Mild Cognitive Impairment

The Role of the Family Physicians

McGill Refresher Course – December 2018

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DISCLOSURES

- **<u>No Conflicts of Interest to Disclose</u>**

Objectives

- *Discuss the updated criteria of Mild Cognitive Impairment and how they differ from the criteria of Dementia.*

- *Describe the practical tools and pertinent investigations indicated for a patient with a cognitive complaint.*

- *Determine the best management and treatment approach in a patient with a cognitive complaint.*

INTRODUCTION

Should We Screen for Cognitive Impairment ?

- ***NO*** systematic screening
- Subjective complaint
- Caregiver complaint
- ***Case-Finding***
  - Age ≥ 80
  - Delirium
  - De novo depression
  - Multiple vascular risk factors
  - Other clinical indices
    - Unexplained weight loss
    - Doubt about medication compliance
    - Frequent calls or medical visits (to the ER)
    - Forgetting appointments
    - « Bad historian » - Inconsistent history, etc.

CLINICAL CASE 1

Clinical Case 1

- You see a 83 y/o lady on yearly follow-up.
- She has well-controlled DM, HBP, and CAD.
- Se is independent in her ADLs and IADLs, and drives her car without difficulty. She had more difficulty organising her documents for tax returns in the previous year.
- She complains of mild forgetfulness, that is more "annoying" than really bothersome to her.
- Her general examination is normal.
- Her MMSE (Folstein) score is 28

What other clinical evaluation would you recommend ?

Do you recommend further work-up ?

What is your clinical diagnosis?

Clinical Case 1
Clinical Evaluation

- History: r/o secondary cause
  - Medication side effects
  - Anxiety or depression
  - Sleep apnea
  - Uncontrolled chronic disease: COPD, CRF, heart failure, etc.
  - Metabolic disorder: thyroid disorder, diabetes

- Neurological Examination

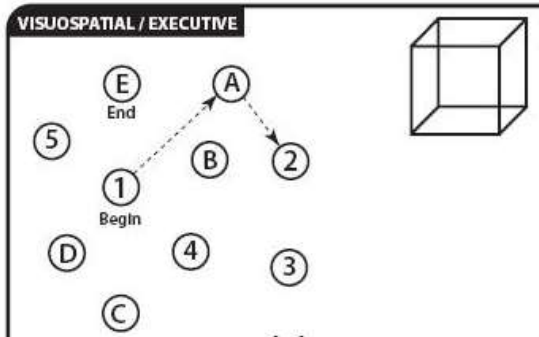
- MOCA = 22 (normal 26)

Montreal Cognitive Assessment (MOCA)

MONTREAL COGNITIVE ASSESSMENT (MOCA)

NAME :
Education : Date of birth :
Sex : DATE :

VISUOSPATIAL / EXECUTIVE — POINTS



Copy cube

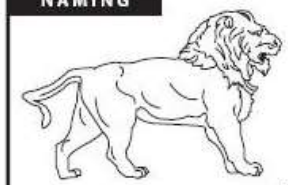
[ ] [ ]

Draw CLOCK (Ten past eleven) (3 points)

[ ] Contour [ ] Numbers [ ] Hands

__/5

NAMING



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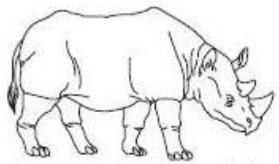

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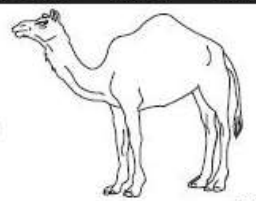

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MEMORY Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.

	FACE	VELVET	CHURCH	DAISY	RED
1st trial					
2nd trial					

No points

ATTENTION Read list of digits (1 digit/ sec).

