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ALZHEIMER'S DISEASE Knowledge Hub

Blood-Based Biomarkers in Alzheimer's Disease -
An APAC Perspective

Prof Nagaendran Kandiah

Nanyang Technological University, Singapore

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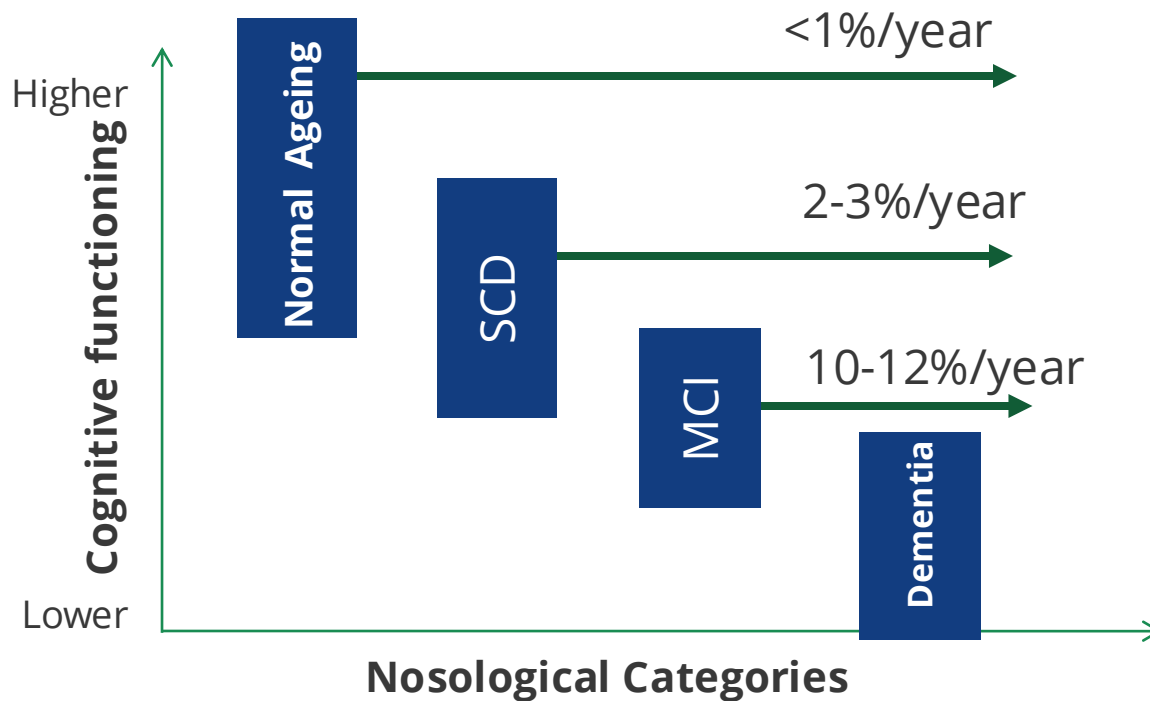
Nagaendran Kandiah has received CME support and honorarium from Schwabe, Eisai, Lilly, Roche, DKSH
Scientific advisor to Neurophet, SG Diagnostics and AllEights and founder of Gray Matter Solutions

Practical Integration: When and How to Use Blood Biomarkers

Nagaendran Kandiah– 10 mins

- Clinical Practice Guidelines- current recommendations, cognitive impairment assessment
- Diagnostic Workflow- patient selection criteria, interpretation of results, integration with clinical assessment and neuropsychological testing
- Clinical Scenario- Differential diagnosis, monitoring disease progression, patient eligibility for DMT

Cognitive Continuum



<p>SCD-Subjective Cognitive Decline</p> <p>Presence of symptoms Nil objective deficits</p>
<p>MCI-Mild Cognitive Impairment</p> <p>Presence of symptoms Presence of objective deficits Normal Function</p>
<p>Dementia</p> <p>Presence of symptoms Presence of deficits Impaired Function</p>

