Is there a pre-dementia syndrome?

Is Mild Cognitive Impairment a Myth?

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Myth. def^n

1. A traditional, typically ancient story dealing with supernatural beings, ancestors, or heroes that serves as a fundamental type in the worldview of a people

2. A popular belief or story that has become associated with a person, institution, or occurrence

3. A fiction or half-truth, especially one that forms part of an ideology
Global increase in dementia
Global increase in dementia

Cognitive Impairment 5X more common in the community than dementia (Unverzagt et al, 2001)
I'm going to carry out a little memory test...
Who am I?

I'd say you failed
Introduction

• There is usually a period between appearance of first symptoms and a clinical diagnosis of dementia

e.g. Subjects who report subjective memory loss more likely to develop AD\textsuperscript{1}

\textsuperscript{1}Tyas et al, 2001
Rate of memory decline increases 5.1 years before dementia diagnosis (Hall et al, 2000)
• Changes may occur even before the first symptoms
e.g. Neuritic plaques and neurofibrillary tangles found in adults without dementia\textsuperscript{1,2}
e.g. Idea density in autobiographies written at mean age 23 correlated with post-mortem neurofibrillary tangle count in frontal, temporal, parietal lobe\textsuperscript{3}

\textsuperscript{1}Price & Morris, 1999; \textsuperscript{2}Braak & Braak, 1991; \textsuperscript{3}Snowdon et al, 2000
Benefits of early identification

The accurate identification of individuals who will develop dementia allows for:

• earlier interventions
• pharmacotherapy
• cognitive training
• legal, financial and other decisions to be made while person is still competent
Delay = prevention

If onset of AD can be delayed
• by 2 yrs, ↓ prevalence by >20%
• by 5 yrs, ↓ prevalence by 50%¹

¹Brookmeyer et al. (1998)
A pharmaceutical opportunity

- Annual sales of Aricept worldwide for 2002 totalled over US$850 million\(^1\)
- Aricept Alzheimer's disease agent saw brisk sales of 141.56 million yen, up 22.8 percent\(^2\)

\(^1\)Esai Annual Report, 2002; \(^2\)Kyodo News Service 5.11.04
Proposed treatments for MCI

- NSAIDs
- Antioxidants
- Statins
- AChE Inhibitors
- Estrogen?
- Ginkgo biloba
- Memantine
- AMPAkinines
- PD4 Inhibitors
- Secretase inhibitors
- Immunotherapy
- Tau inhibitors
Cognitive training for older adults

- RCT of N = 2832 aged 65-94 years
- Randomised to 10 sessions of group training for memory, reasoning, speed of processing or no-contact
- 60% randomly received 4-session booster after 11 months
- Interventions ↑ the targeted cognitive ability
- Booster ↑ training gains in speed & reasoning at 2 year follow-up

¹Ball et al JAMA 2002:288:2271-81
Does MCI have clinical validity?
Kendell’s Criteria *plus one for validating clinical syndromes*¹

1. Identification & description
2. Demonstration of boundaries or ‘points of rarity’ between related syndromes
   
   *2b. Concurrent validity*

3. Establish a distinct course or outcome
4. Establish a distinct treatment response
5. Establish the syndrome ‘breeds true’
6. Association with more fundamental abnormality

Criterion 1:
Identification & description
Pre-dementia syndromes

- Age Associated Memory Impairment (AAMI)
- Age Related Memory Decline (ARMD)
- Age Related Cognitive Decline (ARCD)
- Benign Senescent Forgetfulness (BSF)
- Cognitive Impairment No Dementia (CIND)
- Memory Impairment
- Mild Cognitive Disorder (MCD)
- Mild Cognitive Impairment (MCI)
- Mild Neurocognitive Disorder (MND)
- Questionable dementia (QD)
Problems with criteria

• Multiple definitions
• Heterogenous criteria eg subjective, objective
• Vary in content and amount of detail eg which tests to use
Mild Cognitive Impairment

Cognitive Performance

Normal  MCI  Dementia

‘MCI refers to the state of cognition and functional ability between normal aging and very mild AD’

(Petersen, 2001)
Amnestic MCI (Petersen, 1995)

- Cognitive complaint, usually memory
- Cognitive screening test in normal range for age (eg MMSE)
- 1.5 SDs below age-appropriate norms on memory tests or memory component of other cognitive tests - *clinician judgement*
- ADLs not significantly affected
- Not meeting DSM dementia criteria
But there are problems with each of these criteria
The problem with cognitive complaint

• Who complains?
  – Patient or family member

• Does the person complain
  – Spontaneously? or
  – In response to interviewer asking about memory problems?