Subject has to repeat them in the forward order [ ] 2 1 8 5 4

Subject has to repeat them in the backward order [ ] 7 4 2

__/2

Read list of letters. The subject must tap with his hand at each letter A. No points if ≥ 2 errors

[ ] F B A C M N A A J K L B A F A K D E A A A J A M O F A A B

__/1

Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 or 5 correct subtractions: **3 pts**, 2 or 3 correct: **2 pts**, 1 correct: **1 pt**, 0 correct: **0 pt**

__/3

LANGUAGE Repeat : I only know that John is the one to help today. [ ]

The cat always hid under the couch when dogs were in the room. [ ]

__/2

Fluency / Name maximum number of words in one minute that begin with the letter F [ ] _____ (N ≥ 11 words)

__/1

ABSTRACTION Similarity between e.g. banana - orange = fruit [ ] train – bicycle [ ] watch - ruler

__/2

DELAYED RECALL

	Has to recall words WITH NO CUE	FACE	VELVET	CHURCH	DAISY	RED	Points for UNCUED recall only
		[ ]	[ ]	[ ]	[ ]	[ ]	
Optional	Category cue						
	Multiple choice cue						

__/5

ORIENTATION [ ] Date [ ] Month [ ] Year [ ] Day [ ] Place [ ] City

__/6

© Z.Nasreddine MD Version 7.1 **www.mocatest.org** Normal ≥ 26 / 30

TOTAL __/30

Add 1 point if ≤ 12 yr edu

Administered by: _____

MOCATEST.ORG

Clinical Case 1
Work-Up

- CBC, electrolytes, Ca, BUN, creatinine, TSH (B12 / folate)

- Brain Imaging ?

TABLE 4.
Recommendations from CCCDTD2 about CT scan needed if:

- age less than 60 years
- rapid (e.g., 1 or 2 months) unexplained decline in cognition or function
- "short" duration of dementia (less than 2 years)
- recent and significant head trauma
- unexplained neurological symptoms (e.g. new onset of severe headache or seizures)
- history of cancer (especially in sites and types that metastasize to the brain)
- use of anticoagulants or history of bleeding disorder
- history of urinary incontinence and gait disorder early in the course of dementia (as may be found in normal pressure hydrocephalus)
- any new localizing sign (e.g., hemiparesis or a Babinski reflex)
- unusual or atypical cognitive symptoms or presentation (e.g. progressive aphasia)
- gait disturbance