Normal ageing -> SCD -> MCI -> dementia

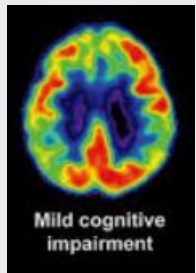
MCI mild cognitive impairment; SCD subjective cognitive impairment

Concept of “Early Dementia”

- Syndrome of “Early Dementia”
 - Stage of disease where irreversible neuronal damage is minimal
 - Functional ability relatively preserved
 - Stage where treatment can substantially alter course of disease
- Includes both MCI and Mild Dementia
- Newer disease modifying treatments are directed towards “Early Dementia”

Barriers to Early Diagnosis of Early Dementia

Need for effective, affordable diagnostic biomarkers



Amyloid PET Scan
\$\$ High Cost



MEMORY	Number of words recalled from list	100%
ATTENTION	Number of digits in span	7
LANGUAGE	Number of words that rhyme with the word 'blue'	4
ABSTRACTION	Number of correct answers to the 'bat and ball' problem	2
RELAYED RECALL	Number of words recalled after 15 minutes	8
ORIENTATION	Number of correct answers to the orientation questions	10

Cognitive Test



Blood Biomarker

Need for personalization of diagnostics & therapeutics

Personalize testing to individual baseline capabilities

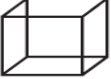
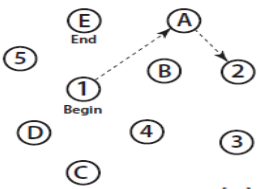


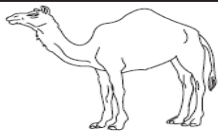
Need for scalability of diagnostic paradigms



Objective Cognitive Evaluation

MONTREAL COGNITIVE ASSESSMENT (MOCA)

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

VISUOSPATIAL / EXECUTIVE		Copy cube 		Draw CLOCK (Ten past eleven) (3 points)		POINTS		
		[] []		[] [] []			___/5	
NAMING								
						___/3		
MEMORY								
Read list of words, subject must repeat them. Do 2 trials, even if 1st trial is successful. Do a recall after 5 minutes.		1st trial	FACE	VELVET	CHURCH	DAISY	RED	No points
		2nd trial						
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 [] FBACMNAAJKLBFAKDEAAJAMOF AAB						___/1		
Serial 7 subtraction starting at 100 [] 93		[] 86		[] 79		[] 65	___/3	
		4 or 5 correct subtractions: 3 pts, 2 or 3 correct: 2 pts, 1 correct: 1 pt, 0 correct: 0 pt						
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	
Category cue		[]	[]	[]	[]	[]		
Multiple choice cue								
Optional								
ORIENTATION		[] Date	[] Month	[] Year	[] Day	[] Place	[] City	___/6
© Z.Nasreddine MD Version 7.1 www.mocatest.org Normal ≥ 26 / 30		TOTAL				___/30		
Administered by: _____						Add 1 point if ≤ 12 yr edu		

Downloaded from <http://jnnp.bmj.com/> on March 9, 2015 - Published by group.bmj.com
 JNNP Online First, published on February 17, 2015 as 10.1136/jnnp-2014-309647

Cognition

RESEARCH PAPER

Early detection of dementia in multilingual populations: Visual Cognitive Assessment Test (VCAT)

Nagaendran Kandiah,^{1,2} Angeline Zhang,¹ Dianne Carol Bautista,^{3,4} Eveline Silva,¹ Simon Kang Seng Ting,¹ Adeline Ng,¹ Pryseley Assam^{3,4}

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/jnnp-2014-309647>).

¹Department of Neurology, National Neuroscience Institute, Singapore, Singapore
²Duke—NUS Graduate Medical School, Singapore, Singapore

ABSTRACT

Background Early diagnosis of cognitive impairment allows timely intervention with pharmacological and non-pharmacological measures. However, current cognitive evaluation tools do not cater for multilingual populations. **Objective** To develop and validate a visual-based cognitive evaluation tool, the Visual Cognitive Assessment Test (VCAT), which can be administered to multilingual populations without the need for translation or adaptation.

matched with appropriate cognitive screening tools that transcend language and cultural barriers.⁴⁻⁸ Equipping neurologists and psychiatrists with effective cognitive screening tools would ensure early diagnosis of dementia and timely intervention with pharmacological and non-pharmacological measures. Early diagnosis would also allow inclusion of appropriate patients into clinical trials and research studies. Screening tools will need to have good sensitivity and specificity for detection of the condition.



