38TH ANNUAL CONFERENCE
OCTOBER 17-20, 2018

BECOMING AGENTS OF CHANGE

SHERATON NEW ORLEANS HOTEL | NEW ORLEANS, LA

How to make evidence based neuropsychology a daily occurrence.

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Catherine Meade,
Leonie Simpson,
Brooke Davis,
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The University of Melbourne,
Australia.

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Financial Disclosure: Bowden

I have financial relationships to disclose:

Employee of:	**University of Melbourne, Australia.**
Consultant for:	**Nil**
Research support from:	**Australian NH&MRC** **Australian Brain Foundation**
Stockholder in:	**Nil**
Book Royalties:	**Oxford University Press** **Taylor & Francis**
Editorial Stipend:	**Nature-Springer**

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What is Evidence Based Practice?

- A value-driven pattern of clinical practice that attempts to integrate "best research" derived from the study of populations to inform clinical decisions about individuals within the context of the provider's expertise and individual patient values . . . . .
  - Adapted From Chelune (2010)
- Evidence-based practice is the use of mathematical estimates of the risk of benefit and harm, derived from high quality research on representative samples, to inform clinical decision-making on the diagnosis or treatment of individual patients.
  - Adapted from Greenhalgh (2010)

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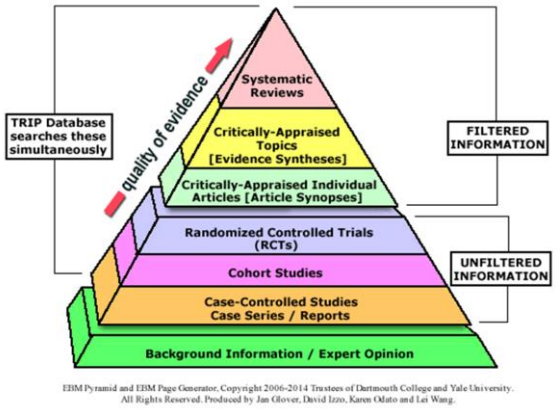

The levels-of-evidence framework and the underlying principles of evidence-based practice may be the most widely-debated, and peer-reviewed, set of quality guidelines in the history of health-care.

In view of the constantly evolving state of knowledge in psychology (and every other health-related profession)

- We need some easily learnt and easily applied, systematic means by which to update our knowledge and stay up to date with recent developments.
- And to identify better quality research so we can rank the validity of published research findings.
- Evidence Based Practice Critical-Appraisal techniques have evolved specifically to address these needs.

5

6

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Frontal Screening for dementia using INECO Frontal Screening (IFS)

Dr Catherine Meade
Neuropsychology Unit
Department of Clinical Neurosciences
St Vincent's Hospital Melbourne
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Financial Disclosure

I have no financial relationships to disclose:

Employee of: St Vincent's Hospital Melbourne
Consultant for: nil
Stockholder in: nil
Research support from: nil
Honoraria from: nil

Frontal screening for bvFTD with INECO: a diagnostic CAT

Dr Catherine Meade,
Senior Clinical Neuropsychologist,
St Vincent's Hospital, Melbourne, Australia
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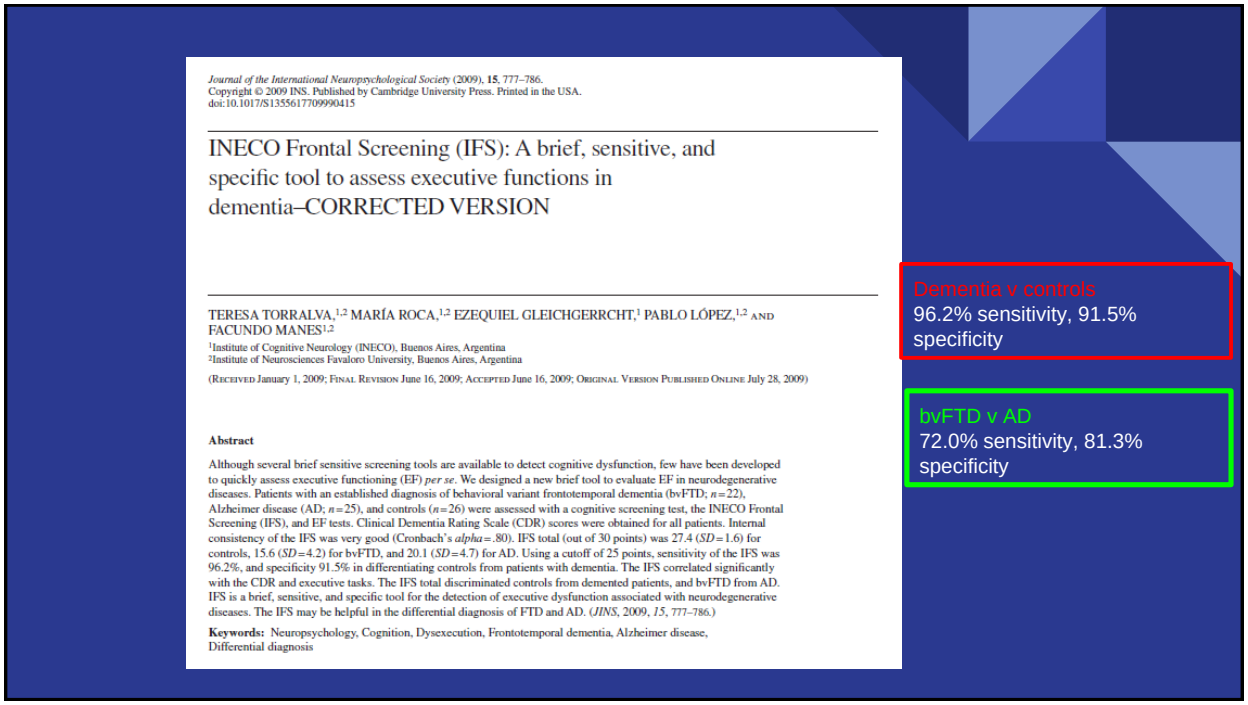
A 66 year old woman, Sue, presents with 12 month hx of personality change, behavioural disturbance, language symptoms and other "executive-type" deficits.



Journal of the International Neuropsychological Society (2009), **15**, 777–786.
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doi:10.1017/S1355617709990415

INECO Frontal Screening (IFS): A brief, sensitive, and specific tool to assess executive functions in dementia–CORRECTED VERSION

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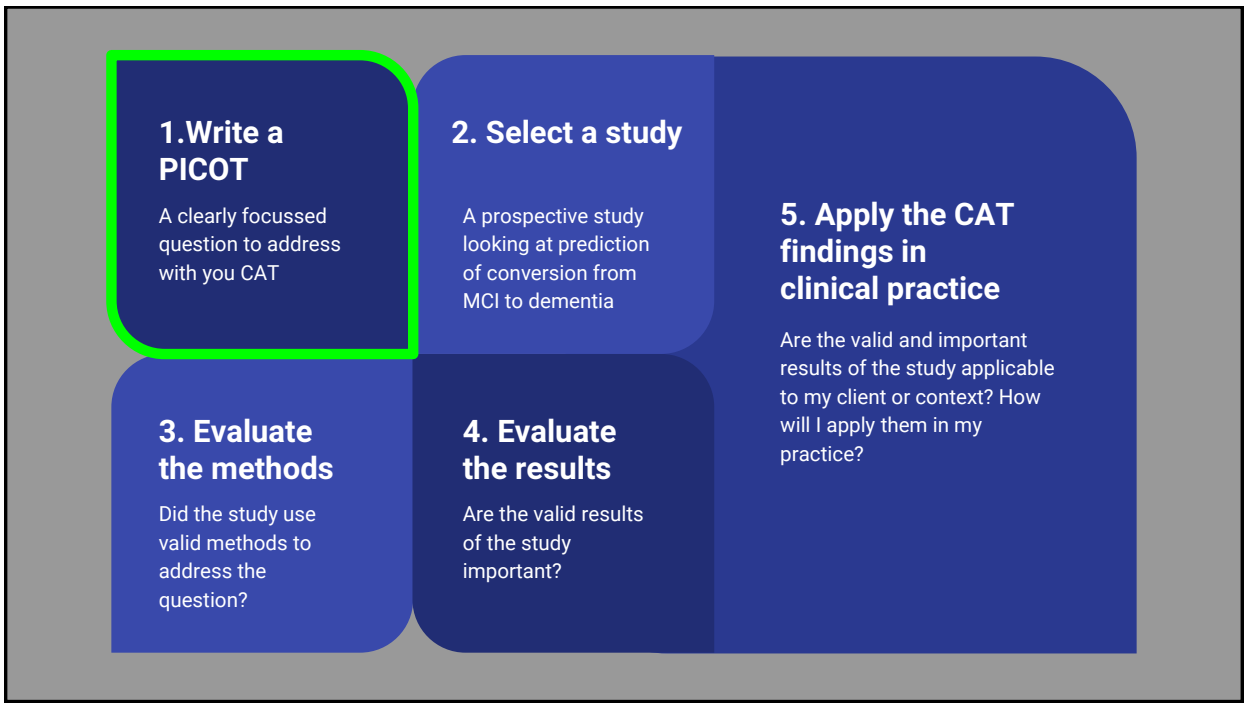
(Received January 1, 2009; Final Revision June 16, 2009; Accepted June 16, 2009; Original Version Published Online July 28, 2009)

Abstract

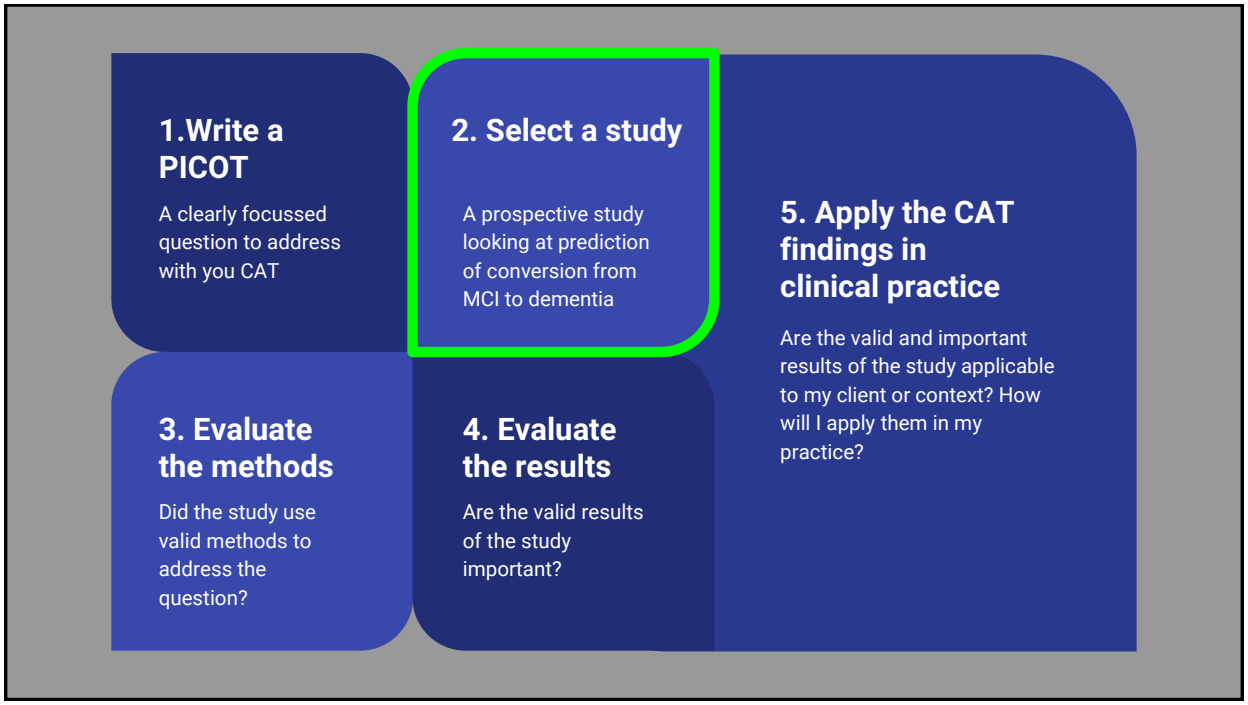
Although several brief sensitive screening tools are available to detect cognitive dysfunction, few have been developed to quickly assess executive functioning (EF) *per se*. We designed a new brief tool to evaluate EF in neurodegenerative diseases. Patients with an established diagnosis of behavioral variant frontotemporal dementia (bvFTD; $n=22$), Alzheimer disease (AD; $n=25$), and controls ($n=26$) were assessed with a cognitive screening test, the INECO Frontal Screening (IFS), and EF tests. Clinical Dementia Rating Scale (CDR) scores were obtained for all patients. Internal consistency of the IFS was very good (Cronbach's *alpha* = .80). IFS total (out of 30 points) was 27.4 ($SD=1.6$) for controls, 15.6 ($SD=4.2$) for bvFTD, and 20.1 ($SD=4.7$) for AD. Using a cutoff of 25 points, sensitivity of the IFS was 96.2%, and specificity 91.5% in differentiating controls from patients with dementia. The IFS correlated significantly with the CDR and executive tasks. The IFS total discriminated controls from demented patients, and bvFTD from AD. IFS is a brief, sensitive, and specific tool for the detection of executive dysfunction associated with neurodegenerative diseases. The IFS may be helpful in the differential diagnosis of FTD and AD. (*JINS*, 2009, *15*, 777–786.)

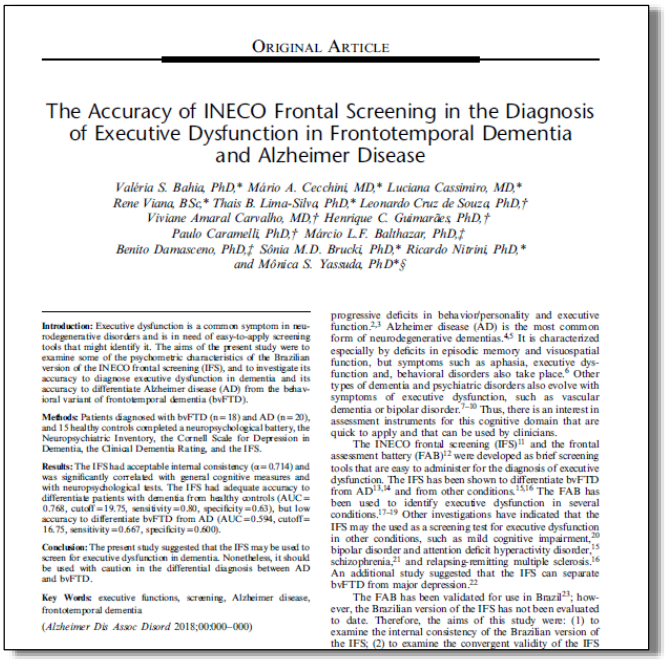
Keywords: Neuropsychology, Cognition, Dysexecution, Frontotemporal dementia, Alzheimer disease, Differential diagnosis



Diagnostic CAT

P	66 year old woman with personality change, behavioural disturbance, language changes and uncertain 'executive-type' deficits
I	diagnostic test of bvFTD
C	AD control group
O	Can we differentiate bvFTD versus AD on the basis of a clinical test
T	Cohort study





ORIGINAL ARTICLE

The Accuracy of INECO Frontal Screening in the Diagnosis of Executive Dysfunction in Frontotemporal Dementia and Alzheimer Disease

Valéria S. Bahia, PhD, Mário A. Cecchini, MD,* Luciana Cassimiro, MD,* Rene Viana, BSc,* Thais B. Lima-Silva, PhD,* Leonardo Cruz de Souza, PhD,† Viviane Amaral Carvalho, MD,† Henrique C. Guimarães, PhD,† Paulo Caramelli, PhD,† Márcio L.F. Balthazar, PhD,‡ Benito Damasceno, PhD,‡ Sônia M.D. Brucki, PhD,* Ricardo Nitrini, PhD,* and Mônica S. Yassuda, PhD*§*

Introduction: Executive dysfunction is a common symptom in neurodegenerative disorders and is in need of easy-to-apply screening tools that might identify it. The aims of the present study were to examine some of the psychometric characteristics of the Brazilian version of the INECO frontal screening (IFS), and to investigate its accuracy to diagnose executive dysfunction in dementia and its accuracy to differentiate Alzheimer disease (AD) from the behavioral variant of frontotemporal dementia (bvFTD).

Methods: Patients diagnosed with bvFTD (n = 18) and AD (n = 20), and 15 healthy controls completed a neuropsychological battery, the Neuropsychiatric Inventory, the Cornell Scale for Depression in Dementia, the Clinical Dementia Rating, and the IFS.