Gauthier S, Can Geriatr J 2012

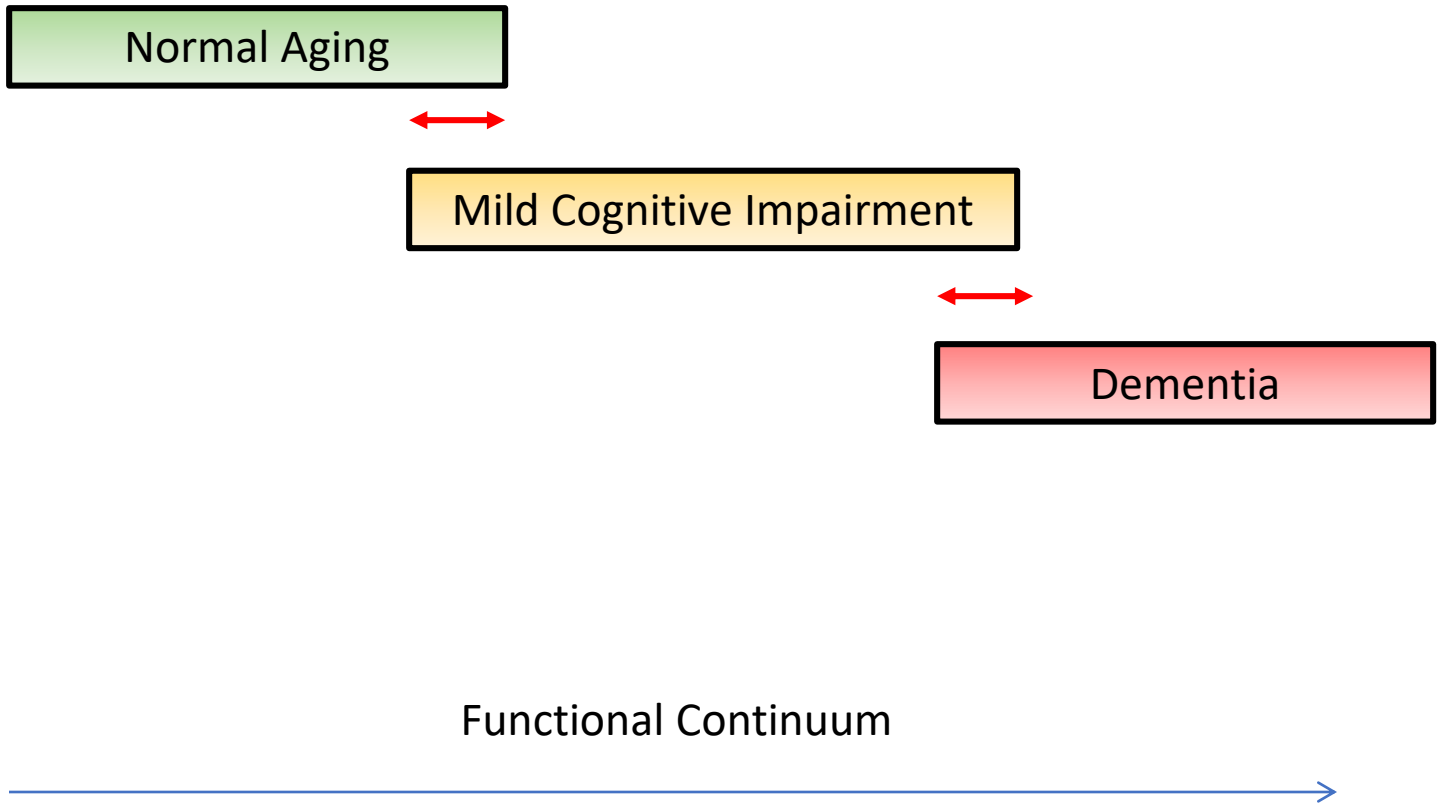
What is your diagnosis ?

Clinical Case 1
Clinical Diagnosis

- Mild Cognitive Impairment (*Mild Neurocognitive Disorder*)

- Why is this not early Alzheimer's Disease?
  - Mild symptoms
  - Don't seem to be progressive
  - No repercussions on functional autonomy

Cognitive Continuum



Petersen RC et al, Neurologia 2000

Normal Cognitive Aging

- Slowing in reaction time

- Mild impairment in executive function (7^{th} decade)
  - Initiation, planning, mental flexibility
  - Capacity to evaluate and accommodate new learning

- Mild impairment in short-term memory (6th decade)
  - ↓ working memory
  - Immediate memory intact
  - Long-term memory intact

- ↓ divided attention (7^{th} decade)

- Mild word-finding difficulty

- Typically
  - Changes are mild
  - Little/not progressive
  - Little/no functional repercussions

Terminology

- *Cognitive Impairment Not Dementia* (CIND) (Can Study of Health and Aging, 1995)
- *Mild Cognitive Impairment* (amnestic) (MCI) (1999)
- *Mild Cognitive Impairment* (multi-domain) (2004)
  - Memory impaired (amnestic): alone or multi-domain
  - Memory spared: other cognitive fct alone or multi-domain
- Prodromal AD (Dubois, 2010)
- *Mild Cognitive Impairment due to AD* (NIA-AA, 2011)
- *Mild Neurocognitive Disorder* (DSM 5) (2013)

Common Elements to All Definitions

- Subjective complaint – Confirmed by caregiver
- Objective evidence of decline (cognitive testing)
- Preservation of functional autonomy (mild impairment or decrease in efficiency accepted)
- Do not meet criteria for dementia
- Gray zone …

Neurocognitive Disorder
DSM 5

- Change in terminology
- ***Dementia***: association with diseases of aging, stigma.
- Proposed Approach
  - Determine the affected cognitive domains
  - Determine severity of impairment / functional repercussions: mild vs major
  - Determine etiology (AD, vascular, Lewy Body, etc.)
    - Probable: typical clinical picture, supported by imaging or other biomarkers
    - Possible

Mild Neurocognitive Disorder
DSM 5

- ***Modest Decline*** *in* ≥ ***1*** cognitive domain
  - On history
  - On objective evaluation
- No functional repercussions
- Exclusion: delirium or psychiatric condition

- Comparable to Dx criteria of MCI (Mayo, IWG, NIA-AA, etc.)