► Alzheimers Res Ther. 2018 Jan 22;10:6. doi: [10.1186/s13195-017-0333-z](https://doi.org/10.1186/s13195-017-0333-z)

A novel language-neutral Visual Cognitive Assessment Test (VCAT): validation in four Southeast Asian countries

Levinia Lim¹, Tze Pin Ng², Anam Paulus Ong³, Maw Pin Tan⁴, Alvin Rae Cenina^{5,6}, Qi Gao², Adeline Ng¹, Nagaendran Kandiah^{1,7,✉}

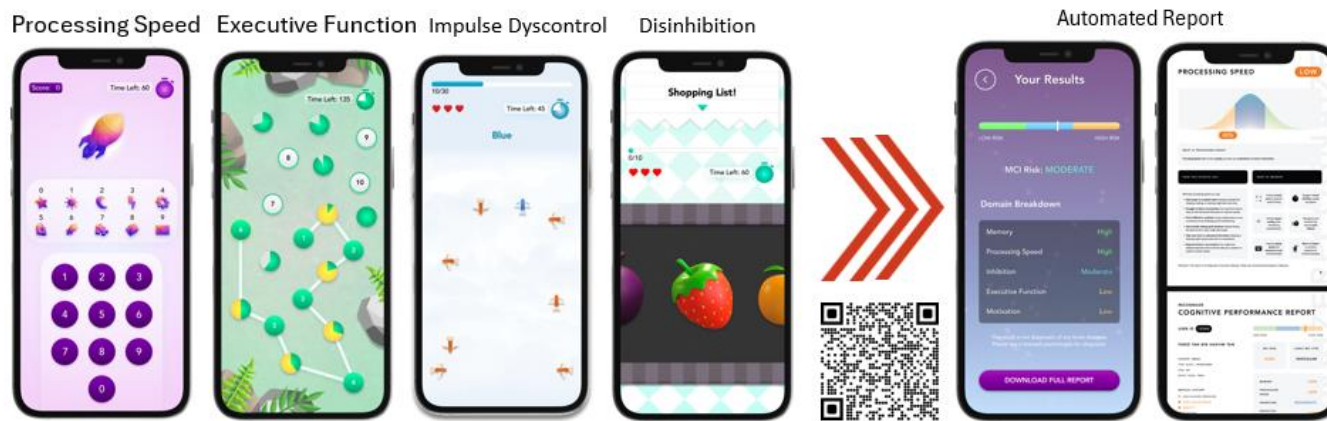
- Evaluates multiple cognitive domains
- Based on figures and pictures, no need for translation
- 10-15 mins
- Validated in Malaysia

Mild Cognitive Impairment		
Education >10years	<27	Sensitivity 94.2%
Education ≤10years	<26	Sensitivity 96%
Mild Dementia		
Education >10years	<25	Sensitivity 90.4%
Education ≤10years	<24	Sensitivity 85%