• Does the person seek assessment/ treatment or is s/he recruited from community survey?
Problem with general cognition normal for age

- Usual to base this on a MMSE score above certain threshold, eg >24
- Does not make allowance for effects of intelligence, education, language, culture
- Person of low intelligence is more susceptible to MMSE decline (than person with high IQ)
Problem with memory impairment

• What is impairment?
  – No specific cut-offs
  – No standard memory tests prescribed

• Standard practice is to define 1.5 SD below population norms corrected for age, education

• BUT criterion is *then* based on clinician judgement
  – this is not operationalised but allows flexibility eg to allow for high intelligence, low education
Problem with intact ADLs

• Intact ADLs can be as simple as still being able to dress, wash

• Or, intact IADLs e.g. driving car, managing housework, catching public transport

• But, are subtle impairments included?
  – Eg ability to weigh up competing investment portfolios and make decisions about finance
Revised Petersen Criteria (2004)

4 subsets of MCI now included:

1. aMCI (single domain)
2. aMCI (multiple domains)
3. Non-amnestic MCI (single domain)
4. Non-amnestic MCI (multiple domains)
Revised Petersen Criteria (2004)

• Proposes a parallel set of procedures to those for diagnosing AD

• Includes clinical judgement for assessment of cognitive performance and ADL performance (no specific instruments or cut-off scores)

• Clinical judgement particularly relevant when assessing people of either high intellect (where performance may now be average) or of low education (where below average performance may not represent cognitive decline)
Revised Petersen Criteria (2004)

Mild Cognitive Impairment

- Cognitive complaint
  - Not normal for age
  - Not demented
  - Cognitive decline
  - Essentially normal functional activities

MCI

Memory impaired?

Yes
- Amnestic MCI
  - Memory impairment only?
    - Yes
      - Amnestic MCI Single Domain
    - No
      - Amnestic MCI Multiple Domain

No
- Non-Amnestic MCI
  - Single non-memory cognitive domain impaired?
    - Yes
      - Non-Amnestic MCI Single Domain
    - No
      - Non-Amnestic MCI Multiple Domain
Criterion 2: Points of rarity between related syndromes
Mild Cognitive Impairment

Cognitive Performance

Normal  MCI  Dementia

‘MCI refers to the state of cognition and functional ability between normal aging and very mild AD’

(Petersen, 2001)
MCI concepts

Cognitive Performance

Normal

MCI

Dementia
Pre-dementia

Cognitive Performance

Normal

Prodrome

Dementia
Pre-dementia

Cognitive Performance

Normal

Prodrome

Prodromes? VaD, LBD, FTD

AD
Criterion 2b: Points of rarity on correlates of MCI
Normal > MCI > AD

On all measures, MCI is intermediate between normal controls and Alzheimer’s disease

- Neuropsychology
- Neuroimaging
- Neuropsychiatry
- Neuropathology
Neuropsychiatry and MCI: Cardiovascular Health Study

- From 3608 participants studied over 10 years
- 362 with dementia; 320 with MCI and 142 NC
- Dementia 270 (75%) had a neuropsychiatric symptom in the past month, (62% clinically sig.)
- MCI 43% NPI Sx and 29% clinically significant
- Normal cognitive (from Cache County Study)

Lyketsos et al, *JAMA*, 2002;288:1475-83
Cardiovascular Health Study

1 Lyketsos et al, *JAMA*, 2002;288:1475-83
Clinically significant symptoms in MCI from Cardiovascular Health Study

Clinically significant Sx = NPI ≥ 4 for the item

- Sleep disturbance (8.8%)
- Irritability (7.5%)
- Depression (6.3%)
- Apathy (6.3%)
- Eating disturbance (6.3%)

1 Lyketsos et al, *JAMA*, 2002;288:1475-83
Neuropsychiatry and MCI: InDDEEx Study

Baseline data from InDDEEx (Investigation into Delay to Diagnosis of AD with Exelon; N = 1000)

