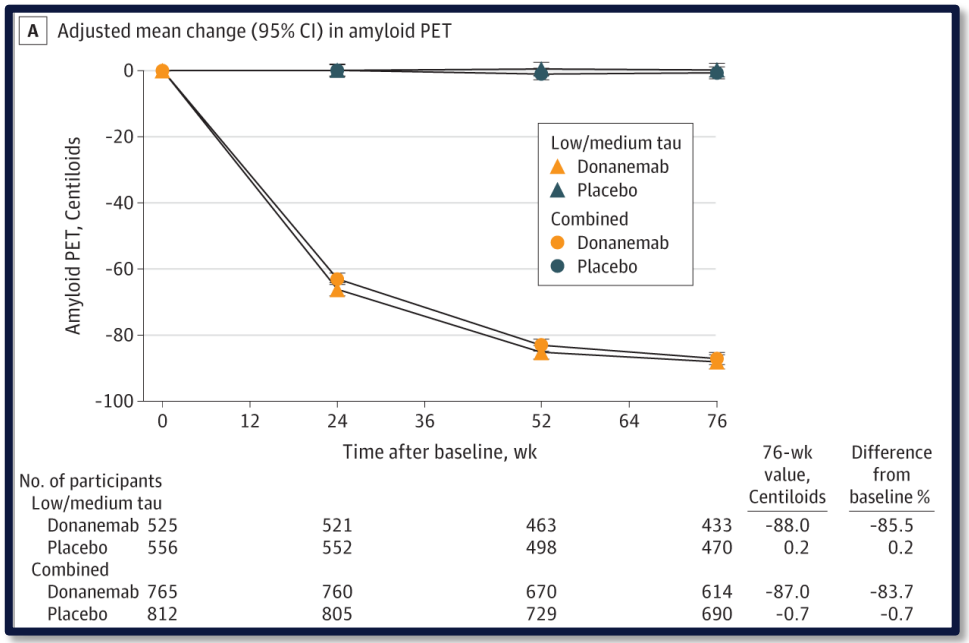
- Targets amyloid -beta protofibrils
- 2 weekly infusion & regular MRI
- Treatment continued until progression to stage 2 "moderate" dementia