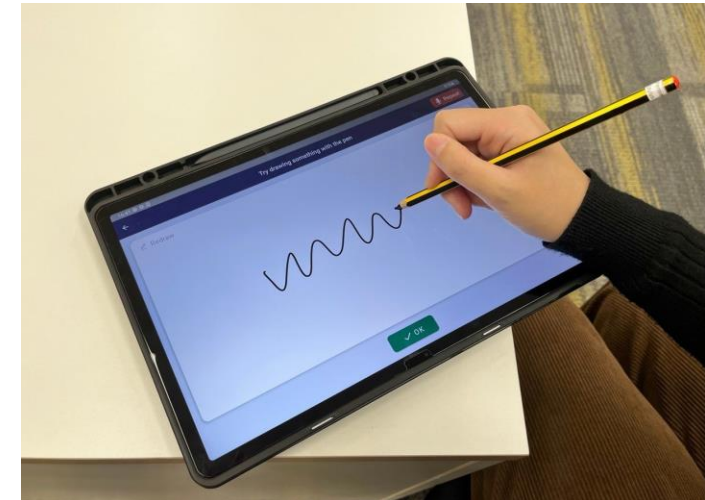


Digital Diagnostic Test

The ReCOGnAlze Assessment: Validated gamified cognitive test to detect MCI and Vascular MCI



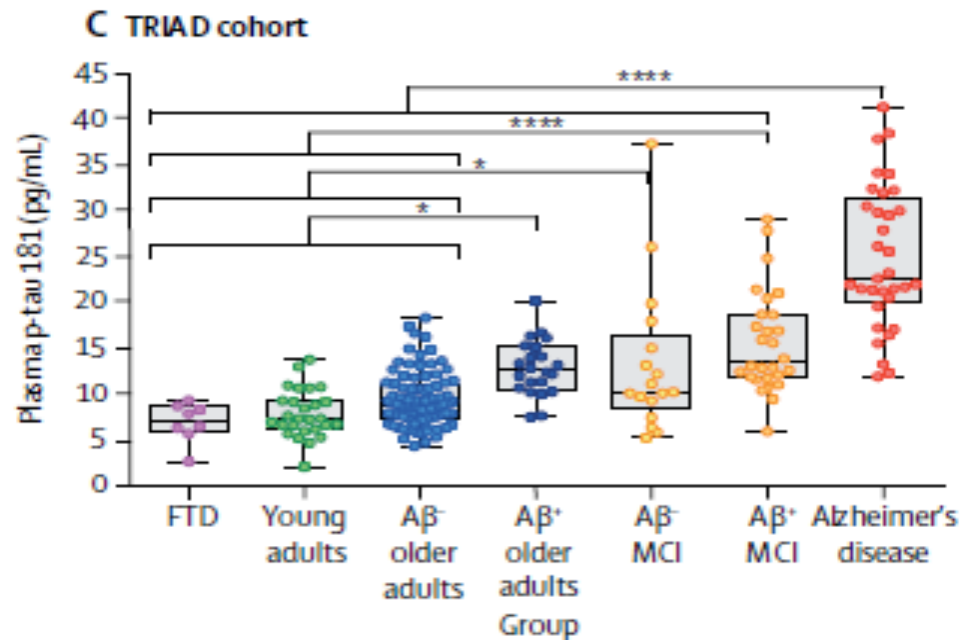
PENSIEVE-AI a brief cognitive test



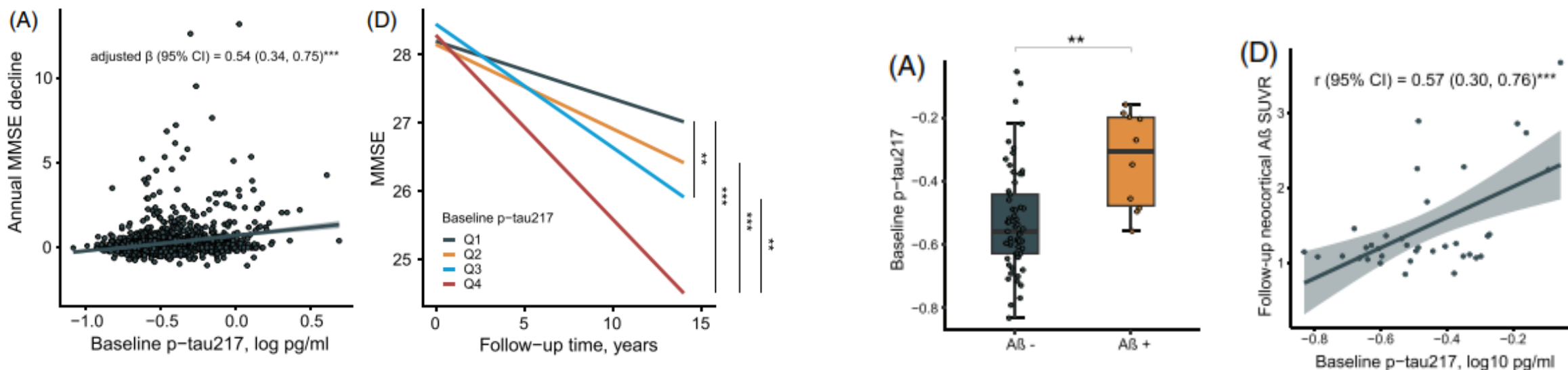
- Superior performance compared to traditional tests for the detection of MCI
- Can be personalized to user profile such as demographics
- Scalable