Mild Cognitive Impairment
Progression (« conversion »)

Table 3. Rates of Progression

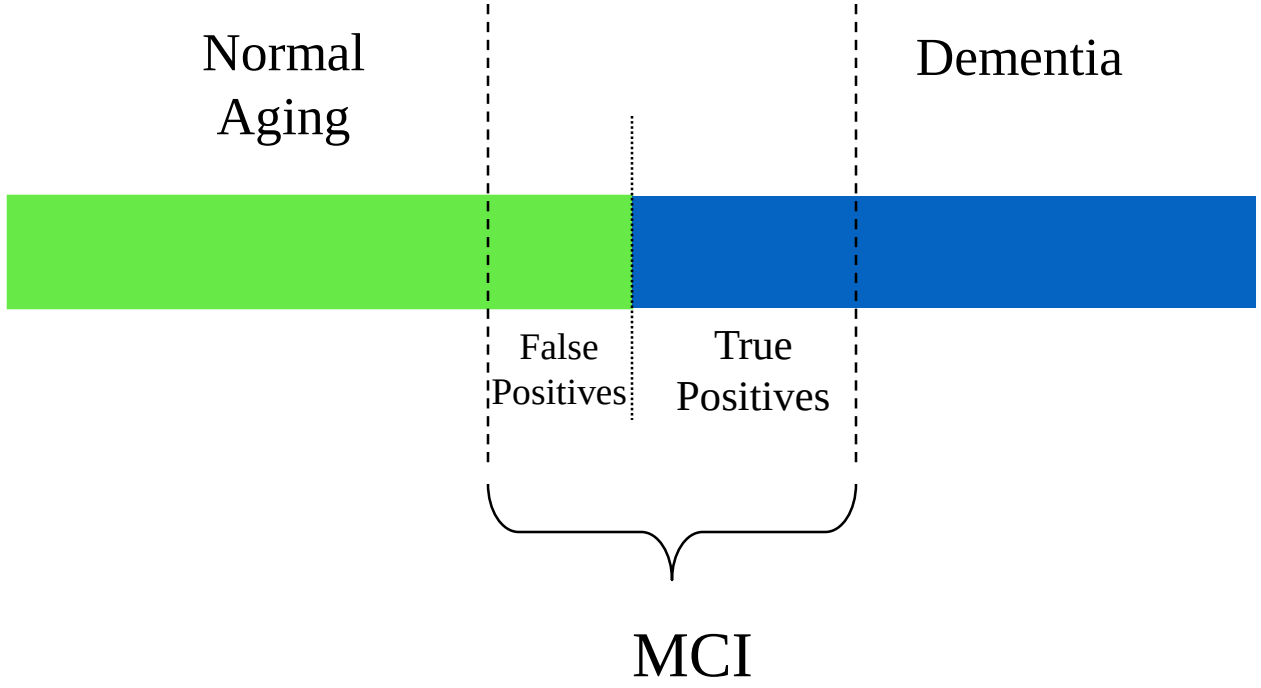
Source	Study Location	No. of Participants	Participant Age, y	Reported Rate of Progression	Annual Crude Progression Rate, %[a]
Solfrizzi et al,[30] 2004	Italy	1524	≥65	3.8/100 person-years	3.8
Busse et al,[12] 2006	Leipzig, Germany	863	≥75	44% per 4.3 y	10.2
Tschanz et al,[31] 2006	Cache County, Utah	3266	≥65	46% per 3 y	15.3
Fischer et al,[24] 2007	Vienna, Austria	476	75-76	33.9% per 30 mo	13.6
Ravaglia et al,[32] 2008	Italy	937	≥65	14% per 1 yr	14.0
Farias et al,[26] 2009	California	111	>60	3% per 1 y[b]	3.0[b]
Petersen et al, unpublished data, 2009	Rochester, MN	1969	70-89	7.5% per 1 y	7.5

[a] Reported or crude rate estimated from data.
[b] Progression rate for clinic cohort reported as 13% per 1 year.