Data From Lecanemab Trial – Amyloid Reduction and Slowing of Symptom Progression

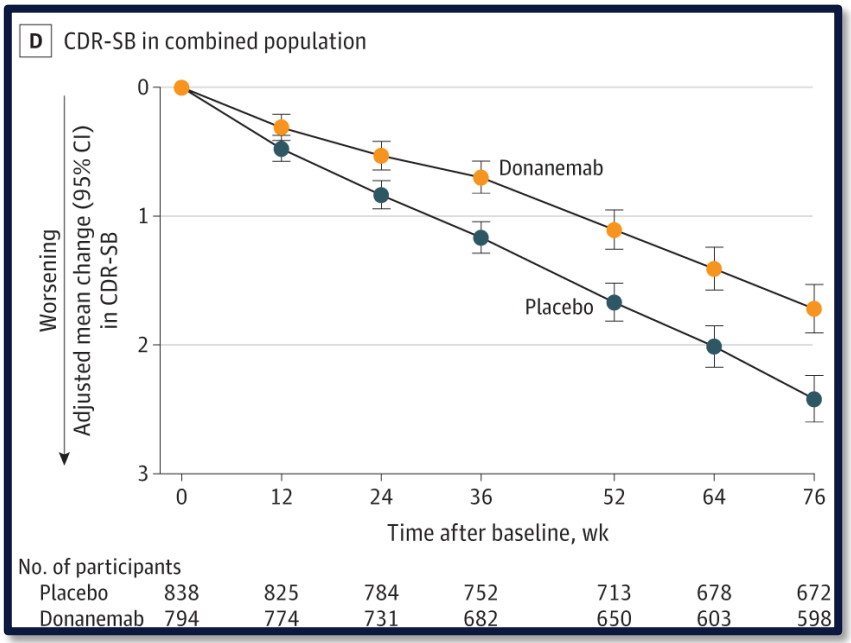




Data From Donanemab Trial – Amyloid Reduction and Slowing of Symptom Progression



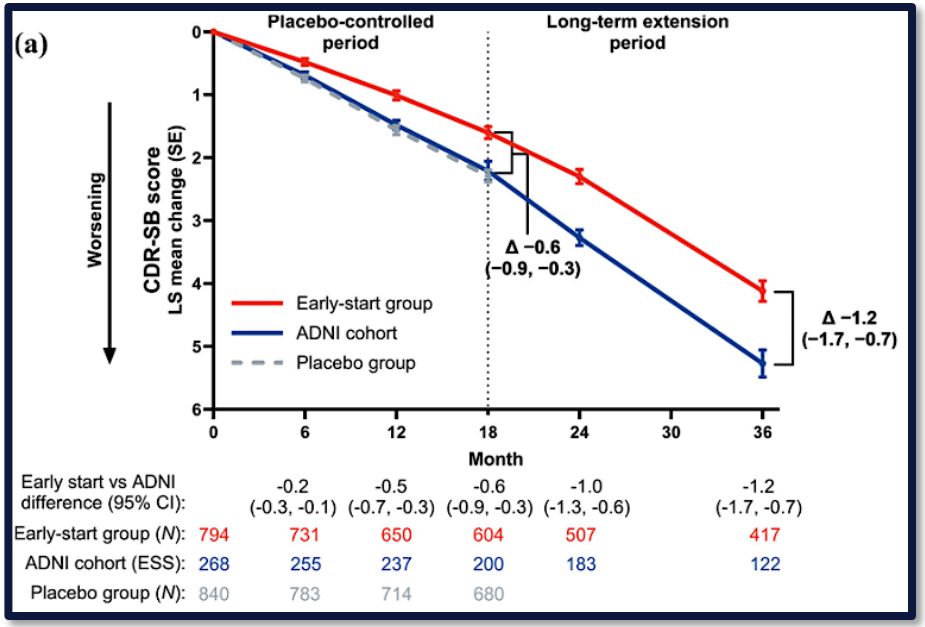
No. of participants					76-wk value, Centiloids	Difference from baseline %
Low/medium tau						
Donanemab	525	521	463	433	-88.0	-85.5
Placebo	556	552	498	470	0.2	0.2
Combined						
Donanemab	765	760	670	614	-87.0	-83.7
Placebo	812	805	729	690	-0.7	-0.7



No. of participants							
Placebo	838	825	784	752	713	678	672
Donanemab	794	774	731	682	650	603	598

Donanemab Extension Trial

Efficacy: Slowing of Clinical Decline in Early Start Donanemab Vs External ADNI Cohort



- Treatment benefit increased even after treatment regimen was completed in most participants
- Donanemab benefit continued to grow over 3 years

Side Effects of Anti-Amyloid Therapies

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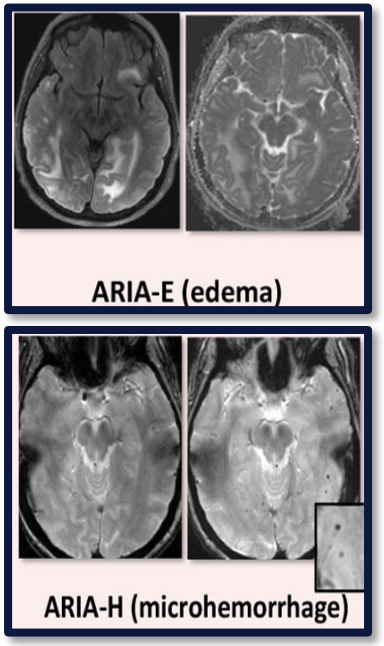
Amyloid Related Imaging Abnormalities (ARIA)

- Greater risk in ApOE4 carriers, higher still in homozygotes
- Most events occurred in first 3 months
- Most events asymptomatic
- ARIA -related deaths have occurred with both with Donanemab and Lecanemab
- Infusion related adverse events