Plasma p-tau 181 in AD Diagnosis

- Plasma p-tau181 distinguished AD dementia from:
 - cognitively unimpaired older adults (AUC >90)**
 - frontotemporal dementia (AUC >82.76) and vascular dementia (AUC=92.13%)
- Plasma p-tau181 was associated with:
 - PET tau (AUC>83.08)
 - PET A β (AUC >76.14)



Plasma p-tau 217



Shanghai Aging Study -1857 dementia-free community residents

- Higher plasma p-tau217:
 - -correlated to higher decline in MMSE
 - -higher risk of incident dementia and AD
- Plasma p-tau 217 significantly correlated with longitudinal neocortical amyloid-beta (A β) deposition ($r = 0.57$ [0.30, 0.76])

Alzheimer's Association Clinical Practice Guidelines for Blood Based Biomarkers for AD

- Key recommendations in this CPG:
 - BBM tests with $\geq 90\%$ sensitivity and $\geq 75\%$ specificity can be used as a triaging test
 - BBM tests with $\geq 90\%$ sensitivity and specificity can serve as a substitute for amyloid PET imaging or CSF AD biomarkers
- Applicable for patients with cognitive impairment in specialised memory clinics with careful consideration of pretest probability of AD pathology
- These tests do not serve as a substitute for comprehensive clinical evaluation and should be used only as part of a full diagnostic workup

FDA NEWS RELEASE

FDA Clears First Blood Test Used in Diagnosing Alzheimer's Disease

New Test Provides Less Invasive Option, Reduces Reliance on PET Scans and Increases Diagnosis Accessibility