- Variable between studies
- Specialized clinics: 10%-15% par année
- Community: 6%-10% par année
- Reversibility: 25% - 30%

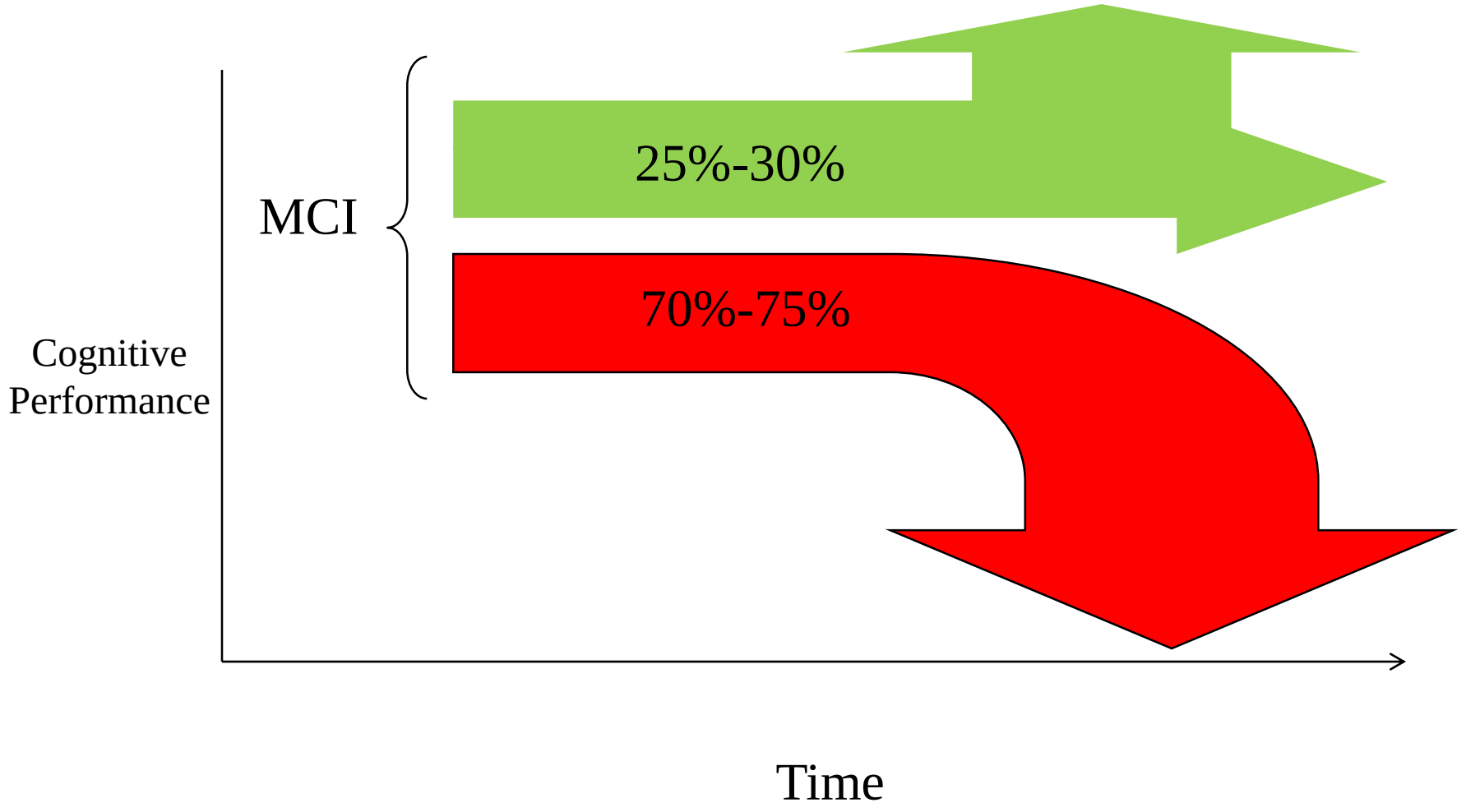
Petersen RC et al, Arch Neurol 2009

Mild Cognitive Impairment
Controversy…



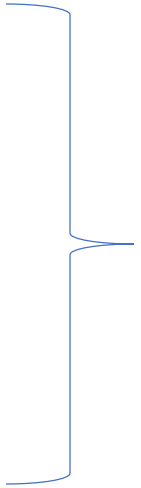
Mild Cognitive Impairment

Natural History



Predictors of Progression

- Clinical