- RCT rivastigmine/placebo for MCI
- 42% score 0 on NPI = NPI – (n 417)
- 59% scored 1+ on NPI (n 593)
  - 40% on one item
  - 24% on two items
  - 36% on 3+ items
- Commonest items: depression irritability anxiety agitation

Neuropsychiatry and MCI: UCLA outpatient study

Any NPI Sx
- 12% in normal cognition (community, n=50)
- 75% in MCI (n=28)
- 89% in mild AD (n=124)

Most common NPI Sx in MCI pts:
- Dysphoria
- Irritability
- Apathy
- Anxiety
Criterion 3:
Course and Outcome
Rate of decline & mortality\textsuperscript{1}

- Older Catholic clergy: 211 MCI, 587 cog\textsuperscript{n} intact
- mean 4.5 yrs f/u
- MCI aged 78.6 ± 6.8, cog\textsuperscript{n} intact 74.3 ± 6.5 yrs
- MCI declined significantly faster on episodic memory, semantic memory & perceptual speed
- MCI mortality 1.7 higher than cog\textsuperscript{n} intact

\textsuperscript{1}Bennett et al, Neurology, 2002;59:198-205
Institutionalisation and mortality

• Population sample: 801 CIND, 883 No Cognitive Impairment (NCI)
• At 5 year follow up available data showed:
  – 29% CIND institutionalised vs 14% NCI
  – 49% CIND had died vs 30% NCI

1 Tuokko et al, Archives of Neurology, 2003; 60: 577-582
Dementia incidence

New cases per year in general population$^1$

- 65-69 years - 0.33%
- 70-74 years - 0.84%
- 75-79 years - 1.82%
- 80-84 years - 3.36%

$^1$Kawas et al, 2001
### Out-patient clinic samples

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Annualized conversion rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Memory impairment</td>
<td>6%</td>
</tr>
<tr>
<td>AAMI</td>
<td>8% - 15%</td>
</tr>
<tr>
<td>MCI</td>
<td>12% - 34%</td>
</tr>
<tr>
<td>MCI (clinical interview)</td>
<td>6% - 34%</td>
</tr>
</tbody>
</table>

## Community samples

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Annualized conversion rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>MCI</td>
<td>12.2% - 16.0%</td>
</tr>
<tr>
<td>MCI (clinical interview rating)</td>
<td>6.5% - 8.2%</td>
</tr>
<tr>
<td>AACD</td>
<td>8.8% - 28.6%</td>
</tr>
</tbody>
</table>

1Ritchie et al, 2001; 2Petersen et al, 1995; 3Daly et al, 2000; 4Bennett et al, 2002
### Population samples

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Annualized conversion rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAMI</td>
<td>3.5% - 4.2%</td>
</tr>
<tr>
<td>Any preclinical syndrome</td>
<td>6%</td>
</tr>
<tr>
<td>Vascular CIND</td>
<td>9.2%</td>
</tr>
<tr>
<td>MCI (clinical interview)</td>
<td>18%</td>
</tr>
</tbody>
</table>

Instability of syndromes

- Memory impairment (<10th percentile)$^1$
  - After 2 years, 35% improved
  - After 5 years, 42% improved

- AACD$^2$
  - After 1 year, 76/174 improved (43%)
  - After 3 years, 69/170 improved (41%)

$^1$Visser et al, 2000; $^2$Ritchie et al, 2001
Instability of syndromes

MCI

• Ritchie (2001) found:
  – After 1 year, 25/27 improved (93%)
  – After 3 years 19/23 improved (83%)

• Wahlund (2003) found:
  – After 3 years, 5/43 improved (11%)
Rates of conversion

• Vary between 0 and 34% p.a.
• Depends on
  – Sample source, clinic vs community vs population
  – Age of sample, higher if older
  – Criteria for defining sample
  – Exclusion criteria
MCI

• Petersen 10-12%pa → dementia

• Ritchie (2001):
  – After 1 year, 25/27 improved (93%); No dementia

• Wahlund (2003):
  – After 3 years, 5/43 improved (11%)
Explanation of discrepancy between Petersen and Ritchie