For Immediate Release: May 16, 2025

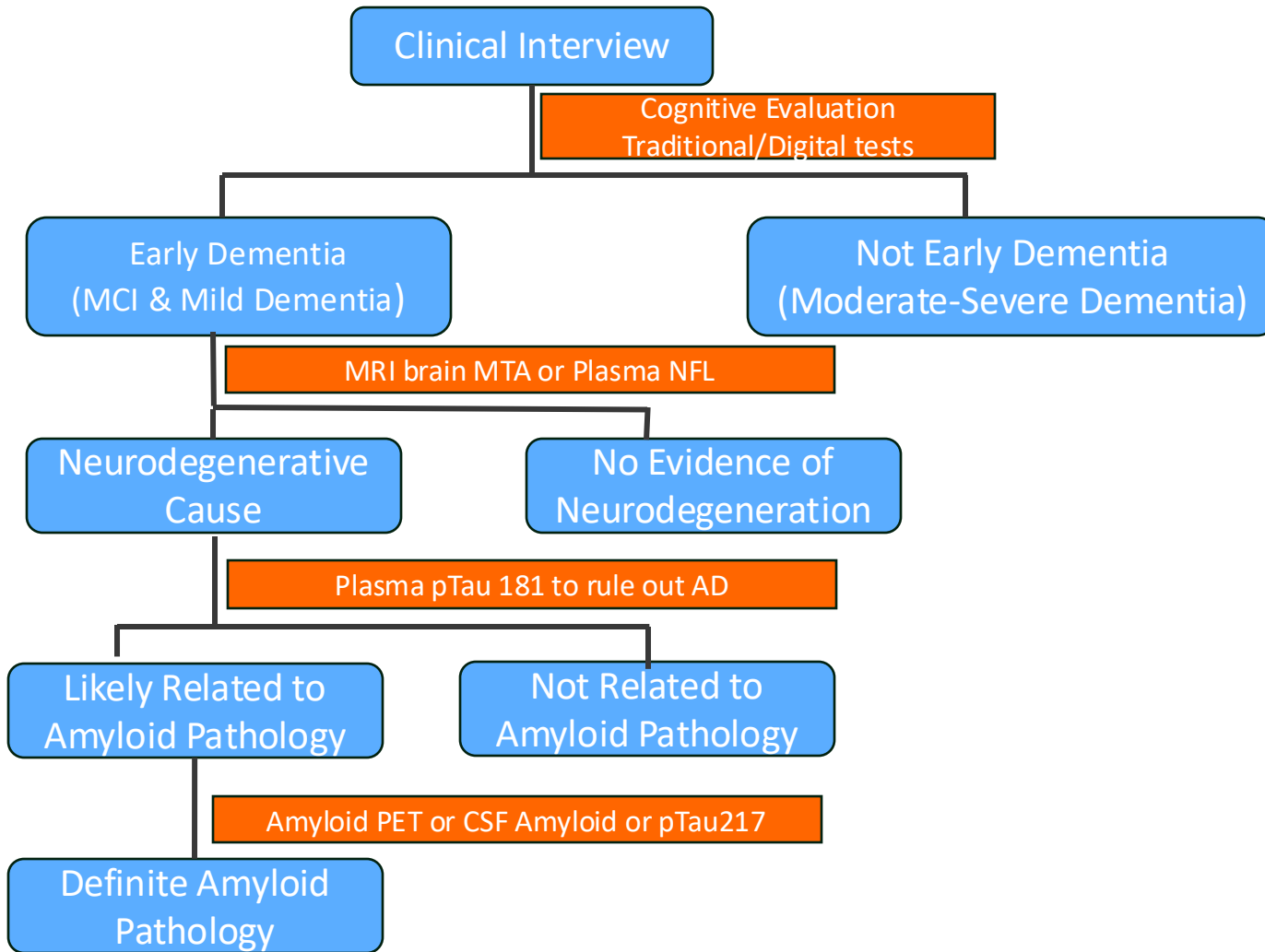
- The Lumipulse G pTau217/ β -Amyloid 1-42 Plasma Ratio
 - for the early detection of amyloid plaques associated with Alzheimer's disease
 - in adult patients, aged 55 years and older, exhibiting signs and symptoms of the disease
- FDA evaluated data from a multi-center clinical study of 499 cognitively normal individuals
 - Lumipulse plasma ratio compared with amyloid PET scan/CSF
 - 91.7% of Lumipulse positive were $A\beta^+$ by PET/CSF
 - 97.3 % of Lumipulse negative were $A\beta^-$ PET/CSF
 - 20% had an indeterminate Lumipulse G result

FDA Clearance of First Blood Test for Use in Primary Care to Rule Out Alzheimer's-Related Amyloid Pathology

October 13, 2025

- Elecsys pTau181 plasma test, developed by Roche
- first blood-based biomarker test for AD cleared for use in the primary care setting, for adults aged >55 years with symptoms of cognitive impairment
- specifically to rule out the presence of amyloid pathology
- helps determine which patients do not require AD tests, such as PET scans or cerebrospinal fluid analysis

Practical Use of Biomarkers



Relevant Biomarkers

- Cognitive Biomarker
 - Digital Test or traditional Test
 - Allows for a diagnosis of clinical syndrome
- Biomarker for Neurodegeneration
 - MRI Brain-medial temporal Atrophy
 - Plasma Neurofilament Light Chain
 - Identifies a brain related disease as the cause for the cognitive impairment
 - Non-specific
- Biomarker for Amyloid Pathology
 - Blood based –pTau 181 & 217
 - Gold Standard Test for amyloid
 - Amyloid PET Scan
 - CSF Amyloid levels