  - Age, education, scores on screening tests, (MMSE, clock drawing)
  - Behavioral changes (anxiety, depression, etc.)
  - Neuropsychology
- Biochemical
  - ApoE4
  - Protein τ / Aβ42 (CSF)
- Neuroimaging
  - Structural (MRI)
  - Functional (SPECT, PET)
  - Molecular (PET-PIB)



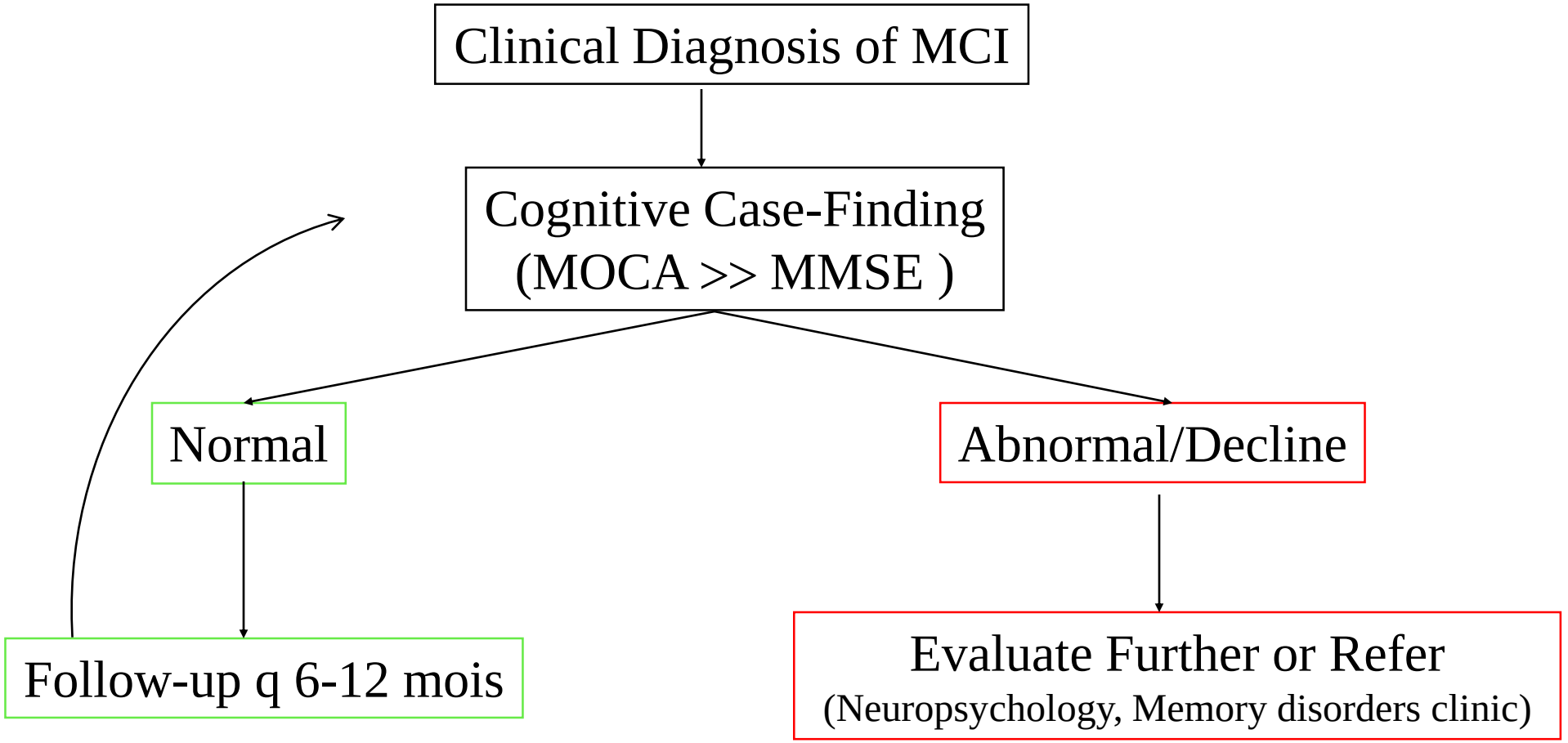
Not recommended for usual clinical management