Results: The IFS had acceptable internal consistency (α = 0.714) and was significantly correlated with general cognitive measures and with neuropsychological tests. The IFS had adequate accuracy to differentiate patients with dementia from healthy controls (AUC = 0.768, cutoff = 19.75, sensitivity = 0.80, specificity = 0.63), but low accuracy to differentiate bvFTD from AD (AUC = 0.594, cutoff = 16.75, sensitivity = 0.667, specificity = 0.600).

Conclusion: The present study suggested that the IFS may be used to screen for executive dysfunction in dementia. Nonetheless, it should be used with caution in the differential diagnosis between AD and bvFTD.

Key Words: executive functions, screening, Alzheimer disease, frontotemporal dementia

(*Alzheimer Dis Assoc Disord* 2018;00:000–000)

progressive deficits in behavior/personality and executive function.[2,3] Alzheimer disease (AD) is the most common form of neurodegenerative dementias.[4,5] It is characterized especially by deficits in episodic memory and visuospatial function, but symptoms such as aphasia, executive dysfunction and, behavioral disorders also take place.[6] Other types of dementia and psychiatric disorders also evolve with symptoms of executive dysfunction, such as vascular dementia or bipolar disorder.[7–10] Thus, there is an interest in assessment instruments for this cognitive domain that are quick to apply and that can be used by clinicians.

The INECO frontal screening (IFS)[11] and the frontal assessment battery (FAB)[12] were developed as brief screening tools that are easy to administer for the diagnosis of executive dysfunction. The IFS has been shown to differentiate bvFTD from AD[13,14] and from other conditions.[15,16] The FAB has been used to identify executive dysfunction in several conditions.[17–19] Other investigations have indicated that the IFS may the used as a screening test for executive dysfunction in other conditions, such as mild cognitive impairment,[20] bipolar disorder and attention deficit hyperactivity disorder,[15] schizophrenia,[21] and relapsing-remitting multiple sclerosis.[16] An additional study suggested that the IFS can separate bvFTD from major depression.[22]

The FAB has been validated for use in Brazil[23]; however, the Brazilian version of the IFS has not been evaluated to date. Therefore, the aims of this study were: (1) to examine the internal consistency of the Brazilian version of the IFS; (2) to examine the convergent validity of the IFS

1.Write a PICOT

A clearly focussed question to address with you CAT

2. Select a study

A prospective study looking at prediction of conversion from MCI to dementia

3. Evaluate the methods

Did the study use valid methods to address the question?

4. Evaluate the results

Are the valid results of the study important?

5. Apply the CAT findings in clinical practice

Are the valid and important results of the study applicable to my client or context? How will I apply them in my practice?

cebm.net/2014/06/critical-appraisal

https://www.cebm.net/2014/06/catmaker-ebm-calculators/

Was there an independent blind comparison with a reference ("gold") standard of diagnosis?

Yes

The behavioral variant of frontotemporal dementia (bvFTD) is the second cause of early-onset neurodegenerative dementia and the third most common cause of all degenerative dementias.[1] This disease is characterized by

Received for publication November 22, 2017; accepted February 1, 2018.
From the Departments of *Neurology; §Gerontology, School of Arts, Sciences and Humanities, University of São Paulo; ‡Department of Neurology, University of Campinas, São Paulo; and †Cognitive and Behavioral Neurology Research group, School of Medicine, Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, Minas Gerais (MG), Brazil.
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with the FAB and its correlation with other cognitive measures; (3) to investigate the diagnostic accuracy of the IFS in patients with dementia; and (4) to compare the accuracy of the IFS and the FAB in the diagnosis of bvFTD.

METHODS

Participants

Dementia patients were recruited from the outpatient neurology clinics in the University of São Paulo, Federal University of Minas Gerais, and in the State University of Campinas. For the bvFTD group, 18 patients were recruited on the basis of the international consensus criteria for this disease.[3] Twenty patients met the criteria for dementia due to probable AD based on the National Institute on Aging—

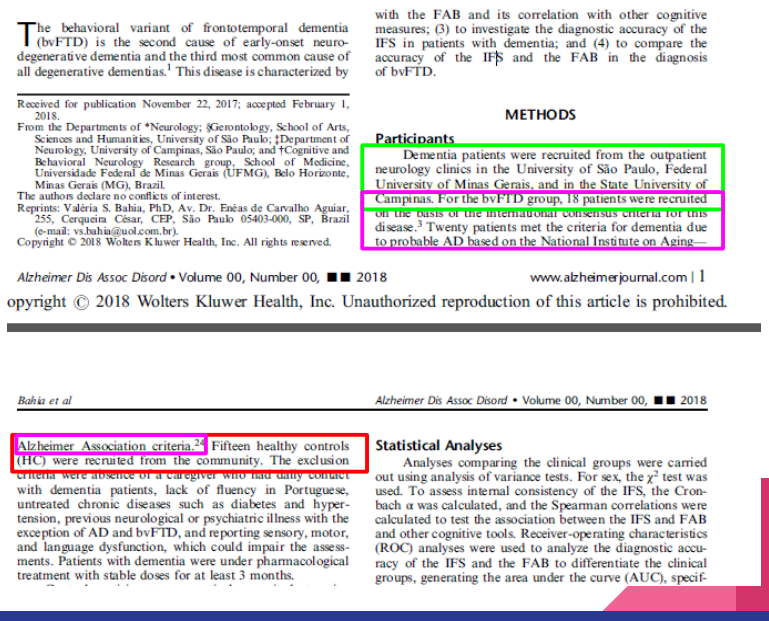
Alzheimer Association criteria.[24] Fifteen healthy controls (HC) were recruited from the community. The exclusion criteria were absence of a caregiver who had daily contact with dementia patients, lack of fluency in Portuguese, untreated chronic diseases such as diabetes and hypertension, previous neurological or psychiatric illness with the exception of AD and bvFTD, and reporting sensory, motor, and language dysfunction, which could impair the assessments. Patients with dementia were under pharmacological treatment with stable doses for at least 3 months.

Statistical Analyses

Analyses comparing the clinical groups were carried out using analysis of variance tests. For sex, the χ^2 test was used. To assess internal consistency of the IFS, the Cronbach α was calculated, and the Spearman correlations were calculated to test the association between the IFS and FAB and other cognitive tools. Receiver-operating characteristics (ROC) analyses were used to analyze the diagnostic accuracy of the IFS and the FAB to differentiate the clinical groups, generating the area under the curve (AUC), specif-

Was the diagnostic test evaluated in a representative group of patients? (ie. similar to your clinic?)

Yes



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Was the reference standard (dx criteria) applied regardless of the index (INECO) test result?

Yes

Instruments and Procedures

All patients were assessed by neurologists, geriatricians, and neuropsychologists. Patients and HC underwent a clinical evaluation and screening tests for dementia: Addenbrooke's Cognitive Examination-Revised (ACE-R),[25,26] Neuropsychiatric Inventory (NPI),[27] Cornell Scale for Depression in Dementia (CSDD),[28,29] and laboratory and neuroimaging examinations. The diagnosis was defined by the clinicians involved in the project, and patients with bvFTD and AD were in the mild stage, according to the Clinical Dementia Rating (CDR).[30–32] FAB, IFS, and neuropsychological tests were applied by trained neuropsychologists (L.C.d.S., M.A.C., M.S.Y.). CDR, NPI, and CSDD were applied by a trained gerontologist (T.B.L.-S.). Patients with CDR = 0.5 and 1.0 were selected.

Results for the neuropsychological tests are shown in Table 2. Three HC participants, one AD and one bvFTD9patient did not complete these tests.

The patients presented worse performance than HC in episodic memory (immediate and delayed recall), verbal fluency, and inhibitory control (Stroop test). Patients with AD had lower scores than bvFTD patients in the delayed recall of both episodic memory tests.

Table 3 presents the results for the IFS and FAB instruments for each group. The IFS total score differentiated dementia patients from HC, but the groups with bvFTD and AD had equivalent scores. In the IFS, the items motor programming, verbal and spatial working memory, and abstraction capacity differentiated AD patients from HC, but not bvFTD patients from HC. The "Response

Was the test (or cluster of tests) validated in a second group, independent group of patients?

No.

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Did the study use valid methods to address the question?

4. Evaluate the results

Are the valid results of the study important?

5. Apply the CAT findings in clinical practice

Are the valid and important results of the study applicable to my client or context? How will I apply them in my practice?

Are the valid results of this diagnostic study important?

		Reference standard (diagnostic criteria)		
		+ve	-ve	
Index test	+ve	a	b	N with +ve test
	-ve	c	d	N with -ve test
		N with condition	N without condition	Total N

TABLE 2. Neuropsychological Test Scores for HC, AD, and bvFTD Patients

	HC (n = 12)	AD (n = 19)	bvFTD (n = 17)	*P*
RAVLT 5 trials	44.50 (8.94)*†	24.84 (5.45)‡	28.71 (11.53)‡	<0.001
RAVLT delayed	10.17 (2.98)*†	0.95 (1.22)†‡	3.35 (3.74)*‡	<0.001
VR immediate	33.50 (5.18)*†	20.16 (7.72)‡	22.53 (8.17)‡	<0.001
VR delayed	26.42 (7.09)*†	2.05 (3.49)†‡	9.29 (8.64)*‡	<0.001
Phonemic verbal fluency	15.40 (4.91)*†	10.30 (4.93)‡	10.94 (3.73)‡	0.004
Semantic verbal fluency	17.73 (3.26)*†	9.90 (3.60)‡	11.78 (4.98)‡	<0.001

TABLE 4. Accuracy Analyses for the IFS and FAB

	Cutoff	AUC	Sensitivity	Specificity
IFS				
HC×AD+bvFTD	19.75	0.768	0.800	0.632
HC×AD	19.75	0.818	0.800	0.700
HC×bvFTD	20.25	0.713	0.733	0.611
AD×bvFTD	16.75	0.594	0.667	0.600
FAB				
HC×AD+bvFTD	15.50	0.717	0.667	0.684
HC×AD	16.50	0.713	0.667	0.700
HC×bvFTD	15.50	0.720	0.667	0.667
AD×bvFTD	13.50	0.544	0.550	0.500

AD indicates Alzheimer disease; AUC, area under the curve; bvFTD, behavioral variant frontotemporal dementia; FAB, frontal assessment battery; HC, healthy controls; IFS, INECO frontal screening.

Calculations

Sensitivity- proportion of people with the disease who get a positive test result	67% (45-88)	a/(a+c) x 100 = 67 a=12
Specificity - proportion of people without the disease who get a negative test result	60% (39-81)	d/(b+d) x 100 = 60 d=12

Are the valid results of this diagnostic study important?

		Reference standard bvFTD v AD		Totals
		+ve	-ve	
Diagnostic Test Result IFS	+ve	a12	b8	20
	-ve	c6	d12	18
		18	20	38

What are the results?

		Reference standard bvFTD v AD		Totals
		+ve	-ve	
Diagnostic Test Result IFS	+ve	a12	b8	20
	-ve	c6	d12	18
		18	20	38

PPV = proportion of people with a positive test result who do have the disease

= 12/(12+8)

= 60% (39-81)

What are the results?

		Reference standard bvFTD v AD		Totals
		+ve	-ve	
Diagnostic Test Result IFS	+ve	12	8	20
	-ve	6	12	18
		18	20	38

NPV = proportion of people with a negative test who don't have the disease

= 12/(6+12)

= 67% (45-88)

Calculations

Likelihood Ratio for a positive result (LR+)	sens/(1-spec)	67%/40% = 1.68 (0.89-3.12)
Likelihood Ratio for a negative result (LR-)	(1-sens)/spec	33%/60% = 0.55 (0.26-1.17)

CATmaker

Use Control-C to **copy** selected text, Control-V to **paste** and Control-X to **cut**.

making a CAT diagnosis

Your Question | the Study Patients | **the Study Evidence** | the Bottom Line | the Other Stuff

Analysis 1 of 1

TEST		TARGET DISORDER: bvFTD — Present	TARGET DISORDER: bvFTD — Absent	
INECO<17	Positive	12 (a)	8 (b)	
	Negative	6 (c)	12 (d)	95% Confidence Intervals
SENSITIVITY		a / (a+c)	67 %	45 to 88
SPECIFICITY		d / (b+d)	60 %	39 to 81
Pre-test Probability ("Prevalence"):		(a+c)/(a+b+c+d)	47 %	31 to 63
Positive Predictive Value:		a / (a+b)	60 %	39 to 81
Negative Predictive Value:		d / (c+d)	67 %	45 to 88
LIKELIHOOD RATIO +		sens / (1 - spec)	1.67	0.89 to 3.12
LIKELIHOOD RATIO −		(1 - sens) / spec	0.56	0.26 to 1.17

Analyse another test in this same study

1.Write a PICOT

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A prospective study looking at prediction of conversion from MCI to dementia

3. Evaluate the methods

Did the study use valid methods to address the question?

4. Evaluate the results

Are the valid results of the study important?

5. Apply the CAT findings in clinical practice

Are the valid and important results of the study applicable to my client or context? How will I apply them in my practice?

Is the diagnostic test available, affordable, accurate, and precise in your setting?

Yes.

Can you generate a clinically sensible estimate of your patient's pre-test probability?

Prevalence, characteristics, and survival of frontotemporal lobar degeneration syndromes

OPEN

Ian T.S. Coyle-Gilchrist, MBBS
Katrina M. Dick, BSc
Karalyn Patterson, FMedSci
Patricia Vázquez Rodríquez, MSc
Eileen Wehmann, MPhil
Alicia Wilcox, MClinNeuroPsy
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ABSTRACT

Objectives: To estimate the lifetime risk, prevalence, incidence, and mortality of the principal clinical syndromes associated with frontotemporal lobar degeneration (FTLD) using revised diagnostic criteria and including intermediate clinical phenotypes.

Methods: Multisource referral over 2 years to identify all diagnosed or suspected cases of frontotemporal dementia (FTD), progressive supranuclear palsy (PSP), or corticobasal syndrome (CBS) in 2 UK counties (population 1.69 million). Diagnostic confirmation used current consensus diagnostic criteria after interview and reexamination. Results were adjusted to the 2013 European standard population.

Results: The prevalence of FTD, PSP, and CBS was 10.8/100,000. The incidence and mortality were very similar, at 1.61/100,000 and 1.56/100,000 person-years, respectively. The estimated lifetime risk is 1 in 742. Survival following diagnosis varied widely: from PSP 2.9 years to semantic variant FTD 9.1 years. Age-adjusted prevalence peaked between 65 and 69 years at 42.6/100,000: the age-adjusted prevalence for persons older than 65 years is double the prevalence for those between 40 and 64 years. Fifteen percent of those screened had a relevant genetic mutation.

Conclusions: Key features of this study include the revised diagnostic criteria with improved specificity and sensitivity, an unrestricted age range, and simultaneous assessment of multiple FTLD syndromes. The prevalence of FTD, PSP, and CBS increases beyond 65 years, with frequent genetic causes. The time from onset to diagnosis and from diagnosis to death varies widely among syndromes, emphasizing the challenge and importance of accurate and timely diagnosis. A high index of suspicion for FTLD syndromes is required by clinicians, even for older patients.

Neurology® 2016;86:1736–1743

GLOSSARY

bvFTD = behavioral variant frontotemporal dementia; **CBS** = corticobasal syndrome; **ESP2013** = European Standard Population 2013; **FTD** = frontotemporal dementia; **FTLD** = frontotemporal lobar degeneration; **MND** = motor neuron disease; **nfvPPA** = nonfluent agrammatic variant primary progressive aphasia; **PiPPIN** = Pick's Disease and Progressive Supranuclear Palsy: Prevalence and Incidence; **PPA** = primary progressive aphasia; **PSP** = progressive supranuclear palsy; **svPPA** = semantic variant primary progressive aphasia.

Narrative review

Diagnosing, monitoring and managing behavioural variant frontotemporal dementia

Olivier Piguet[1,2], Fiona Kumfor[1,2], John Hodges[1,3]

Frontotemporal dementias (FTDs) are progressive neurodegenerative brain conditions characterised by brain atrophy in the prefrontal cortices or the anterior portions of the temporal lobes caused by various intraneuronal inclusions and abnormal protein depositions. FTD has a prevalence of 10–15/100 000 population in individuals aged 45–65 years, and is a common cause of younger onset dementia, although with large variability across studies.[1,2] Recent evidence indicates that the occurrence of FTD beyond 65 years of age appears to be more common than previously assumed.[2]

Unlike Alzheimer disease (AD), the clinical profile and pathology of FTD are heterogeneous and characterised by two main phenotypes: a progressive deterioration in behaviour and personality, known as behavioural variant FTD (bvFTD); and a decline in language skills, known as primary progressive aphasia, which is further subdivided according to the main pattern of language breakdown into progressive non-fluent aphasia and semantic dementia.[3,4] This review focuses on bvFTD. Although bvFTD is recognised as a potential cause of both major and mild neurocognitive disorder in the fifth edition of the *Diagnostic and statistical manual of mental disorders*,[5] the international consensus criteria published in 2011[3] are usually preferred in the clinic.