• Peterson bases diagnosis of MCI on clinical judgement – reduction of memory by 1.5 SDs < norm is guide not definitive.
• Ritchie used a number of tests: many people fell below this threshold on ≥ one test but these would not be considered MCI by Petersen
• How is clinical judgement operationalised?
• Would Petersen’s MCI patients be considered early dementia in other settings?
### Instability of syndromes: AAMI

<table>
<thead>
<tr>
<th></th>
<th>1.5 years</th>
<th>2 years</th>
<th>3.6 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No subjective complaints</strong></td>
<td>12.1%</td>
<td>4.0%</td>
<td></td>
</tr>
<tr>
<td><strong>No objective impairment</strong></td>
<td>21.5%</td>
<td>13.7%</td>
<td>9.7%</td>
</tr>
<tr>
<td><strong>Exclusion met</strong></td>
<td>10.6%</td>
<td>6.0%</td>
<td>8.5%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>44.1%</td>
<td>23.7%</td>
<td>18.2%</td>
</tr>
</tbody>
</table>

1 Helkala et al, 1997; 2 Lane & Snowdon, 1989; 3 Hanninen et al, 1995
Problems with interpretation

- Studies differ greatly—age, syndrome, tests, exclusion, follow-up
- Some do not report type of dementia
- Post-mortem diagnosis rare
- Population studies do not include imaging
- Suitable length of follow-up
- No study investigating individuals not meeting pre-dementia syndrome criteria who subsequently develop dementia
- Definition of impaired ADLs, eg finances - Griffith et al, Neurology 2003; 60:449-57.
Impaired Financial ADLs\(^1\)

- **Subjects:**
  - 21 cognitively normal
  - 21 aMCI
  - 22 mild AD

- The Financial Capacity Instrument (FCI) was administered to assess Financial ADLs

- FCI assesses financial ADLs in 9 domains, such as bill payment, investment decision making, and basic monetary skills

\(^1\)Griffith et al, *Neurology*, 2003; 60: 449-457
Impaired Financial ADL Results

- aMCI subjects impaired relative to controls in:
  - Cash transactions
  - Bank statement management
  - Bill payment
  - Overall financial capacity

- The control and aMCI groups performed significantly better than mild AD subjects

- Suggests the aMCI diagnostic criteria should include impairments in higher order ADLs

Predictors of conversion
Conversion from MCI to AD—Consistently reported

∀ ↑ age¹-³
• Apoe4 genotype³-⁶
∀ ↓ general cognition¹-³,⁷
∀ ↓ memory¹,²,⁵,⁸-¹¹
∀ ↓ function⁵,¹⁰-¹²
• Lower education¹³
∀ ↓ Recall and ↓ executive function

Other predictors

\[ \forall \downarrow \text{baseline olfaction and no complaints of smelling problems}^{1} \]

- Taking longer to walk 30 ft \(^2\)
- Female gender\(^1\)
- Non-drinking and frequent drinking\(^2\)
- Hippocampal atrophy\(^3\) & volume loss\(^4\)\(^-\)\(^6\)
- Medial temporal lobe loss\(^6\)
- Presence of neuropsychiatric symptoms\(^7\)
- Decreased perfusion on SPECT\(^8\)

\(^1\)Devanand et al, 2000; \(^2\)Marquis et al, 2002; \(^3\)Anttila et al, 2004; \(^4\)Jack et al, 1999; \(^4\)Jack et al, 2000; \(^5\)Marquis et al, 2002; \(^6\)Visser et al, 2002; \(^7\); \(^8\)Johnson et al, 1998
Conversion from MCI to AD
Neuropsychological tests

- Recall (particularly delayed)
  - Verbal auditory learning tests\(^1,^2\)
  - Word list delayed recall\(^3\)
  - Shopping list task, misplaced objects task\(^4\)
  - Buschke selective reminding test\(^5,^6,^7\)
  - Logical Memory\(^8,^9\)/ Narrative recall\(^10\)

\(^1\)Visser et al, 2000; \(^2\)Tierney et al, 1996; \(^3\)Chen et al, 2000; 
\(^4\)Flicker et al, 1991; \(^5\)Hanninen et al, 1995; \(^6\)Wentzel et al, 2001; 
\(^7\)Devanand et al, 1997; \(^8\)Morris et al, 2001; 
\(^9\)Marquis et al, 2002; \(^10\)Artero et al, 2003
Conversion from MCI to AD
Neuropsychological tests