Mild Cognitive Impairment
Recommendations (CCCDT 2006)

- There is inadequate evidence to consider this state as equivalent to early dementia, and to treat it as such **(C, II)**
- Regular follow-up is recommended **(B, II)**
- If the MMSE is within normal limits, other ***tests such as the MOCA***, or the DemTect, or the CMC can be used **(B, II)**
- Full ***Neuropsychological*** evaluation can be used to support the diagnosis **(A, I)**

Chertkow H et al, Alzheimer's and Dementia 2007

Mild Cognitive Impairment
Practical Recommendation



Clinical Case
Counseling / Management

- Your patient is very worried about her memory
- She thinks it is early Alzheimer's disease, and wants to inform her family about the diagnosis.
- She plans on updating her will and on making a power of attorney.
- She wants medication to slow progression of her memory loss.

Mild Cognitive Impairment
General Management

- Counseling about the uncertainty of diagnosis and progression
- Insist on regular follow-up
- Opportunity to discuss medico-legal issues (will, power of attorney)
- Driving
  - Look for red flags (getting lost, tickets, difficulty with road signs, etc.)
  - Formal evaluation as needed

Mild Cognitive Impairment
General Management

- ***Optimal management of comorbidities***
  - Chronic diseases
    - COPD, heart failure, DM, etc.
  - Metabolic disorders
    - Thyroid disease, etc.
  - Depression / anxiety

- ***Vascular prevention***
  - Optimal treatment of HBP (evidence-based data)
  - Dyslipidemia (non evidence-based data)
  - Healthy (Mediterranean) diet
  - D/C smoking
  - ***NOT*** Moderate alcohol consumption ???

- ***Rationalise medication***
  - Psychotropic medications, anticholinergic Rx, etc.

Mild Cognitive Disorder
Non-Pharmacological Management

- Stay Active
  - Physically : aerobic physical exercise according to individual capacity and other medical conditions
  - Intellectually: reading, cross-word puzzles / sudoku, bridge, chess, etc.
  - Socially: movies, theatre, volunteering, etc.

- Structured Programs of Cognitive Stimulation
  - Beneficial but limited and inconsistent access

- Cognitive Stimulation Software or Apps
  - Temporarily improve specific performances (task being stimulated)
  - Little or no data showing they prevent progression

- Multi-dimensional Approach
  - FINGER study (Lancet, 2015): vascular prevention / diet / physical exercise / intellectual and social stimulation.
  - Prevents cognitive deterioration in a normal population.

Mild Cognitive Impairment
Pharmacological Management – CCCDT 2006

- Data is insufficient to recommend use of ***ChEI*** in MCI **(C, I)**

- Recommend ***against*** the use of the following in MCI **(D, I):**
  - NSAIDs
  - Estrogens
  - Vitamin E
  - Ginkgo Biloba

- BUT, many potentially disease-modifying drugs under study

CLINICAL CASE 2

Clinical Case 2

- A patient's wife calls you because she is worried about her husband's driving.
- He got lost for several hours in a familiar district on two recent occasions, and was unable to find his way back. He called her in panic, and she had to explain how to get back.
- During the visit, your 78 y/o patient minimizes his difficulties and keeps on repeating that he hasn't gotten a ticket in 20 years. He blames getting lost on road wok !!!
- On history, his wife mentions that he's repeating himself, and forgot to pays a couple of bills recently. These symptoms started about 12 months ago and are getting worse.
- On examination, his MMSE score is 22: he misses the date by several days, he forgets 2/3 words, and has difficulty with copying the pentagons.