Substantial clinical and pathological overlap exists between FTD and motor neuron disease (MND) as well as other extrapyramidal motor disorders. About 10% of patients with FTD have features of MND.[6,7] Similarly, about 40% of patients with MND will develop behavioural or language deficits. In some instances, these deficits are severe enough to meet the FTD diagnostic criteria.[8] FTD can also overlap with two other movement disorders — corticobasal degeneration and progressive supranuclear palsy — with which it shares abnormal tau pathology.[9]

Summary

- Behavioural variant frontotemporal dementia is characterised by insidious changes in personality and interpersonal conduct that reflect progressive disintegration of the neural circuits involved in social cognition, emotion regulation, motivation and decision making.
- The underlying pathology is heterogeneous and classified according to the presence of intraneuronal inclusions of tau, TDP-43 or, occasionally, fused in sarcoma proteins. Biomarkers to detect these histopathological changes in life are increasingly important with the development of disease-modifying drugs.
- A number of gene abnormalities have been identified, the most common being an expansion in the *C9orf72* gene, which together account for most familial cases.
- The 2011 international consensus criteria propose three levels of diagnostic certainty: possible, probable and definite. Detailed history taking from family members to elicit behavioural features underpins the diagnostic process, with support from neuropsychological testing designed to detect impairment in decision making, emotion processing and social cognition. Brain imaging is important for increasing the level of diagnosis certainty over time. Carer education and support remain of paramount importance.

The presence of socially inappropriate behaviours (eg., disinhibition, socially inappropriate comments), stereotypical motor behaviour, and changes in eating habits (eg, increased food intake, hyperorality) are features that most clearly help distinguish bvFTD from AD in the early stages of the disease.[13,14] As the condition advances, agitation and general irritability (ie, shortness of temper) seem to become more frequent, generally mixed with periods of apathy,[15,16] while restless-

11.2 - 14.7 per 100,000!

Coyle-Gilchrist, ITS et al. (2016)
Piguet O, Kumfor F, Hodges JR (2017)

Prevalence figures for bvFTD...

AIHW (2016)

8.8% prevalence dementia (65 and older)

80% AD

Hogan et al., (2016)

FTD accounts for 2.7% of all dementia (65 and older)

Back home to our Memory Clinic….

National Survey of Memory Clinics in Australia
Woodward & Woodward (2009)

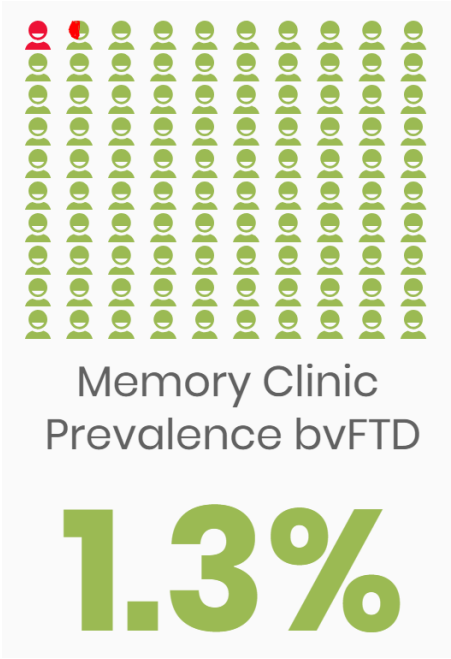
37.8% AD

⇩

If 80% of all dementias are AD
then total dementia cases = 47%

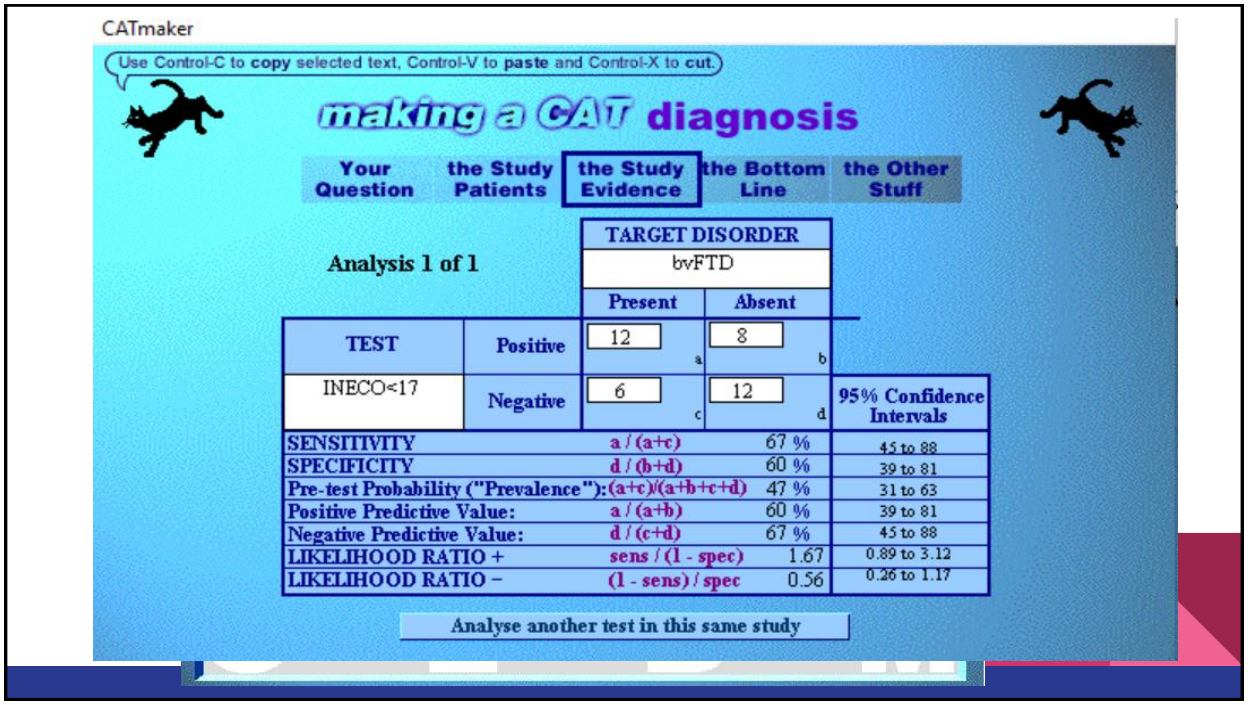
⇩

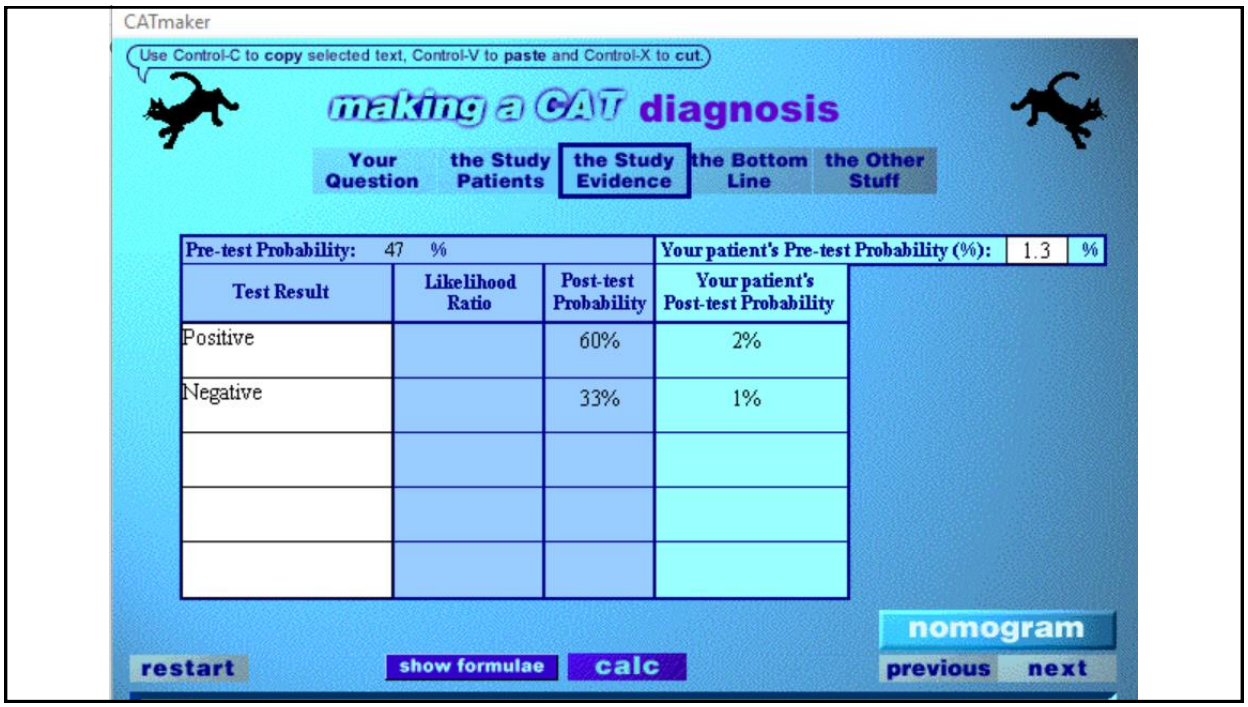
If 2.7% of all dementia are FTD then the prev of FTD in our Australian Memory Clinic sample would be...



Can you generate a clinically sensible estimate of your patient's pre-test probability?

Yes.


CATmaker
Use Control-C to copy selected text, Control-V to paste and Control-X to cut.
making a CAT diagnosis
Your Question
the Study Patients
the Study Evidence
the Bottom Line
the Other Stuff
Analysis 1 of 1
TARGET DISORDER
bvFTD
Present
Absent
TEST
Positive
INECO<17
Negative
12
8
6
12
95% Confidence Intervals
SENSITIVITY a / (a+c) 67 % 45 to 88
SPECIFICITY d / (b+d) 60 % 39 to 81
Pre-test Probability ("Prevalence"): (a+c)/(a+b+c+d) 47 % 31 to 63
Positive Predictive Value: a / (a+b) 60 % 39 to 81
Negative Predictive Value: d / (c+d) 67 % 45 to 88
LIKELIHOOD RATIO + sens / (1 - spec) 1.67 0.89 to 3.12
LIKELIHOOD RATIO − (1 - sens) / spec 0.56 0.26 to 1.17
Analyse another test in this same study


CATmaker
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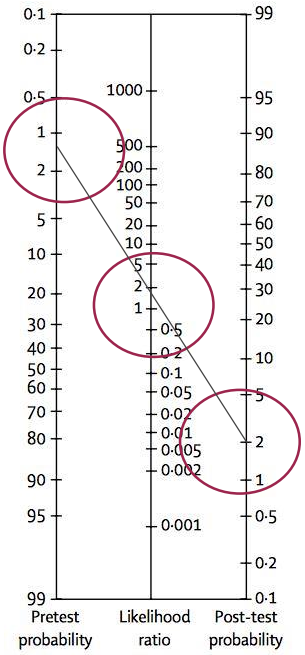
making a CAT diagnosis
Your Question
the Study Patients
the Study Evidence
the Bottom Line
the Other Stuff
Pre-test Probability: 47 %
Your patient's Pre-test Probability (%): 1.3 %
Test Result
Likelihood Ratio
Post-test Probability
Your patient's Post-test Probability
Positive
60%
2%
Negative
33%
1%
nomogram
restart
show formulae
calc
previous
next

LR +ve = Odds that will have a diagnosis of bvFTD if you get a positive test result.

= 1.67 (times more likely to have the condition)

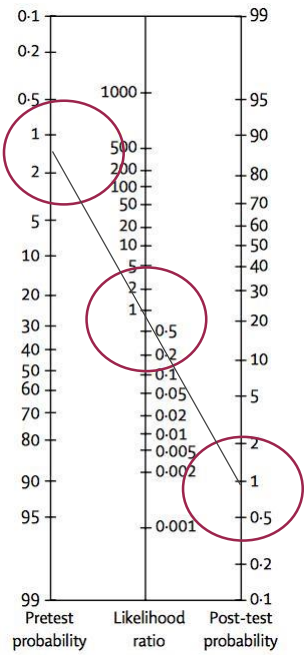


Post-test probability = 2%

(PPV = 60%)

LR -ve = Odds that you will have bvFTD if you get a negative test result

= 0.56 (times more likely to have the condition)



Post test probability = 1%

(NPV = 67%)

Will the resulting post-test probabilities affect your management and help your patient?

No!

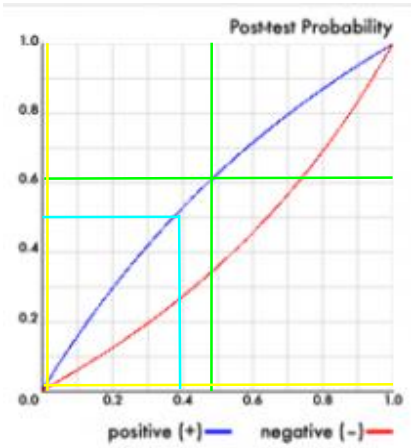
Given a positive test result on INECO (score<17) , the likelihood that Sue has bvFTD

2%

Given a negative test result on INECO (score ⩾17), the likelihood that Sue will be incorrectly classified (actually has bvFTD)

1%

A graphical representation...



Study prevalence = 18/38 = .47

Setting (Memory clinic) prevalence = 0.013

?base-rate to reach 0.5 decision threshold

JOURNAL OF CLINICAL AND EXPERIMENTAL NEUROPSYCHOLOGY
2011, 33 (9), 997–1004

Psychology Press
Taylor & Francis Group

Comparing the clinical usefulness of the Institute of Cognitive Neurology (INECO) Frontal Screening (IFS) and the Frontal Assessment Battery (FAB) in frontotemporal dementia

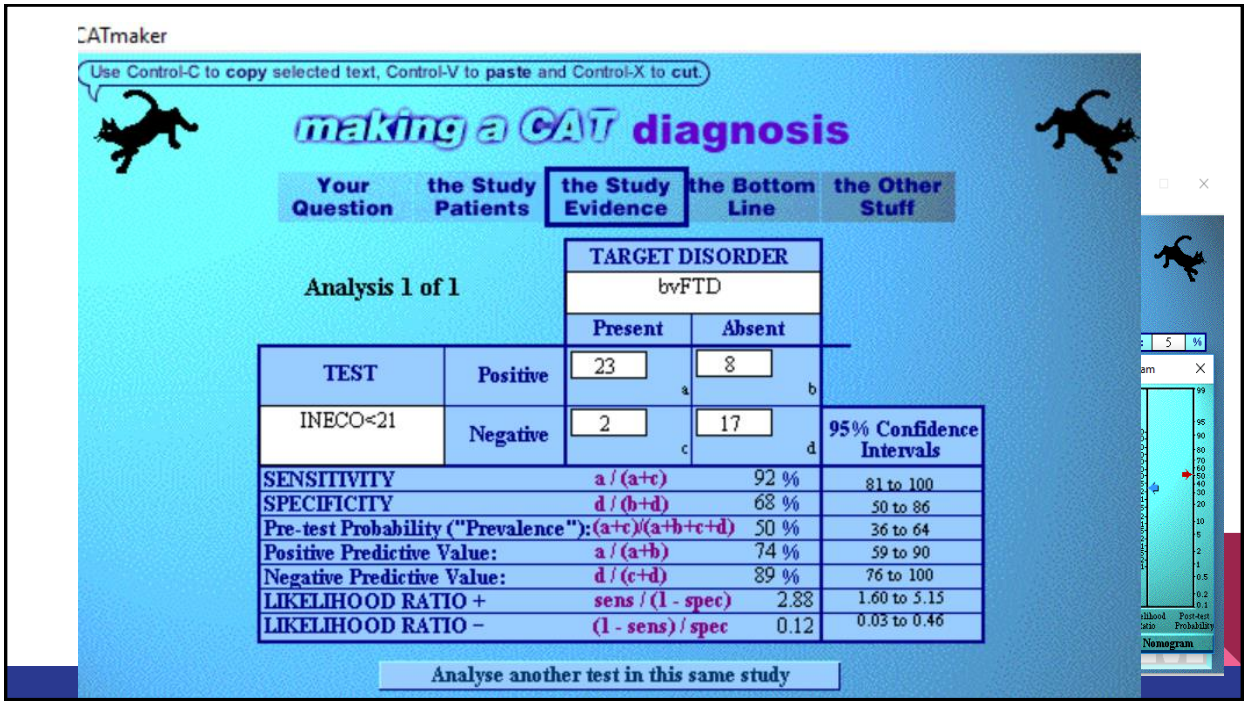
Ezequiel Gleichgerrcht[1,3], María Roca[1,2,3], Facundo Manes[1,3], and Teresa Torralva[1,3]

[1]Institute of Cognitive Neurology (INECO), Buenos Aires, Argentina
[2]Laboratory of Neuroscience, Universidad Diego Portales, Santiago, Chile
[3]Institute of Neurosciences, Favaloro University, Buenos Aires, Argentina

We compared the utility of two executive-function brief screening tools, the Institute of Cognitive Neurology (INECO) Frontal Screening (IFS) and the Frontal Assessment Battery (FAB), in their ability to detect executive dysfunction in a group of behavioral variant frontotemporal dementia (bv-FTD, $n = 25$) and Alzheimer's disease (AD, $n = 25$) patients in the early stages of their disease and in comparison to a group of age-, gender-, and education-matched controls ($n = 26$). Relative to the FAB, the IFS showed (a) better capability to differentiate between types of dementia; (b) higher sensitivity and specificity for the detection of executive dysfunction; (c) stronger correlations with standard executive tasks. We conclude that while both tools are brief and specific for the detection of early executive dysfunction in dementia, the IFS is more sensitive and specific in differentiating bvFTD from AD, and its use in everyday clinical practice can contribute to the differential diagnosis between types of dementia.