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Anti-Amyloid Medications

- Need to consider risk vs. benefit
- Both intervention and treatment groups have cognitive decline, but cognitive decline is slower in the treatment group
- Treatment needs to be in early stage
- Not much data in diverse populations

Finding the Right Balance…

- Ensure the tests are used on the correct population
- Concern surrounding equity of access to biomarkers and treatment
- Concerns about eligibility for treatment
- Diversion of resources away from prevention and existing interventions
- “What price do you put on a potential slowing in symptom progression? ”

Case Study: Sue

Sue has expressed interest in exploring Anti-Amyloid treatment.

Accessing Anti-Amyloid Therapy

- Currently not PBS-subsidised, thus only available privately
- Requires referral to a local specialist who is linked to an infusion centre
- The specialist will organise:
  - Validated Alzheimer's disease biomarker; usually amyloid PET
  - MRI to look for any exclusion criteria
  - APOE4 gene testing
- Review of medical history and medication (including anti-coagulants)

Basic dark green background could be used as divider pages.

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Accessing Anti-Amyloid Therapy (Continued)

- Different infusion centres may have different Inclusion and Exclusion criteria
- Wait times will vary per centre
- Managing expectations, either active or four weekly infusion process, often for 18 months
- MRIs – multiple times along the journey (at least five)
- Trial centres can be reviewed via ADNET website

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Managing Patients Who Are Ineligible for Anti-Amyloid Therapy

- Many patients are ineligible for Anti -Amyloid therapy due to the Exclusion Criteria or MRI precautions

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- Acknowledge the potential psychological impact
- Continue with standard care for all patients living with dementia and MCI, regardless of biomarker positivity or treatment eligibility

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Optimising Brain Health

- Address vascular risks
- Optimise diabetes management
- Cognitive stimulation
- Address hearing and vision impairment
- Optimise mental health
- Physical activity
- Social engagement
- Minimise alcohol intake
- Medication review
- Diet
- Sleep
- Vaccinations
- Consider Souvenaid