What other clinical evaluation would you recommend ?

Do you recommend further work-up ?

What is your clinical diagnosis?

Clinical Case 2
Clinical Evaluation

- History: r/o secondary cause
  - Medication side effects
  - Anxiety or depression
  - Sleep apnea
  - Chronic disease: COPD, CRF, heart failure, etc.
  - Metabolic disorder: thyroid disorder, diabetes

- Neurological Examination

- MOCA = 18 (normal 26)

Clinical Case 2
Work-Up

- CBC, electrolytes, Ca, BUN, creatinine, TSH (B12 / folate)

- Brain Imaging ?

What is your diagnosis ?

Clinical Case 2
Clinical Diagnosis

- Dementia (*Major Neurocognitive Disorder*) – Probable Alzheimer's Disease
  - Mild: impairment in IADLs
  - Moderate: impairment in ADLs
  - Severe: impairment in all ADLs (+ incontinence)

- Why is this not Mild Cognitive Impairment?
  - Progressive symptoms
  - Significant repercussions on IADLs (driving and managing $)

Mild Dementia
Non-Pharmacological Management

- **Reveal and discuss diagnosis**

- **Refer to community resources**

- **Insure home security issues**
  - *Risks*: fire, medication compliance / medication toxicity, wandering, falls, neglecting hygiene, malnutrition / food poisoning, etc.
- **Medico-Legal Dispositions** :
  - Will
  - Power of attorney
  - Competency issues
  - Driving

Mild Dementia
General Management

- ***Optimal management of comorbidities***
  - Chronic diseases
    - COPD, heart failure, DM, etc.
  - Metabolic disorders
    - Thyroid disease, etc.
  - Depression / anxiety

- ***Vascular prevention***
  - Optimal treatment of HBP (evidence-based data)
    - Eventually, adapt Tx targets to disease stage (same for DM)
  - Dyslipidemia (non evidence-based data)
  - Healthy (Mediterranean) diet
  - D/C smoking

- ***Rationalise medication***
  - Psychotropic medications, anticholinergic Rx, etc.

Mild Alzheimer's Disease
Standard Symptomatic Treatment

- Cholinesterase Inhibitors
  - ***Donepezil (Aricept):*** mild-severe AD
  - ***Rivastigmine (Exelon):*** mild-severe AD, parkinsonian dementia, patch approved
  - ***Galantamine (Reminyl ER):*** mild-sev AD
  - Restricted reimbursment (In Qc, exception medications → MMSE: 10-26)
- Glutamate NMDA-Receptor Antagonist
  - ***Memantine (Ebixa)*** : mod-sev
  - Restricted reimbursment (In Qc, exception medications → MMSE: 3-14)

Standard Symptomatic Treatment
Efficacy

Cholinesterase Inhibitors

- Modest improvement or stabilisation of cognition (12 months on average)
- Stabilisation of functional impairment (6-12 months)
- May delay onset of certain behavioral symptoms
- *The three ChEI have shown efficacy in mild-severe AD. We recommend un trial with a ChEI in the majority of patients with AD (1, A)(CCCDTD 2012)*

Memantine

- Added benefit to ChEI unclear
- *Combined treatment is rational and seems safe. However, there is no sufficient data to recommend for or against this approach (2,B) (CCCDTD 2012)*

Standard Symptomatic Treatment
Managing Expectations

- Benefits are mild and symptomatic
- There is no modification of disease progression
- Pharmacoeconomic benefits are controversial
  - Decreasing Caregiver burden
  - Delaying NH placement
  - Decreasing disease cost