Keywords: Behavioral variant frontotemporal dementia; Alzheimer's disease; Institute of Cognitive Neurology Frontal Screening; Frontal Assessment Battery; Executive functions; Cognitive screening.

of 10 points. On the contrary, a 21-point cutoff score on the IFS showed 92.0%, CI = [74.0, 99.0], sensitivity and 67.7%, CI = [52.2, 73.8], specificity. Again, the IFS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Analysis 1 of 1
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bvFTD
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a
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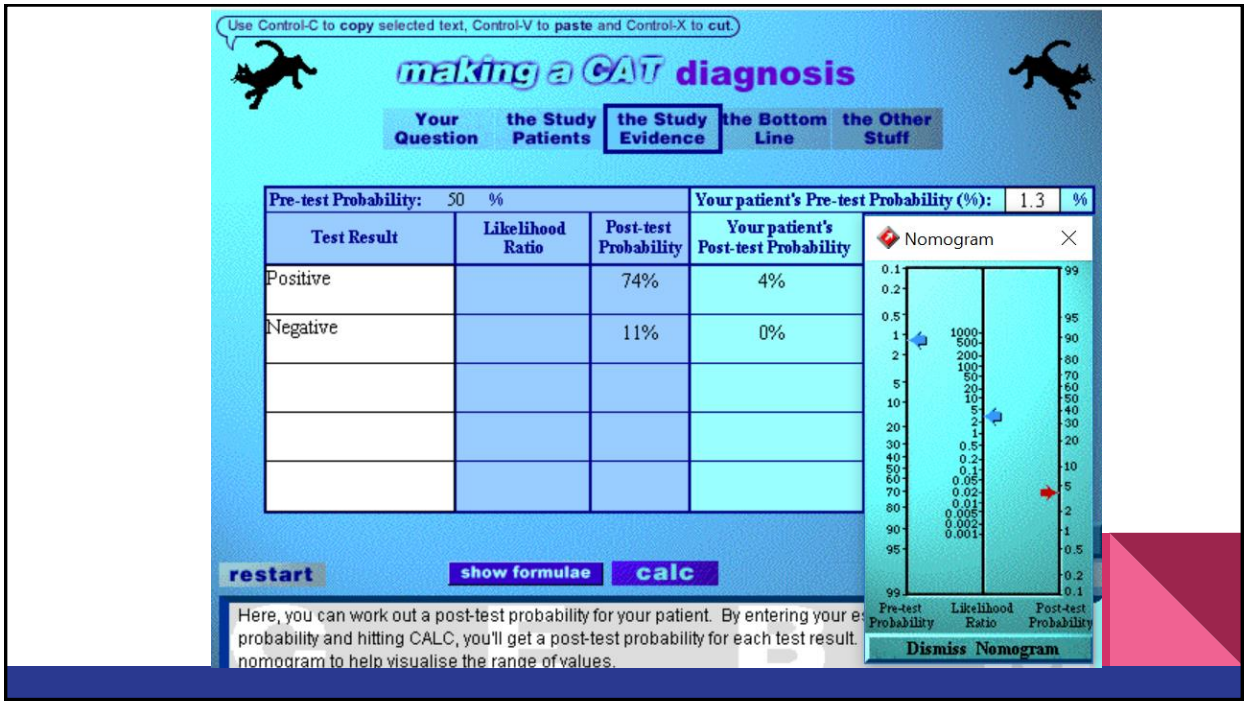
95% Confidence Intervals
SENSITIVITY a / (a+c) 92 % 81 to 100
SPECIFICITY d / (b+d) 68 % 50 to 86
Pre-test Probability ("Prevalence"): (a+c)/(a+b+c+d) 50 % 36 to 64
Positive Predictive Value: a / (a+b) 74 % 59 to 90
Negative Predictive Value: d / (c+d) 89 % 76 to 100
LIKELIHOOD RATIO + sens / (1 - spec) 2.88 1.60 to 5.15
LIKELIHOOD RATIO − (1 - sens) / spec 0.12 0.03 to 0.46
Analyse another test in this same study
Nomogram


Use Control-C to copy selected text, Control-V to paste and Control-X to cut.
making a CAT diagnosis
Your Question
the Study Patients
the Study Evidence
the Bottom Line
the Other Stuff
Pre-test Probability: 50 %
Your patient's Pre-test Probability (%): 1.3 %
Test Result
Likelihood Ratio
Post-test Probability
Your patient's Post-test Probability
Positive
74%
4%
Negative
11%
0%
restart
show formulae
calc
Here, you can work out a post-test probability for your patient. By entering your e
probability and hitting CALC, you'll get a post-test probability for each test result.
nomogram to help visualise the range of values.
Nomogram
Pre-test Probability
Likelihood Ratio
Post-test Probability
Dismiss Nomogram

Our feedback to the Neurologist?

INECO does not add value in **any** likely clinical setting

Revert to **prevalence** rates as the best predictor of bvFTD dx

Dement Neuropsychol 2013 March;7(1):33-39

Original Article

The INECO Frontal Screening tool differentiates behavioral variant - frontotemporal dementia (bv-FTD) from major depression

Natalia Fiorentino[1], Ezequiel Gleichgerrcht[2], María Roca[2], Marcelo Cetkovich[2], Facundo Manes[2], Teresa Torralva[3]

ABSTRACT. Executive dysfunction may result from prefrontal circuitry involvement occurring in both neurodegenerative diseases and psychiatric disorders. Moreover, multiple neuropsychiatric conditions, may present with overlapping behavioral and cognitive symptoms, making differential diagnosis challenging, especially during earlier stages. In this sense, cognitive assessment may contribute to the differential diagnosis by providing an objective and quantifiable set of measures that has the potential to distinguish clinical conditions otherwise perceived in everyday clinical settings as quite similar. **Objective:** The goal of this study was to investigate the utility of the INECO Frontal Screening (IFS) for differentiating bv-FTD patients from patients with Major Depression. **Methods:** We studied 49 patients with bv-FTD diagnosis and 30 patients diagnosed with unipolar depression compared to a control group of 26 healthy controls using the INECO Frontal Screening (IFS), the Mini Mental State Examination (MMSE) and the Addenbrooke's Cognitive Examination-Revised (ACE-R). **Results:** Patient groups differed significantly on the motor inhibitory control ($U=437.0$, $p<0.01$), verbal working memory ($U=298.0$, $p<0.001$), spatial working memory ($U=300.5$, $p<0.001$), proverbs ($U=341.5$, $p<0.001$) and verbal inhibitory control ($U=316.0$, $p<0.001$) subtests, with bv-FTD patients scoring significantly lower than patients with depression. **Conclusion:** Our results suggest the IFS can be considered a useful tool for detecting executive dysfunction in both depression and bv-FTD patients and, perhaps more importantly, that it has the potential to help differentiate these two conditions.

Key words: frontotemporal dementia, major depression and executive dysfunction.

38TH ANNUAL CONFERENCE
OCTOBER 17-20, 2018

BECOMING AGENTS OF CHANGE

SHERATON NEW ORLEANS HOTEL | NEW ORLEANS, LA

Predicting who will develop dementia

Dr Leonie Simpson
Neuropsychology Unit
Department of Clinical Neurosciences
St Vincent's Hospital Melbourne
Honorary Staff Member, The University of Melbourne

38TH ANNUAL CONFERENCE
OCTOBER 17-20, 2018

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Financial Disclosure

I have no financial relationships to disclose:

Employee of: St Vincent's Hospital Melbourne
Consultant for: nil
Stockholder in: nil
Research support from: nil
Honoraria from: nil

Predicting who will develop dementia

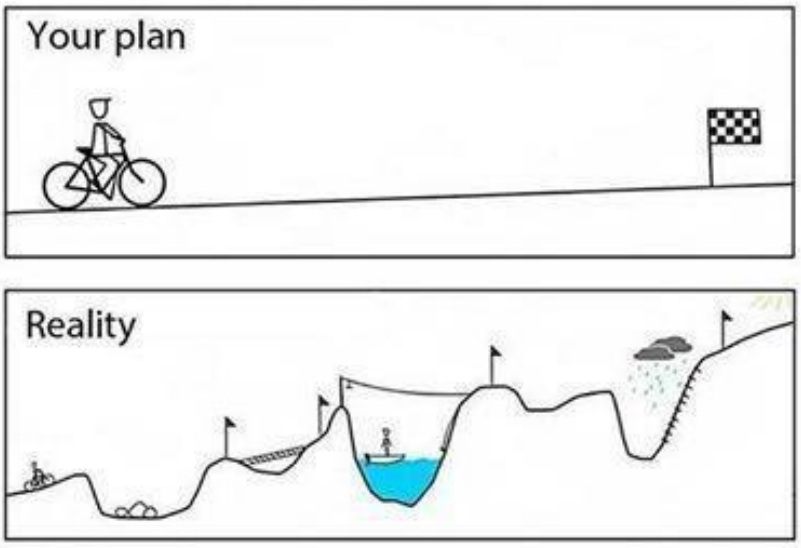
Dr Leonie Simpson
Senior Clinical Neuropsychologist, St Vincent's Hospital, Melbourne
leonie.simpson2@svha.org.au

Michael the commercial pilot

Should he go back to work?

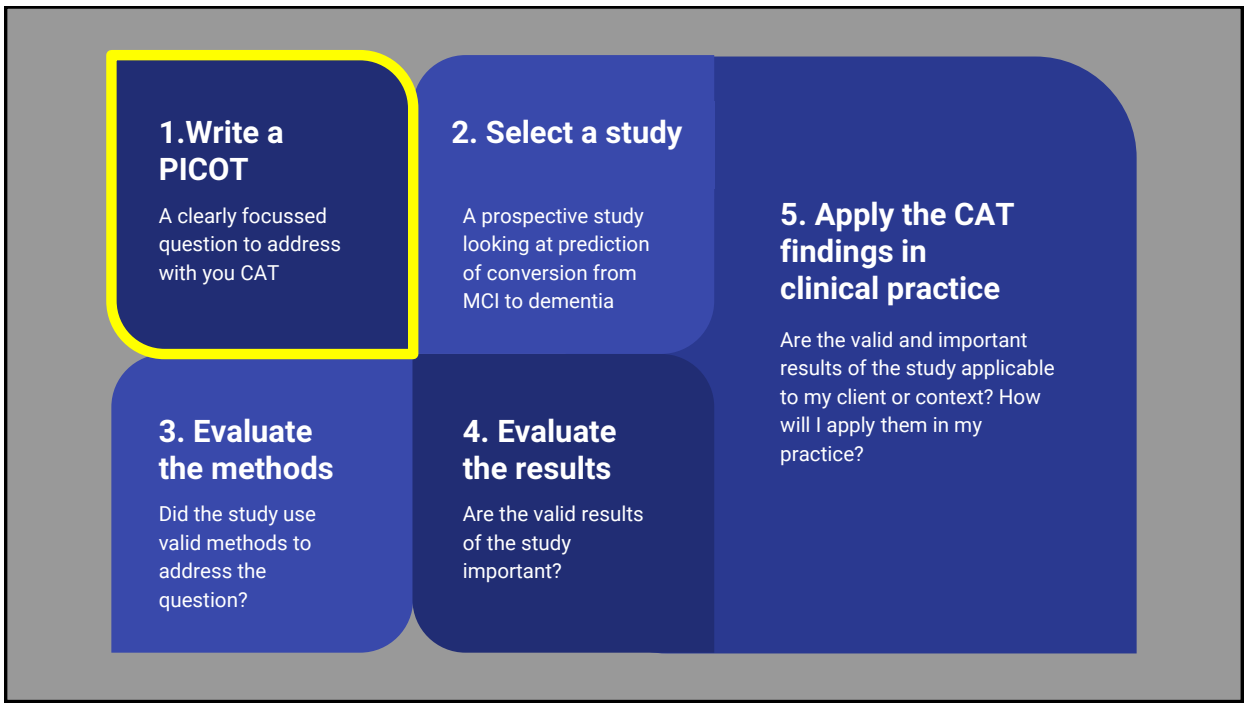
Diagnostic CAT

P	50 year old commercial pilot with moderate head injury
I	neuropsychological test e.g. PSI from WAIS-IV, etc
C	people who are cognitively incompetent to fly
O	successful return to flying, e.g. acceptable degree of flight path deviation or appropriate landing decision on a flight simulator
T	Diagnosis or prognosis (although unlikely to find prognosis as rigorous return to work)


Your plan
Reality

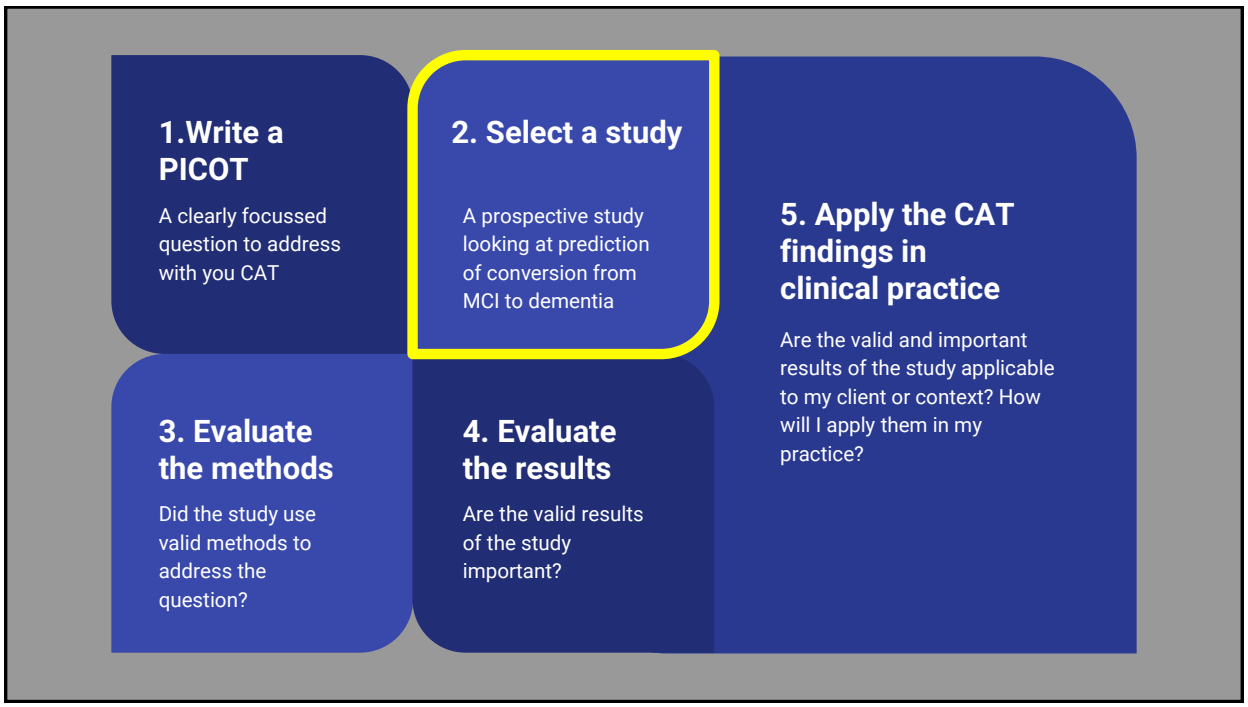
Mary, 69, is forgetting things

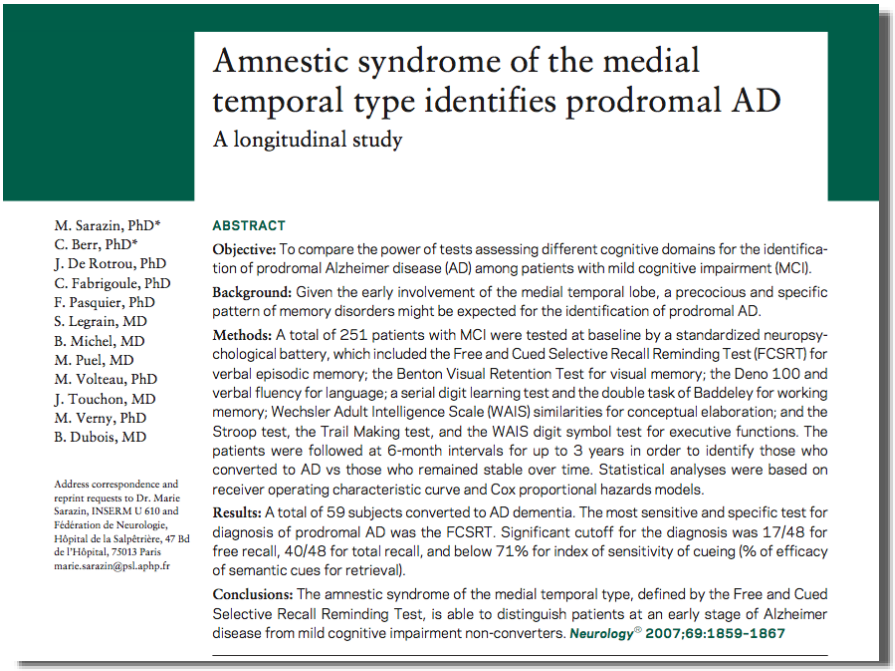
(but not much)