- Fronto-executive:
  - WAIS-R digit symbol, picture arrangement, block design\(^1\)
  - Trails B\(^2\)
  - Verbal fluency\(^1,3,4,5\)

\(^1\)Devanand et al, 1997; \(^2\)Chen et al, 2000; \(^3\)Wentzel et al, 2001; \(^4\)Hanninen et al, 1995; \(^5\)Artero et al, 2003
SPECT as predictor

\( \forall \downarrow \) perfusion\(^1\)

- hippocampal-amygdaloid
- posterior cingulate
- anterior thalamus
- anterior cingulate

• No predictors\(^2\)

\( \forall \downarrow \) Ratio between CFS tau and blood flow in the posterior cingulate\(^3\)

\(^1\)Johnson et al, 1998; \(^2\)McKelvey et al, 1999; \(^3\)Okamura et al, 2002
Criterion 4: Treatment
### AD: Prevention & Treatment Strategies

<table>
<thead>
<tr>
<th>Clinical State</th>
<th>Normal</th>
<th>Pre-symptomatic AD</th>
<th>Mild Cognitive Impairment</th>
<th>AD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Strategies</td>
<td>Identify at-risk Prevent AD</td>
<td>Prevent or Delay Emergence Of Symptoms</td>
<td>Stimulate Memory; Slow progression</td>
<td>Treat cognition Treat behaviours Slow progression</td>
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<tr>
<td>Treatment</td>
<td>NSAIDs</td>
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<td>NSAIDs</td>
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<td>Tau inhibitors</td>
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- **Prevention & Treatment Strategies**
- **NSAIDs**
- **Antioxidants**
- **Statins**
- **Gingko biloba**
- **Estrogen**
- **Secretase inhibitors**
- **Immunother.**
- **Tau inhibitors**
- **AChE Inhibitors**
- **AMPAKines**
- **PD4 Inhibitors**
- **Secretase inhibitors**
- **Immunotherapy**
- **Tau inhibitors**
Preventing Pre-dementia syndrome

• Higher education protective for MCI

• Exercise & social activity programs
  – exercise protective for CIND in women
  – decreased risk with increased level of physical exercise

• HRT
  – estrogen plus progestin shown not to prevent MCI in postmenopausal women

1Tervo et al, 2004; 2Laurin et al, 2001; 3Shumaker et al, 2003
Improving cognition in pre-dementia

- 24-wk RCT Ginkgo biloba\(^1\)
- 12-wk RCT phosphatidylserine (a phospholipid)\(^2\)
- 6-month CBT vs no-treatment\(^3\)

→ All showed no benefit on cognition

- A dopamine agonist (piribidel) did improve MMSE score over 90-days RCT \(^4\)

\(^1\)van Dongen et al, 2000; \(^2\)Jorisse et al, 2001; \(^3\)Rapp et al, 2002; \(^4\)Nagaraja et al, 2001;
Vitamin E and Donepezil Trial for MCI

- Prevent development of AD
- Slow decline on cognitive impairment

- Vitamin E 2,000 IU/day
- Donepezil 10 mg/day
- Placebo
- (Open-label donepezil after conversion to AD)

- 790 participants in 69 centers
Vitamin E and Donepezil trial for MCI

• No overall effect of donepezil or vitamin E on progression to AD over 36 months.

• Donepezil reduced the risk of progressing from MCI to AD for up to 18 months.

• Donepezil had an effect on overall function, memory and language for up to 18 months.

• Vitamin E had no effect on progression to AD and had a minor effect on secondary outcomes.

Galantamine trial for MCI

- Study objectives
  - Prevent development of AD
  - Effects on cognition and global function
- Treatments
  - Galantamine 16 or 24 mg/day
  - Placebo
- 2-year duration
- 50 years old and over
  - 2057 elderly (17 countries)
Galantamine trial for MCI

- **Amnestic-placebo (n=17)**
- **Amnestic+placebo (n=434)**
- **Amnestic-galantamine (n=25)**
- **Amnestic+galantamine (n=411)**