Management of MCI

Cognition/Mental Health

- Education
- Brain health
- Medications

Function

- Legal
- Safety
- Driving

Changed Behaviour

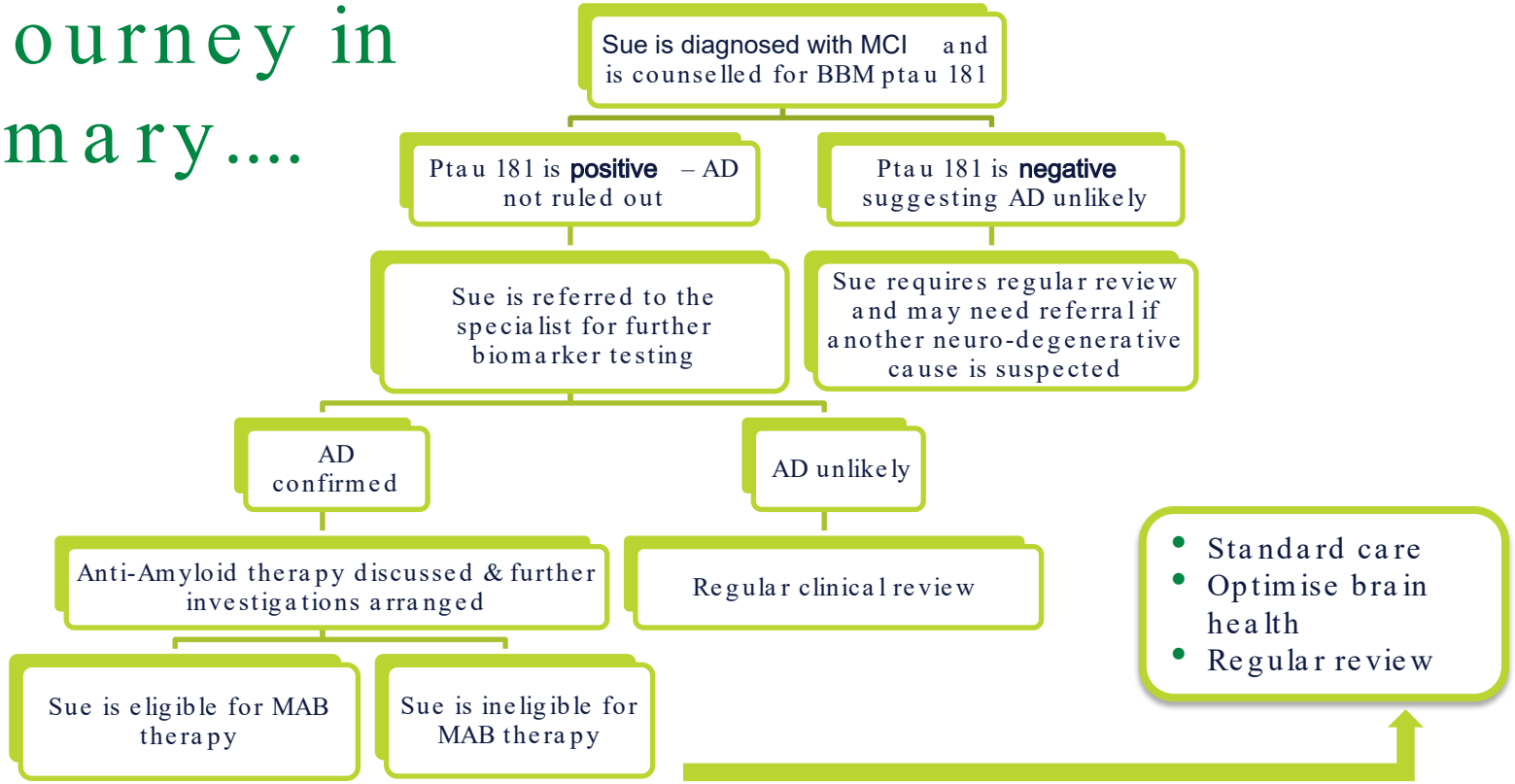
Physical

- GPCCMP

- ☐ **Goals for care*** – consider person with MCI as well as family/care partners
- ☐ **Education*** – answer questions about MCI, prognosis and risk reduction
  - ○ Refer to Dementia Australia: Thinking Ahead small group program for MCI
- ☐ **Brain health*** – discuss exercise, staying cognitively and socially active, limit alcohol and drugs, stop smoking, healthy diet
  - ○ Ask patients to complete CogDRisk – will give them personalised recommendations for reducing risk
  - ○ BrainHQ or Cognifit – evidence based computerised training (payment required)
- ☐ **Medications** – review current medications, especially those with anti-cholinergic load
- ☐ **Legal planning*** – will, enduring powers of attorney (legal/financial, lifestyle, medical), advance care directive
- ☐ **GP chronic condition management plan*** - update or develop

(Adapted from Facing Dementia Together checklist) https://facingdementiatogether.au/en/wp-content/uploads/sites/2/2024/04/Face-Dementia-MCI-review-checklist.pdf

Sue's Journey in Summary....



Sue's Journey in Summary....

- Sue presents to you with cognitive concerns
- Using Inclusion and Exclusion criteria you diagnose her with MCI
- She is counselled for BBM and decides to have the ptau 181 test

- If her ptau 181 test is positive, Sue will need referral to specialist services for further clarification of possible Alzheimer's disease
- If Alzheimer's disease is confirmed, she can be offered therapies

- If her ptau 181 test is negative, she can be reassured that Alzheimer's disease is unlikely, but she should be carefully reviewed for progression of her cognitive changes
- Sue should be referred if a different type of neurodegenerative condition is considered likely

- Standard care for MCI and dementia should be continued through this process, including [illegible] and treatment considerations

Basic dark green background could be used as divider pages.

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