Diagnostic CAT

P	69 year old lady with mild concerns about her memory seen in a tertiary referral centre.
I	Does a low memory test result
C	Compared to people who don't develop dementia
O	Predict a diagnosis of dementia within 2-3 years.
T	(Diagnosis)





Amnestic syndrome of the medial temporal type identifies prodromal AD

A longitudinal study

M. Sarazin, PhD*
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F. Pasquier, PhD
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M. Verny, PhD
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ABSTRACT

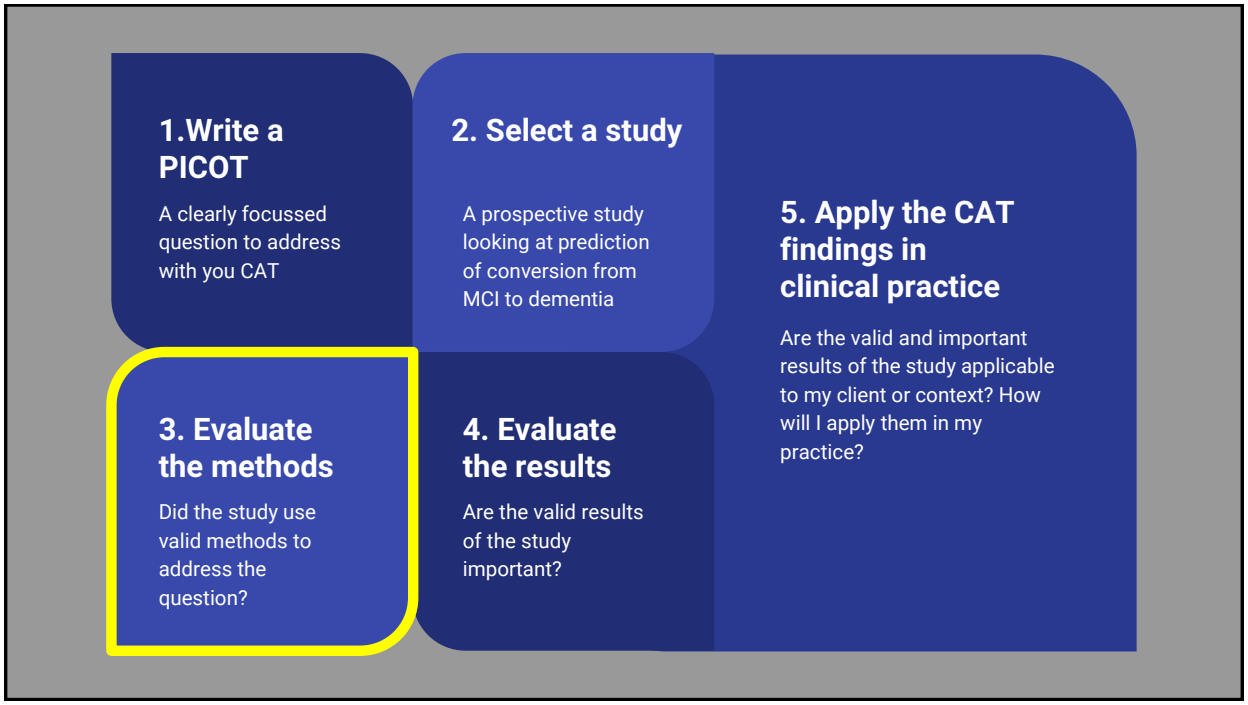
Objective: To compare the power of tests assessing different cognitive domains for the identification of prodromal Alzheimer disease (AD) among patients with mild cognitive impairment (MCI).

Background: Given the early involvement of the medial temporal lobe, a precocious and specific pattern of memory disorders might be expected for the identification of prodromal AD.

Methods: A total of 251 patients with MCI were tested at baseline by a standardized neuropsychological battery, which included the Free and Cued Selective Recall Reminding Test (FCSRT) for verbal episodic memory; the Benton Visual Retention Test for visual memory; the Deno 100 and verbal fluency for language; a serial digit learning test and the double task of Baddeley for working memory; Wechsler Adult Intelligence Scale (WAIS) similarities for conceptual elaboration; and the Stroop test, the Trail Making test, and the WAIS digit symbol test for executive functions. The patients were followed at 6-month intervals for up to 3 years in order to identify those who converted to AD vs those who remained stable over time. Statistical analyses were based on receiver operating characteristic curve and Cox proportional hazards models.

Results: A total of 59 subjects converted to AD dementia. The most sensitive and specific test for diagnosis of prodromal AD was the FCSRT. Significant cutoff for the diagnosis was 17/48 for free recall, 40/48 for total recall, and below 71% for index of sensitivity of cueing (% of efficacy of semantic cues for retrieval).

Conclusions: The amnestic syndrome of the medial temporal type, defined by the Free and Cued Selective Recall Reminding Test, is able to distinguish patients at an early stage of Alzheimer disease from mild cognitive impairment non-converters. *Neurology*® 2007;69:1859-1867

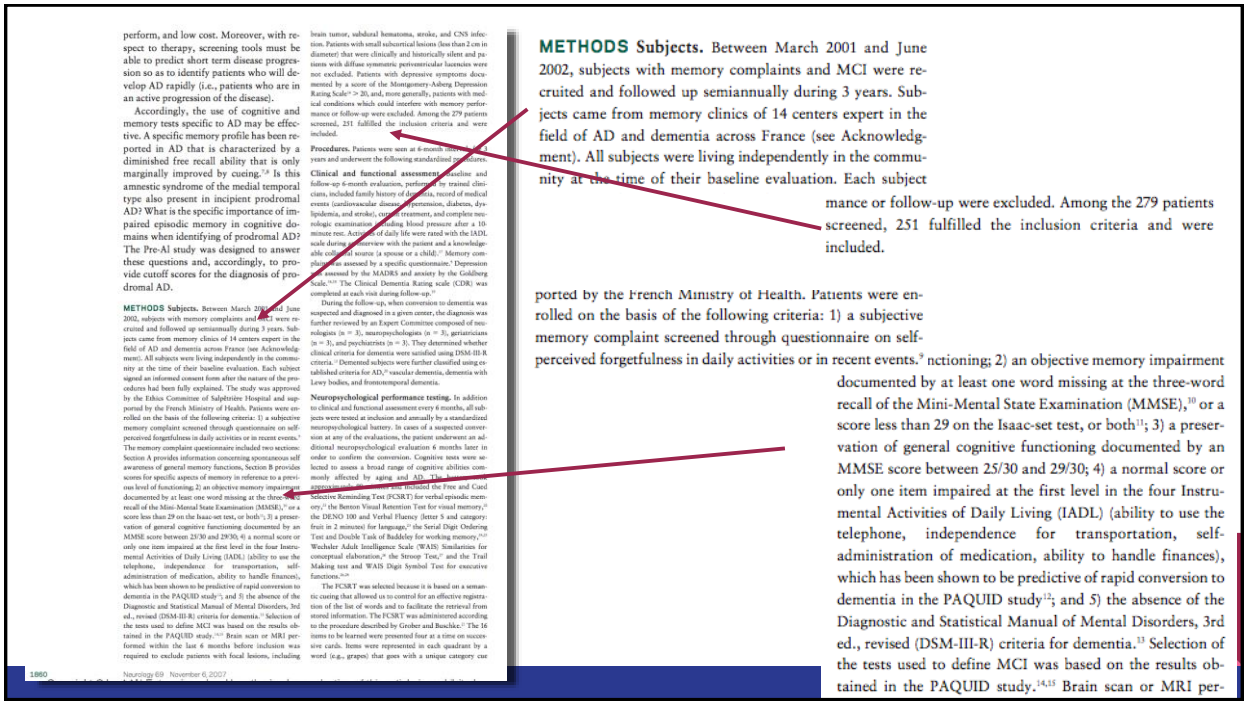


https://www.cebm.net/category/ebm-resources/tools/

Or

https://ebm-tools.knowledgetranslation.net/calculator/diagnostic/

Was the diagnostic test evaluated in a representative spectrum of patients (like those in whom it would be used in practice)?



METHODS Subjects. Between March 2001 and June 2002, subjects with memory complaints and MCI were recruited and followed up semiannually during 3 years. Subjects came from memory clinics of 14 centers expert in the field of AD and dementia across France (see Acknowledgment). All subjects were living independently in the community at the time of their baseline evaluation. Each subject

mance or follow-up were excluded. Among the 279 patients screened, 251 fulfilled the inclusion criteria and were included.

ported by the French Ministry of Health. Patients were enrolled on the basis of the following criteria: 1) a subjective memory complaint screened through questionnaire on self-perceived forgetfulness in daily activities or in recent events.[9] nctioning; 2) an objective memory impairment documented by at least one word missing at the three-word recall of the Mini-Mental State Examination (MMSE),[10] or a score less than 29 on the Isaac-set test, or both[11]; 3) a preservation of general cognitive functioning documented by an MMSE score between 25/30 and 29/30; 4) a normal score or only one item impaired at the first level in the four Instrumental Activities of Daily Living (IADL) (ability to use the telephone, independence for transportation, self-administration of medication, ability to handle finances), which has been shown to be predictive of rapid conversion to dementia in the PAQUID study[12]; and 5) the absence of the Diagnostic and Statistical Manual of Mental Disorders, 3rd ed., revised (DSM-III-R) criteria for dementia.[13] Selection of the tests used to define MCI was based on the results obtained in the PAQUID study.[14,15] Brain scan or MRI per-

maybe

Was the diagnostic test evaluated in a representative spectrum of patients (like those in whom it would be used in practice)?

Was the reference standard applied regardless of the index test result?

perform, and low cost. Moreover, with respect to therapy, screening tools must be able to predict short term disease progression so as to identify patients who will develop AD rapidly (i.e., patients who are in an active progression of the disease).

Accordingly, the use of cognitive and memory tests specific to AD may be effective. A specific memory profile has been reported in AD that is characterized by a diminished free recall ability that is only marginally improved by cueing.[7,8] Is this amnestic syndrome of the medial temporal type also present in incipient prodromal AD? What is the specific importance of impaired episodic memory in cognitive domains when identifying of prodromal AD? The Pre-Al study was designed to answer these questions and, accordingly, to provide cutoff scores for the diagnosis of prodromal AD.

METHODS Subjects. Between March 2001 and June 2002, subjects with memory complaints and MCI were recruited and followed up semiannually during 3 years. Subjects came from memory clinics of 14 centers expert in the field of AD and dementia across France (see Acknowledgment). All subjects were living independently in the community at the time of their baseline evaluation. Each subject signed an informed consent form after the nature of the procedures had been fully explained. The study was approved by the Ethics Committee of Salpêtrière Hospital and supported by the French Ministry of Health. Patients were enrolled on the basis of the following criteria: 1) a subjective memory complaint screened through questionnaire on self-perceived forgetfulness in daily activities or in recent events.[9] The memory complaint questionnaire included two sections: Section A provides information concerning spontaneous self awareness of general memory functions, Section B provides scores for specific aspects of memory in reference to a previous level of functioning; 2) an objective memory impairment documented by at least one word missing at the three-word recall of the Mini-Mental State Examination (MMSE),[10] or a score less than 29 on the Isaac-set test, or both[11]; 3) a preservation of general cognitive functioning documented by an MMSE score between 25/30 and 29/30; 4) a normal score or only one item impaired at the first level in the four Instrumental Activities of Daily Living (IADL) (ability to use the telephone, independence for transportation, self-administration of medication, ability to handle finances), which has been shown to be predictive of rapid conversion to dementia in the PAQUID study[12]; and 5) the absence of the Diagnostic and Statistical Manual of Mental Disorders, 3rd ed., revised (DSM-III-R) criteria for dementia.[13] Selection of the tests used to define MCI was based on the results obtained in the PAQUID study.[14,15] Brain scan or MRI performed within the last 6 months before inclusion was required to exclude patients with focal lesions, including brain tumor, subdural hematoma, stroke, and CNS infection. Patients with small subcortical lesions (less than 2 cm in diameter) that were clinically and historically silent and patients with diffuse symmetric periventricular lucencies were not excluded. Patients with depressive symptoms documented by a score of the Montgomery-Asberg Depression Rating Scale[16] > 20, and, more generally, patients with medical conditions which could interfere with memory performance or follow-up were excluded. Among the 279 patients screened, 251 fulfilled the inclusion criteria and were included.

Procedures. Patients were seen at 6-month intervals for 3 years and underwent the following standardized procedures.

Clinical and functional assessment. Baseline and follow-up 6-month evaluation, performed by trained clinicians, included family history of dementia, record of medical events (cardiovascular disease, hypertension, diabetes, dyslipidemia, and stroke), current treatment, and complete neurologic examination including blood pressure after a 10-minute rest. Activities of daily life were rated with the IADL scale during an interview with the patient and a knowledgeable collateral source (a spouse or a child).[17] Memory complaint was assessed by a specific questionnaire.[9] Depression was assessed by the MADRS and anxiety by the Goldberg Scale.[16,18] The Clinical Dementia Rating scale (CDR) was completed at each visit during follow-up.[19]

During the follow-up, when conversion to dementia was suspected and diagnosed in a given center, the diagnosis was further reviewed by an Expert Committee composed of neurologists (n = 3), neuropsychologists (n = 3), geriatricians (n = 3), and psychiatrists (n = 3). They determined whether clinical criteria for dementia were satisfied using DSM-III-R criteria.[13] Demented subjects were further classified using established criteria for AD,[20] vascular dementia, dementia with Lewy bodies, and frontotemporal dementia.