Mean (±SEM) change from baseline

- **Baseline**
- **Month:** 3, 6, 9, 12, 15, 18, 21, 24

Improvement in CDR-SB

p H0.05 vs baseline  p H0.05 vs placebo  p H0.01 vs baseline
p H0.01 vs baseline  p H0.01 vs placebo  p H0.002 vs baseline
Rate of change in whole brain volume

Rate of brain atrophy over 24 months in galantamine vs placebo

*Placebo (n=142), galantamine (n=127), p=0.003, p<0.001 with sex (additional covariate) +Placebo (n=59), galantamine (n=70), p<0.001, ++Placebo(n=83), galantamine (n=57), p=0.145
Other Potential Interventions

- Vaccine?
- Nerve-growth factor?
- Statins?
- Other antioxidants?
- Anti-inflammatory?
- Nutrition? Regular alcohol? Fish?
- Education?
Criterion 5: Family/Genetic Studies
Apoe4 and MCI

• Apoe4 frequency controls $< \text{ARMD} \approx \text{AD}^1$

• However,
  – Other studies show no difference in Apoe4 status between MCI and controls$^2$
  – Non-carriers can still develop MCI$^3$

$^1\text{Blesa et al, 1996}; \ ^2\text{Collie et al, 2002}; \ ^3\text{Anttila et al, 2004}$
Criterion 6: pathology
MCI: Macro-pathology

∀↓ hippocampal volume\(^1-^4\) (associated with decreased memory but not non-memory cognitive performance)\(^5\)

∀↓ entorhinal cortex volume\(^2\)

∀↑ entorhinal neuron atrophy\(^6\)

• ventricular enlargement\(^2\)

∀↓ cortical grey matter\(^2\)

\(^1\)Convit et al, 1997; \(^2\)Du et al, 2001; \(^3\)Mega et al, 2002; \(^4\)Grundman et al, 2004; \(^5\)Grundman et al, 2003; \(^6\)Kordower et al, 2001
Subjects were followed up for 3 ± 1 years

$^1$Jack et al, 2000
MCI: micro-pathology

• Average # neurofibrillary tangles$^1$
  controls < MCI < AD

• Cholinergic basal forebrain neurons$^2$
  controls > MCI ≅ AD

• Beta-amyloid$^3$
  controls < MCI < AD

$^1$Mitchell et al, 2002; $^2$Mufson et al, 2002; $^3$Mufson et al, 1999
∀ ↑ Choline acetyl transferase activity in superior frontal cortex & hippocampus\(^1\)
MCI > controls

- Quantitative differences in EEG during haptic tasks\(^2\)
  Controls \(\neq\) MCI
- Marker of in vivo lipid peroxidation\(^3\)
  MCI > controls

\(^1\)DeKosky, 2002; \(^2\)Grundwald et al, 2002; \(^3\)Pratico et al, 2002
Kendell’s criteria

Validating clinical syndromes:

1. Identification & description
2. Demonstration of boundaries or ‘points of rarity’ between related syndromes
2b. Concurrent validity
3. Establish a distinct course or outcome
4. Establish a distinct treatment response
5. Establish the syndrome ‘breeds true’
6. Association with more fundamental abnormality

Arbitrary divisions, different slopes

Normal

MCI

Dementia

Death
Arbitrary divisions, different slopes

Normal

MCI

Dementia

Death
Conclusions

• Pre-dementia syndromes heterogenous
• Higher risk of dementia
• Predictors of conversion similar to AD
• Validity questionable
• Specificity not known

→ No syndrome obviously superior to others though perhaps higher rates of conversion using clinical interviews
MCI conclusions

- Pre-dementia syndrome definition still debatable
- Validity questionable
- Specificity not known
- But there appears to be a state intermediate between normal and dementia with a higher risk of dementia
- Predictors of conversion similar to AD
- No intervention proven to work but many trials current to prevent AD
- New MCI types (non-amnestic) being studied
Future directions

• A clinical judgement? (including family info)
• Focus on *decline* rather than impairment
  – Detailed informant reports
  – Comparison of current performance to estimate of premorbid level
  – Longitudinal assessment
• May be specific to dementia types
  – e.g. probable AD pre-dementia
• Imaging & biomarkers
Thank you

www.med.unsw.edu.au/adfoap

“Happiness is nothing more than good health and a bad memory”

Albert Schweitzer (1875-1965)

Kamato Hongo, world’s oldest woman in 2003 - died aged 116