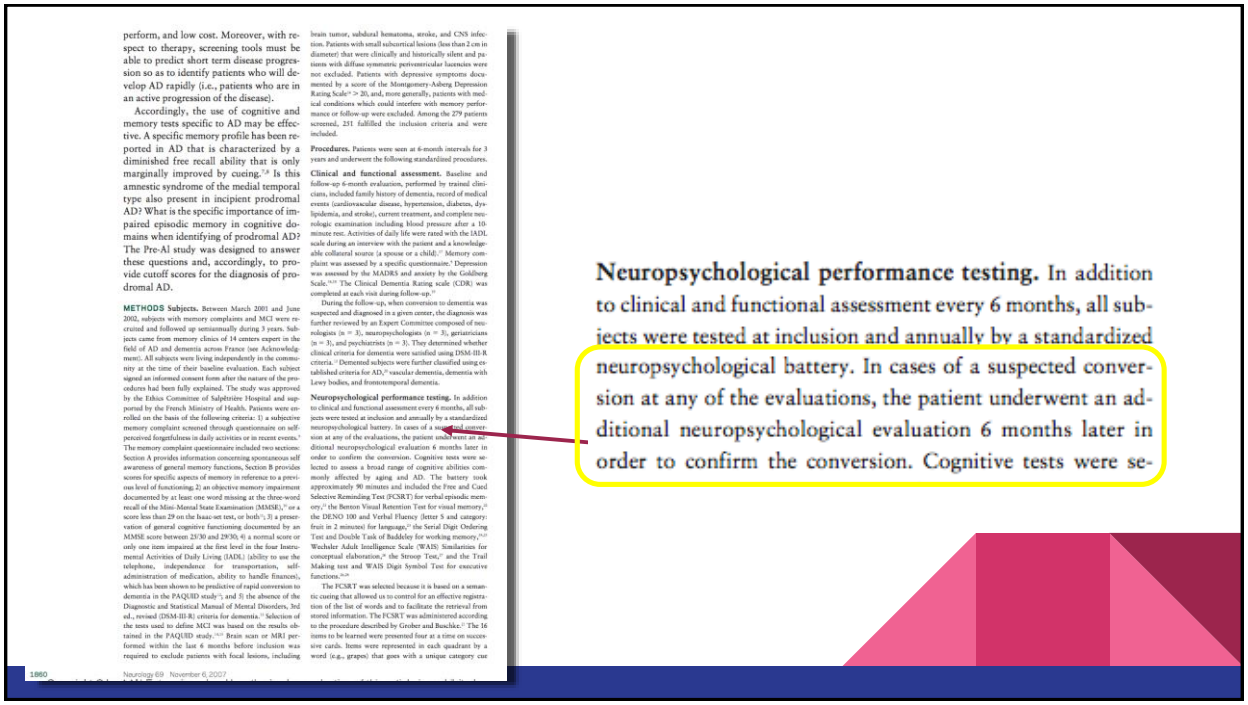
Neuropsychological performance testing. In addition to clinical and functional assessment every 6 months, all subjects were tested at inclusion and annually by a standardized neuropsychological battery. In cases of a suspected conversion at any of the evaluations, the patient underwent an additional neuropsychological evaluation 6 months later in order to confirm the conversion. Cognitive tests were selected to assess a broad range of cognitive abilities commonly affected by aging and AD. The battery took approximately 90 minutes and included the Free and Cued Selective Reminding Test (FCSRT) for verbal episodic memory,[21] the Benton Visual Retention Test for visual memory,[22] the DENO 100 and Verbal Fluency (letter S and category: fruit in 2 minutes) for language,[23] the Serial Digit Ordering Test and Double Task of Baddeley for working memory,[24,25] Wechsler Adult Intelligence Scale (WAIS) Similarities for conceptual elaboration,[26] the Stroop Test,[27] and the Trail Making test and WAIS Digit Symbol Test for executive functions.[26,28]

The FCSRT was selected because it is based on a semantic cueing that allowed us to control for an effective registration of the list of words and to facilitate the retrieval from stored information. The FCSRT was administered according to the procedure described by Grober and Buschke.[21] The 16 items to be learned were presented four at a time on successive cards. Items were represented in each quadrant by a word (e.g., grapes) that goes with a unique category cue

yes

Was the reference standard applied regardless of the index test result?

Was there an independent, blind comparison between the index test and an appropriate reference ('gold') standard of diagnosis?



perform, and low cost. Moreover, with respect to therapy, screening tools must be able to predict short term disease progression so as to identify patients who will develop AD rapidly (i.e., patients who are in an active progression of the disease).

Accordingly, the use of cognitive and memory tests specific to AD may be effective. A specific memory profile has been reported in AD that is characterized by a diminished free recall ability that is only marginally improved by cueing.[7,8] Is this amnestic syndrome of the medial temporal type also present in incipient prodromal AD? What is the specific importance of impaired episodic memory in cognitive domains when identifying of prodromal AD? The Pre-Al study was designed to answer these questions and, accordingly, to provide cutoff scores for the diagnosis of prodromal AD.

METHODS Subjects. Between March 2001 and June 2002, subjects with memory complaints and MCI were recruited and followed up semiannually during 3 years. Subjects came from memory clinics of 14 centers expert in the field of AD and dementia across France (see Acknowledgment). All subjects were living independently in the community at the time of their baseline evaluation. Each subject signed an informed consent form after the nature of the procedures had been fully explained. The study was approved by the Ethics Committee of Salpêtrière Hospital and supported by the French Ministry of Health. Patients were enrolled on the basis of the following criteria: 1) a subjective memory complaint screened through questionnaire on self-perceived forgetfulness in daily activities or in recent events,[9] The memory complaint questionnaire included two sections: Section A provides information concerning spontaneous self awareness of general memory functions, Section B provides scores for specific aspects of memory in reference to a previous level of functioning; 2) an objective memory impairment documented by at least one word missing at the three-word recall of the Mini-Mental State Examination (MMSE),[10] or a score less than 29 on the Isaac-set test, or both[11]; 3) a preservation of general cognitive functioning documented by an MMSE score between 25/30 and 29/30, 4) a normal score or only one item impaired at the first level in the four Instrumental Activities of Daily Living (IADL) (ability to use the telephone, independence for transportation, self-administration of medication, ability to handle finances), which has been shown to be predictive of rapid conversion to dementia in the PAQUID study[12]; and 5) the absence of the Diagnostic and Statistical Manual of Mental Disorders, 3rd ed., revised (DSM-III-R) criteria for dementia.[13] Selection of the tests used to define MCI was based on the results obtained in the PAQUID study.[14,15] Brain scan or MRI performed within the last 6 months before inclusion was required to exclude patients with focal lesions, including brain tumor, subdural hematoma, stroke, and CNS infection. Patients with small subcortical lesions (less than 2 cm in diameter) that were clinically and historically silent and patients with diffuse symmetric periventricular lucencies were not excluded. Patients with depressive symptoms documented by a score of the Montgomery-Asberg Depression Rating Scale[16] > 20, and, more generally, patients with medical conditions which could interfere with memory performance or follow-up were excluded. Among the 279 patients screened, 231 fulfilled the inclusion criteria and were included.

Procedures. Patients were seen at 6-month intervals for 3 years and underwent the following standardized procedures.

Clinical and functional assessment. Baseline and follow-up 6-month evaluations, performed by trained clinicians, included family history of dementia, record of medical events (cardiovascular disease, hypertension, diabetes, dyslipidemia, and stroke), current treatment, and complete neurologic examination including blood pressure after a 10-minute rest. Activities of daily life were rated with the IADL scale during an interview with the patient and a knowledgeable collateral source (a spouse or a child).[17] Memory complaint was assessed by a specific questionnaire.[9] Depression was assessed by the MADRS and anxiety by the Goldberg Scale.[16,18] The Clinical Dementia Rating scale (CDR) was completed at each visit during follow-up.[19]

During the follow-up, when conversion to dementia was suspected and diagnosed in a given center, the diagnosis was further reviewed by an Expert Committee composed of neurologists (n = 3), neuropsychologists (n = 3), geriatricians (n = 3), and psychiatrists (n = 3). They determined whether clinical criteria for dementia were satisfied using DSM-III-R criteria.[13] Demented subjects were further classified using established criteria for AD,[20] vascular dementia, dementia with Lewy bodies, and frontotemporal dementia.

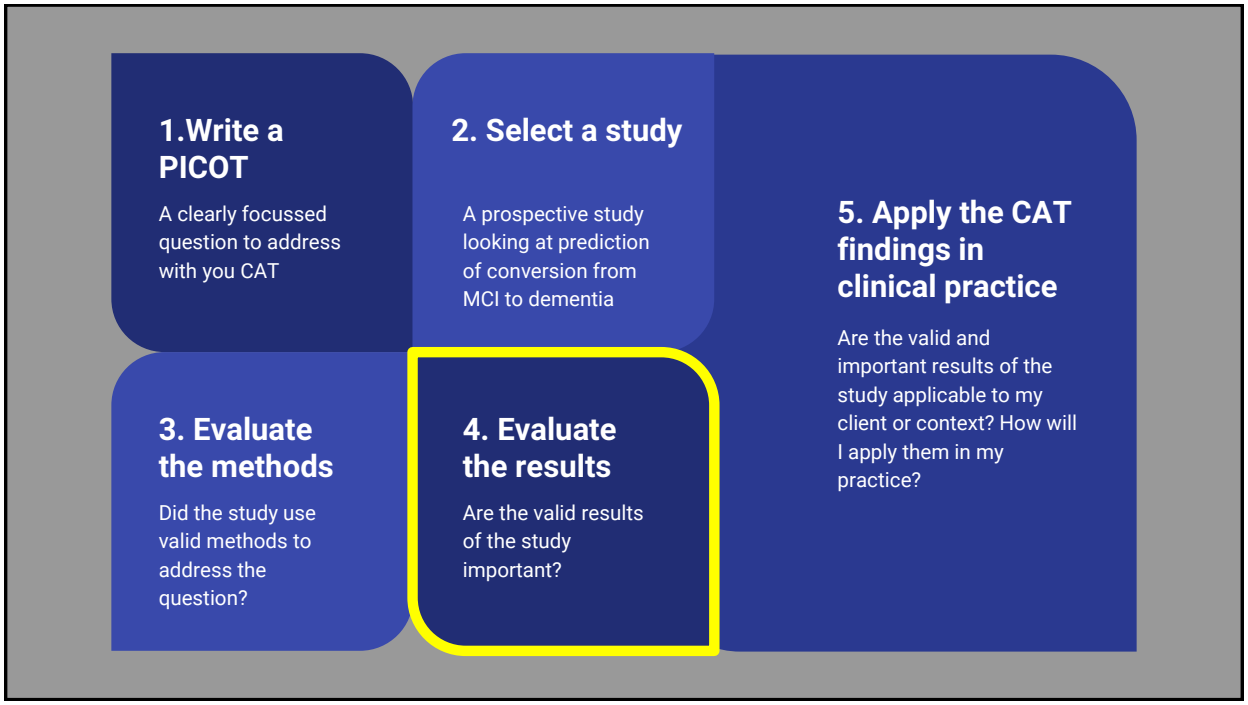
Neuropsychological performance testing. In addition to clinical and functional assessment every 6 months, all subjects were tested at inclusion and annually by a standardized neuropsychological battery. In cases of a suspected conversion at any of the evaluations, the patient underwent an additional neuropsychological evaluation 6 months later in order to confirm the conversion. Cognitive tests were selected to assess a broad range of cognitive abilities commonly affected by aging and AD. The battery took approximately 90 minutes and included the Free and Cued Selective Reminding Test (FCSRT) for verbal episodic memory,[21] the Benton Visual Retention Test for visual memory,[22] the DENO 100 and Verbal Fluency (letter S and category: fruit in 2 minutes) for language,[23] the Serial Digit Ordering Test and Double Task of Baddeley for working memory,[24,25] Wechsler Adult Intelligence Scale (WAIS) Similarities for conceptual elaboration,[26] the Stroop Test,[27] and the Trail Making test and WAIS Digit Symbol Test for executive functions.[26,28]

The FCSRT was selected because it is based on a semantic cueing that allowed us to control for an effective registration of the list of words and to facilitate the retrieval from stored information. The FCSRT was administered according to the procedure described by Grober and Buschke.[21] The 16 items to be learned were presented four at a time on successive cards. Items were represented in each quadrant by a word (e.g., grapes) that goes with a unique category cue

Neuropsychological performance testing. In addition to clinical and functional assessment every 6 months, all subjects were tested at inclusion and annually by a standardized neuropsychological battery. In cases of a suspected conversion at any of the evaluations, the patient underwent an additional neuropsychological evaluation 6 months later in order to confirm the conversion. Cognitive tests were se-

Maybe not

Was there an independent, blind comparison between the index test and an appropriate reference ('gold') standard of diagnosis?



Are the test characteristics presented?

What are the results?

		Reference standard		
		+ve	-ve	
Index test	+ve	TP	FP	N with +ve test
	-ve	FN	TN	N with -ve test
		N with condition	N without condition	Total N

Step 2: What are the results?

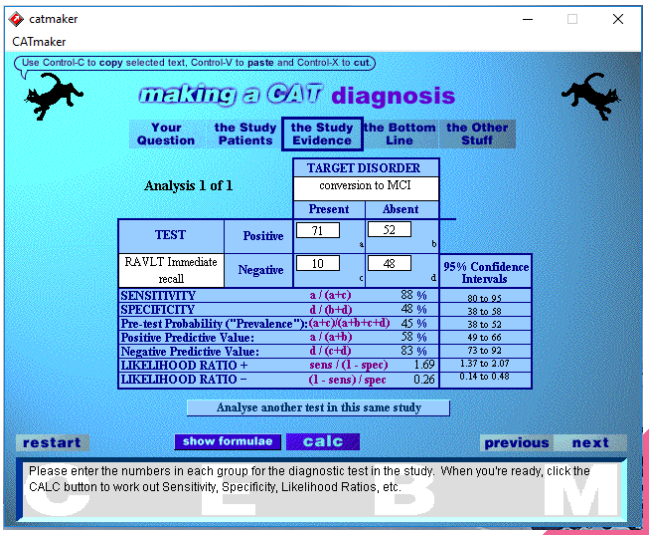


Table 3 Receiver operating characteristic analysis: Demographic factors and neuropsychological tests associated with incident AD dementia

	AUC	CI (AUC)	p Value	Cutoff	Se	Sp
Age	0.72	(0.65, 0.79)				
Age + gender	0.72	(0.65, 0.79)	0.21			
Age + education	0.72	(0.65, 0.79)	0.79			
Age + gender + education	0.73	(0.66, 0.80)	0.49			
FCSRT total recall*	0.94	(0.91, 0.97)	<0.0001	40	79.7	89.9
FCSRT index of cueing*	0.93	(0.89, 0.96)	<0.0001	71	78.0	84.8
FCSRT free recall*	0.92	(0.88, 0.96)	<0.0001	17	71.2	91.8
FCSRT delayed free recall*	0.92	(0.89, 0.96)	<0.0001	6	76.3	90.5
FCSFT delayed total recall*	0.89	(0.85, 0.94)	<0.0001	14	69.5	88.6
FCSRT number of intrusions*	0.87	(0.81, 0.92)	<0.0001	2	64.4	85.4
Verbal fluency (category)*	0.80	(0.74, 0.87)	0.003	13	55.9	82.3
WAIS similarities*	0.78	(0.72, 0.85)	0.04	11	49.2	72.2
FCSRT false recognition*	0.78	(0.71, 0.84)	0.002	1	20.3	98.1
Serial digit learning test*	0.77	(0.7, 0.84)	0.04	80	57.6	67.7
DENO 100*	0.76	(0.7, 0.83)	0.07	89	55.9	67.7
Benton Visual Retention Test*	0.76	(0.69, 0.83)	0.07	11	42.4	77.2
Trail Making test B*	0.75	(0.68, 0.82)	0.09	138	62.7	67.1
WAIS digit symbol test*	0.74	(0.67, 0.81)	0.15	10	37.3	71.5

Areas under the curve (AUC) are presented with their 95% CI. p Values are given for comparison between and for each factor added. Optimal cutoff was determined for each neuropsychological test associat dementia. Results for tests are presented in order of statistical power.
*Age is included in models for computing AUC.
AD = Alzheimer disease; FCSRT = Free and Cued Selective Recall Reminding Test; WAIS = Wechsler Adult

Determination of the optimal neuropsychological cutoff for predicting AD dementia. A first ROC curve analysis showed that only age changed the statistical level, whereas sex and level of education did not. Results are presented in table 3. The ROC analysis provides information about the more sensitive and specific neuropsychological tools which can predict the development of AD dementia. The FCSRT scores (total recall, index of cuing free recall, free recall, delayed free recall, delayed total recall, and number of intrusions) all have the best areas under the curve with AUC values higher than 0.87. Then, only Verbal Fluency (category), WAIS Similarities, and the Serial Digit Learning Test add significant information to predict the incidence of AD dementia (compared to a model with age only) with AUC between 0.77 and 0.80. All other tests did not add significant information.

We further tried to increase accuracy by combining different neuropsychological performances. No combination significantly improved the accuracy of the models presented in table 3.

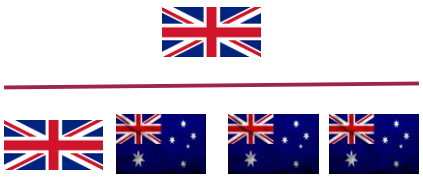
The significant threshold of FCSRT for identifying MCI-A baseline was 17/48 for free recal recall, 6/16 for delayed free recal delayed recall, and 71% for index cuing (table 3). Respective sens ficity are also presented in table ity and specificity were provided FCSRT scores, total recall bein the highest sensitivity (79.7%), v of 89.9%. The highest specificity (91.8%), with sensitivity equal to 71.2%. In addition to the FCSRT scores were the Verbal Fluency scores, but these values were far less sensitive and specific than those of the FCSRT subscores (sensitivity = 55.9%, specificity = 82.3%).

Relation between baseline neuropsychological performance and risk of developing AD. The Kaplan-Meier survival curves (figure) graphically show the dramatic difference in the development of AD dementia between the groups, according to the

MCI-non AD (n = 158)	MCI-AD (n = 59)
70.0 ± 5.4	74.8 ± 4.1

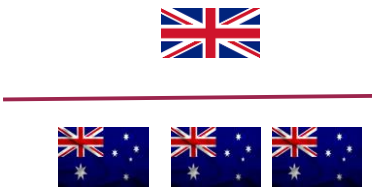
LR = odds of having the condition (compared to not having it

probability



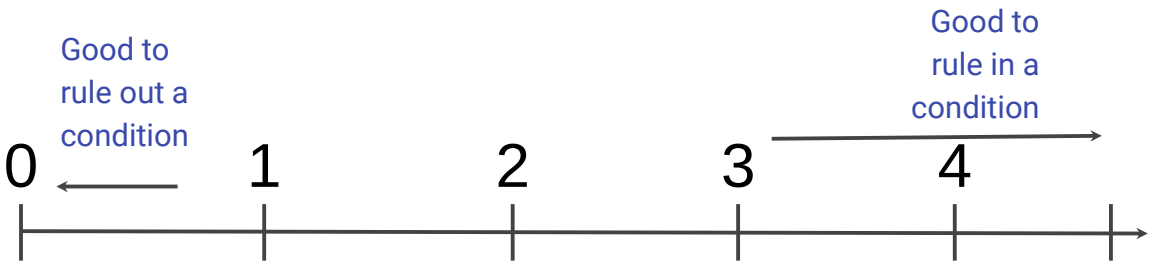
P = 0.25 (25%)

odds



odds = 0.33

What's useful in LRs



throw your test in the bin

	AUC	CI (AUC)	*p* Value	Cutoff	Se	Sp
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Age + gender	0.72	(0.65, 0.79)	0.21			
Age + education	0.72	(0.65, 0.79)	0.79			
Age + gender + education	0.73	(0.66, 0.80)	0.49			
FCSRT total recall*	0.94	(0.91, 0.97)	<0.0001	40	79.7	89.9

MCI-non AD (n = 158)	MCI-AD (n = 59)

Specificity = proportion of people without the disease who get a negative test result

0.899 = TN/(158)

142 = TN

FP = 158-142 = 16

		Reference standard: MCI prog	Reference standard: Stable MCI	
Index test	FCSRT <40	47	16	63
	FCSRT >40	12	142	154
		59	158	217

	AUC	CI (AUC)	*p* Value	Cutoff	Se	Sp
Age	0.72	(0.65, 0.79)				
Age + gender	0.72	(0.65, 0.79)	0.21			
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Age + gender + education	0.73	(0.66, 0.80)	0.49			
FCSRT total recall*	0.94	(0.91, 0.97)	<0.0001	40	79.7	89.9

MCI-non AD (n = 158)	MCI-AD (n = 59)

Sensitivity = proportion of people with the disease who get a positive test result

0.797 = TP / 59

TP = 47

FN = 59 - TP = 10

		Reference standard: MCI prog	Reference standard: Stable MCI	
Index test	FCSRT <40	47	16	63
	FCSRT >40	12	142	154
		59	158	217

	AUC	CI (AUC)	*p* Value	Cutoff	Se	Sp
Age	0.72	(0.65, 0.79)				
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Age + gender + education	0.73	(0.66, 0.80)	0.49			
FCSRT total recall*	0.94	(0.91, 0.97)	<0.0001	40	79.7	89.9

PPV = proportion of people with a positive test result who do have the disease

= 47/(47+16)

= 75% (64-85)

		Reference standard: MCI prog	Reference standard: Stable MCI	
Index test	FCSRT <40	47	16	63
	FCSRT >40	12	142	154
		59	158	217

	AUC	CI (AUC)	*p* Value	Cutoff	Se	Sp
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Age + gender + education	0.73	(0.66, 0.80)	0.49			
FCSRT total recall*	0.94	(0.91, 0.97)	<0.0001	40	79.7	89.9

NPV = proportion of people with a negative test who don't have the disease

= 142/(12+142)

= 93% (88-96)

		Reference standard: MCI prog	Reference standard: Stable MCI	
Index test	FCSRT <40	47	16	63
	FCSRT >40	12	142	152
		59	158	217

LR+ve = Ratio of chance of getting a positive result if patient is a converter : chance of getting a positive result if patient isn't a converter

= 47/(47+12) : 16/(142+16)

= 7.9

95% CI 4.9-12.7

		Reference standard: MCI prog	Reference standard: Stable MCI	
Index test	FCSRT <40	47	16	63
	FCSRT >40	12	142	152
		59	158	217

LR = Odds (ratio of chances of X compared to all the things there are out there)

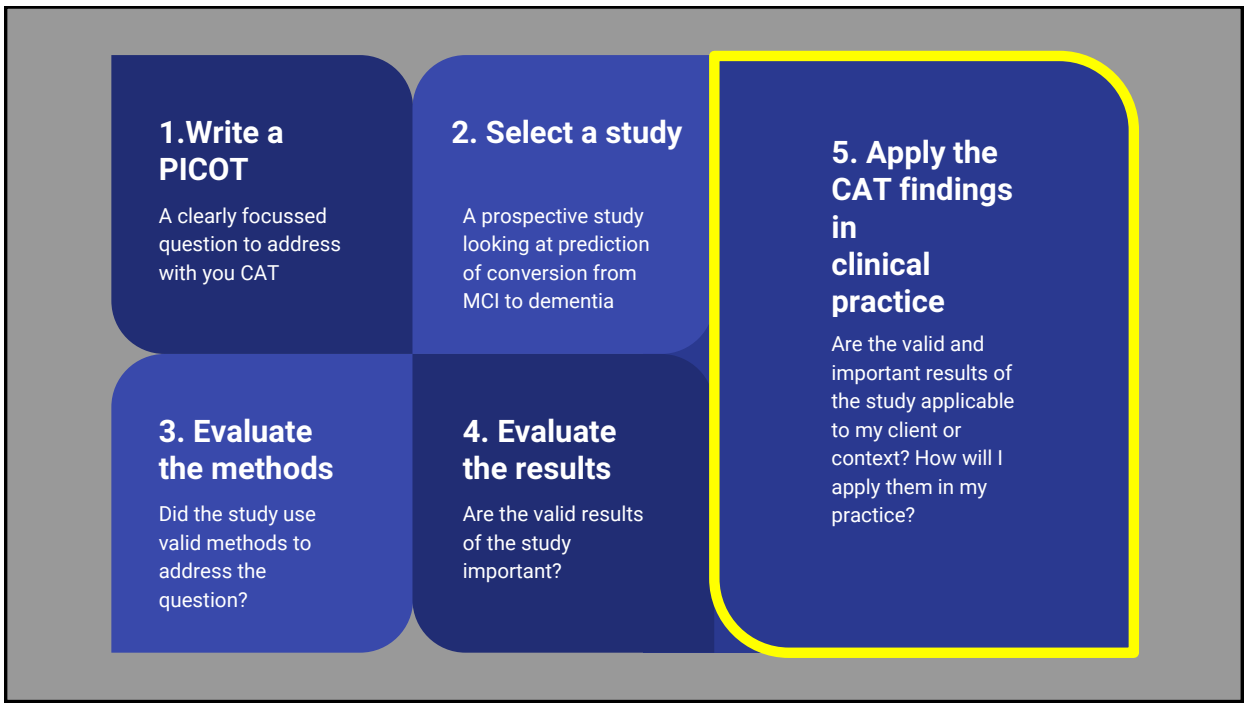
LR-ve = Ratio of chances of getting a negative result if patient is a converter : chances of getting a positive result if patient isn't a converter

= 12/(12+47) : 142/(142+16)

= 0.2

95% CI 0.1-0.4

		Reference standard: MCI prog	Reference standard: Stable MCI	
Index test	FCSRT <40	47	16	63
	FCSRT >40	12	142	152
		59	158	217



Were the methods for performing the test described in sufficient detail to permit replication?

Is the diagnostic test available, affordable, accurate, and precise in your setting?

Can you generate a clinically sensible estimate of your patient's pre-test probability?

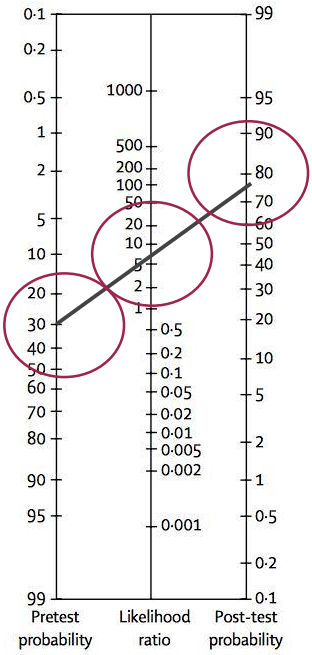
Will the resulting post-test probabilities affect your management and help your patient?

Could it move you across a test-treatment threshold?

LR +ve = Odds that will convert to dementia if you get a positive test result

= (X times more likely to convert)

= 7.9



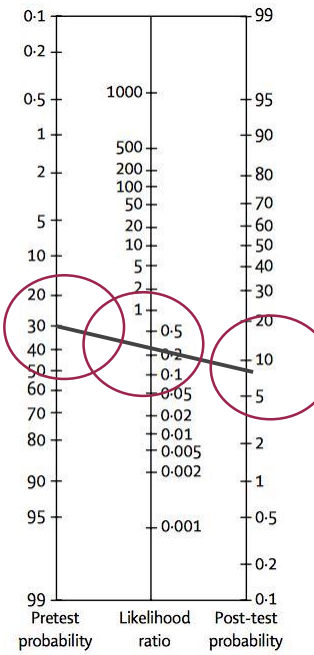
Post-test p = 77%

(PPV = 75%)

LR -ve = Odds that will convert to dementia if you get a negative test result

= (X times more likely to convert)

= 0.2 (0.14-0.48)



Post test p = 9%

(NPV = 92%)

77%

probability that Mary will develop dementia within 3 years given her FCSRT score of 38

9%

probability that Mary will develop dementia within two years given her reasonably good FCSRT score (over the cut score)

But we could do better

FCSRT helps

LR+ FCSRT = 7.9

LR+ Fluency = 3.2

Table 3 Receiver operating characteristic analysis: Demographic factors and neuropsychological tests associated with incident AD dementia

	AUC	CI (AUC)	*p* Value	Cutoff	Se	Sp
	0.72	(0.65, 0.79)				
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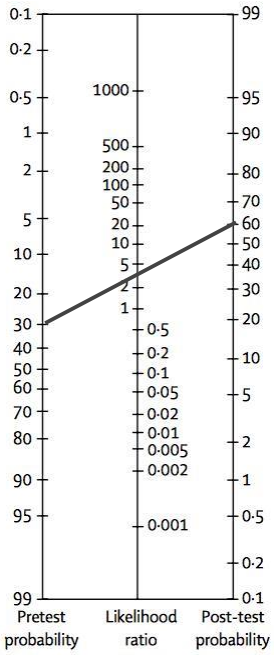
Verbal fluency (category)*	0.80	(0.74, 0.87)	0.003	13	55.9	82.3

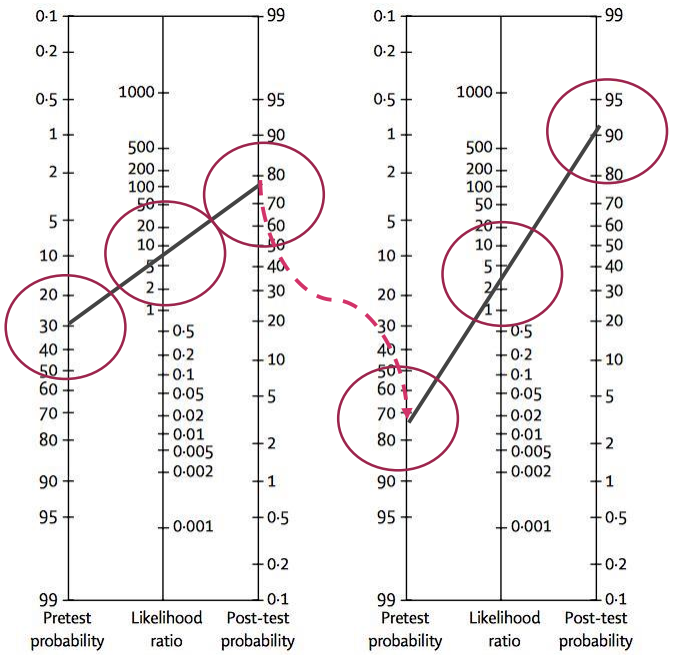
LR +ve = Odds that will convert to dementia if you get a positive test result

= 3.2



Post-test p = 58%

Chaining



92%

probability that Mary will develop dementia within 2 years given her FCSRT of 38 AND her fluency score of 10

38TH ANNUAL CONFERENCE
OCTOBER 17-20, 2018

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SHERATON NEW ORLEANS HOTEL | NEW ORLEANS, LA

CBT for treating fatigue in MS

Dr Brooke Davis
Neuropsychology Unit
Department of Clinical Neurosciences
St Vincent's Hospital Melbourne
Honorary Staff Member, The University of Melbourne

38TH ANNUAL CONFERENCE
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SHERATON NEW ORLEANS HOTEL | NEW ORLEANS, LA

Financial Disclosure

I have no financial relationships to disclose:

Employee of: St Vincent's Hospital Melbourne
Consultant for: nil
Stockholder in: nil
Research support from: nil
Honoraria from: nil

CBT for treating fatigue in MS

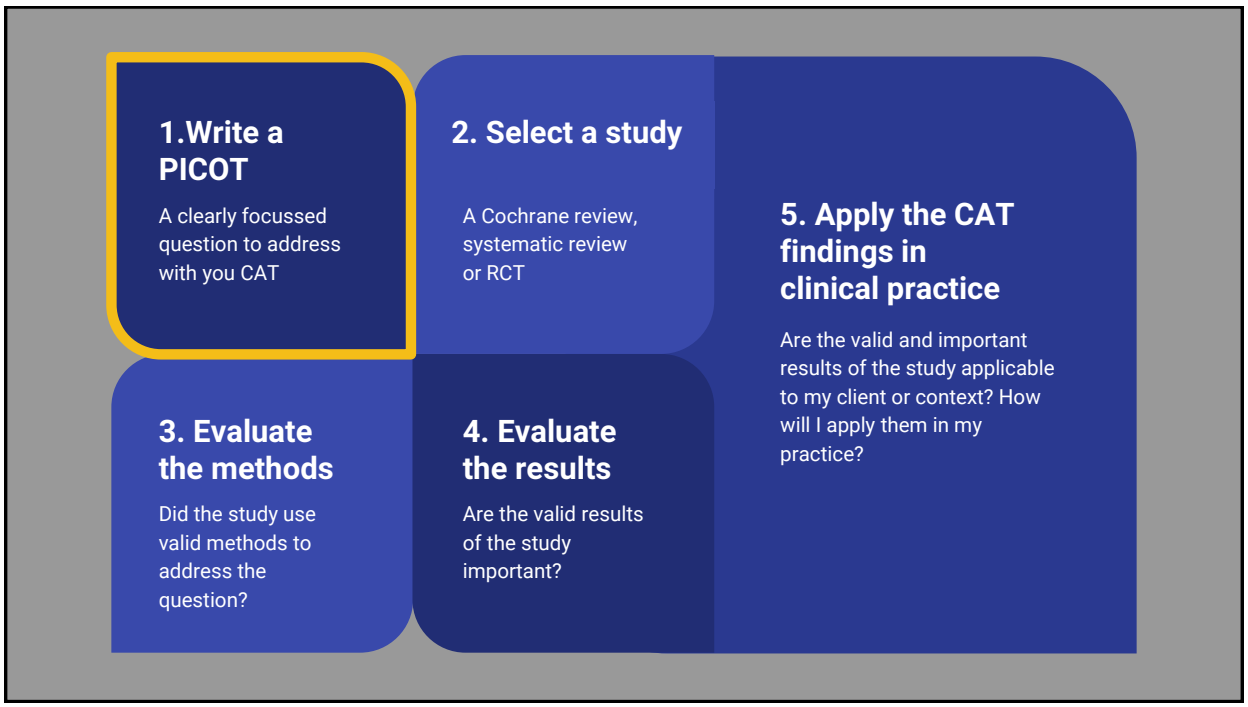
A Treatment CAT

Dr Brooke Davis
Senior Clinical Neuropsychologist, St Vincent's Hospital, Melbourne Australia
brooke.davis@svha.org.au

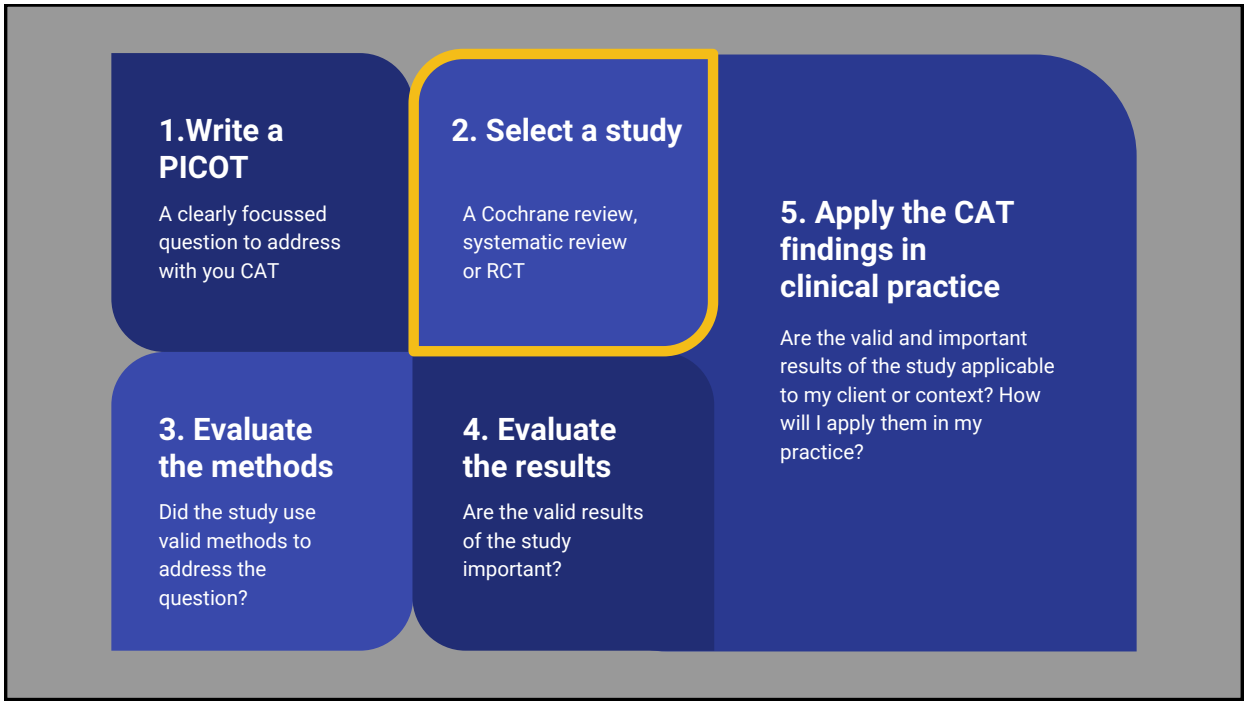
Quality is key

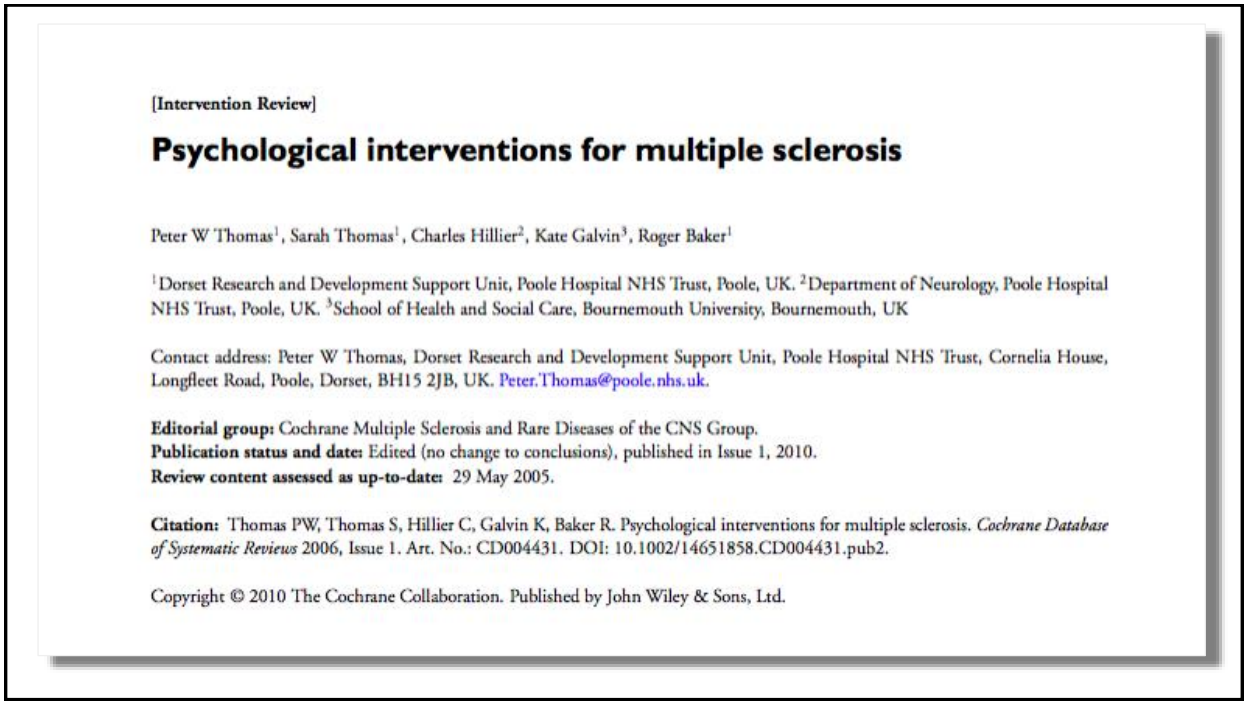
Don't believe everything you read

Amy, 22, has MS and fatigue.



In Australian young women with Multiple Sclerosis (P), how does CBT (I) compare with other psychological therapies (C) for management of fatigue (O)?





[Intervention Review]

Psychological interventions for multiple sclerosis

Peter W Thomas[1], Sarah Thomas[1], Charles Hillier[2], Kate Galvin[3], Roger Baker[1]

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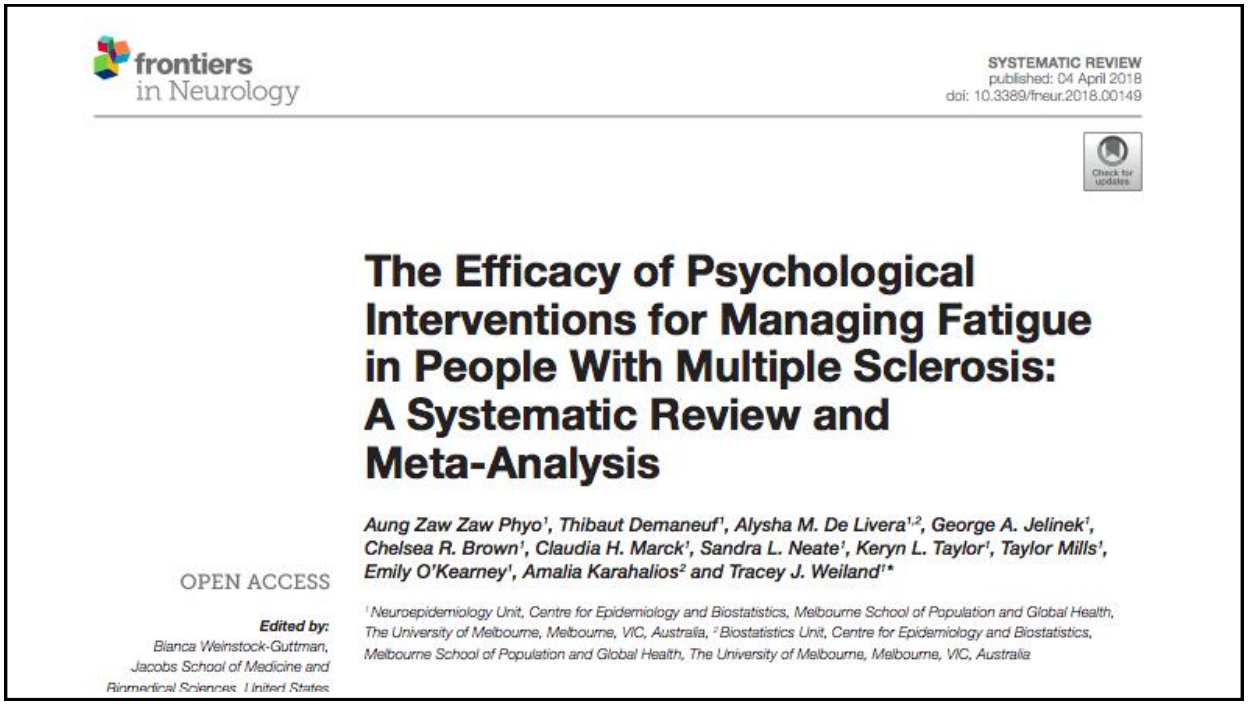
Editorial group: Cochrane Multiple Sclerosis and Rare Diseases of the CNS Group.
Publication status and date: Edited (no change to conclusions), published in Issue 1, 2010.
Review content assessed as up-to-date: 29 May 2005.

Citation: Thomas PW, Thomas S, Hillier C, Galvin K, Baker R. Psychological interventions for multiple sclerosis. *Cochrane Database of Systematic Reviews* 2006, Issue 1. Art. No.: CD004431. DOI: 10.1002/14651858.CD004431.pub2.

What can psychologists do for people with MS?

(Some sad info about study quality)

Who knows.



frontiers in Neurology

SYSTEMATIC REVIEW
published: 04 April 2018
doi: 10.3389/fneur.2018.00149

The Efficacy of Psychological Interventions for Managing Fatigue in People With Multiple Sclerosis: A Systematic Review and Meta-Analysis

*Aung Zaw Zaw Phyo[1], Thibaut Demaneuf[1], Alysha M. De Livera[1,2], George A. Jelinek[1], Chelsea R. Brown[1], Claudia H. Marck[1], Sandra L. Neate[1], Keryn L. Taylor[1], Taylor Mills[1], Emily O'Kearney[1], Amalia Karahalios[2] and Tracey J. Weiland[1]**

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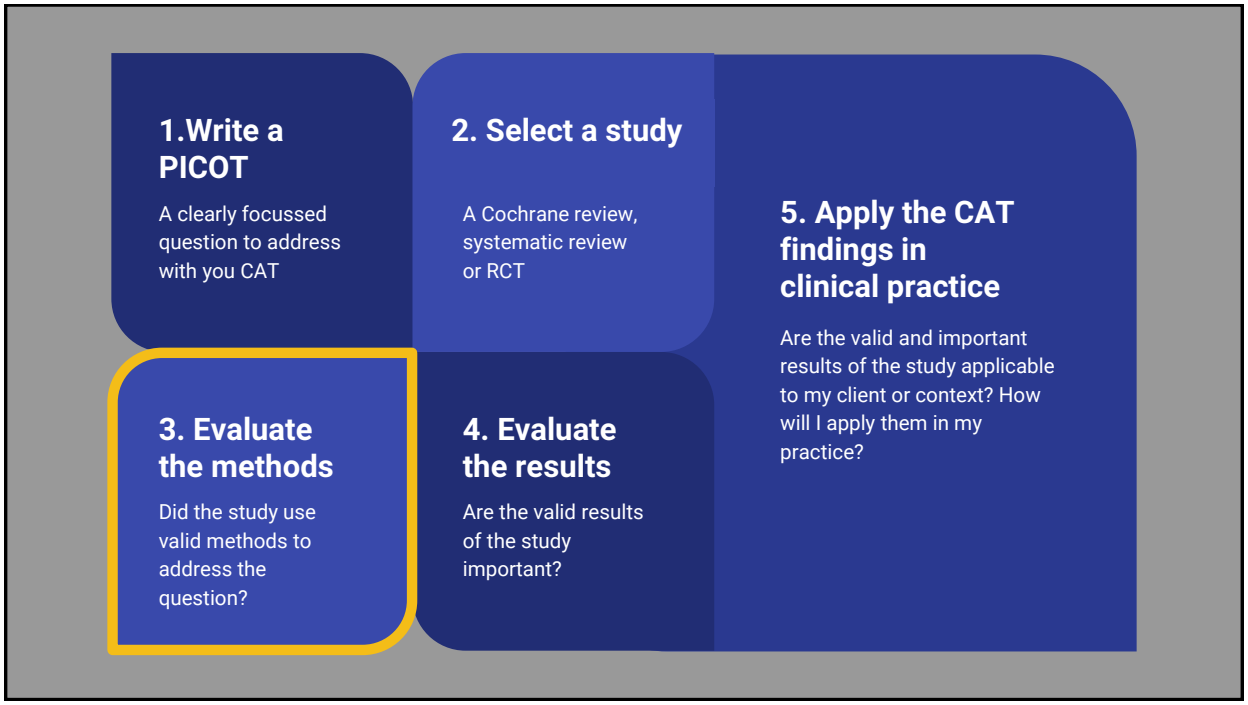
OPEN ACCESS

Edited by:
Bianca Weinstock-Guttman, Jacobs School of Medicine and Biomedical Sciences, United States



1.Write a PICOT

A clearly focussed question to address with you CAT

2. Select a study

A Cochrane review, systematic review or RCT

3. Evaluate the methods

Did the study use valid methods to address the question?

4. Evaluate the results

Are the valid results of the study important?

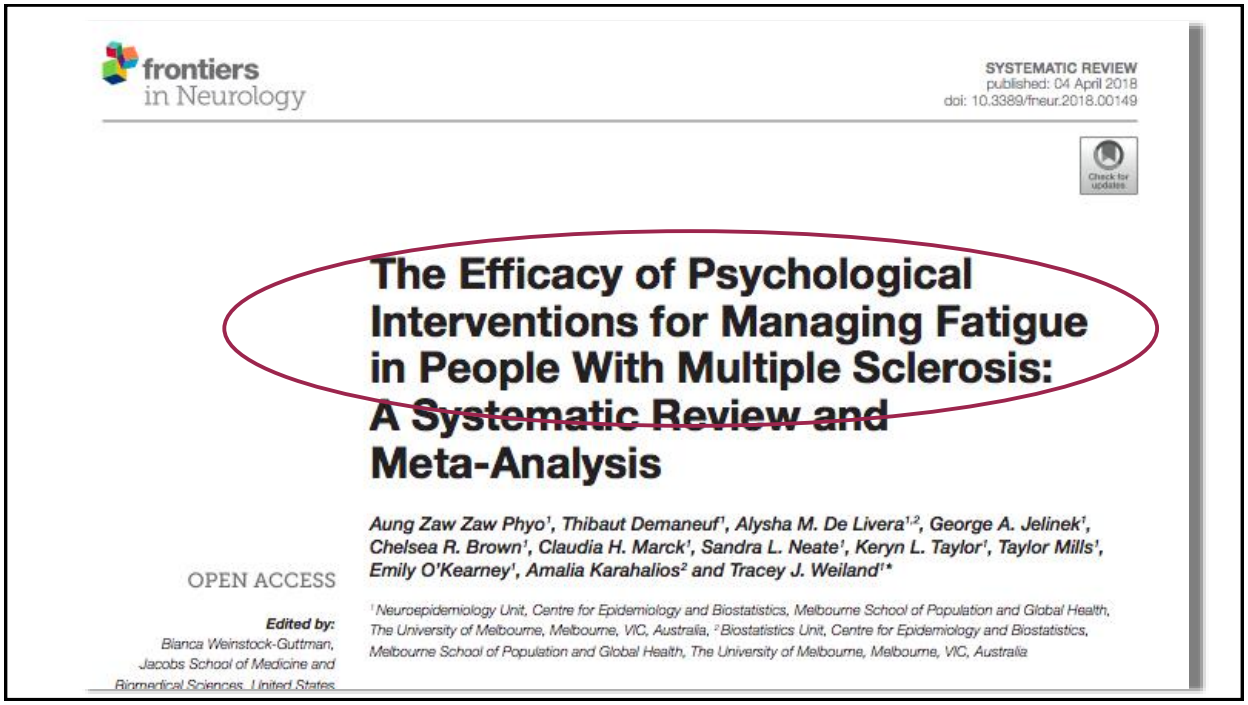
5. Apply the CAT findings in clinical practice

Are the valid and important results of the study applicable to my client or context? How will I apply them in my practice?

cebm.net/2014/06/critical-appraisal

Is the clinical question clearly stated?

Yes.



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doi: 10.3389/fneur.2018.00149

The Efficacy of Psychological Interventions for Managing Fatigue in People With Multiple Sclerosis: A Systematic Review and Meta-Analysis

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OPEN ACCESS

Edited by:
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Is it unlikely that important, relevant studies were missed?

Papers not written in English were excluded

METHODS

To determine the efficaciousness of psychological intervention in managing fatigue in PwMS, we defined terms of interest as follow: (a) the population of interest was PwMS who were aged 18 years or older; (b) interventions were psychological interventions; (c) comparators were non-active/active controls; (d) the outcome was fatigue; and (e) study designs included all types of studies except reviews, case reports, case series, and qualitative studies.

Search Methods

Phyo et al.

PROSPERO, registration number-CRD42017060497. The following electronic bibliographic databases were searched for articles published from database inception to April 5, 2017: Medline (Ovid), EMBASE, PsycINFO, and CINAHL. We consulted with a professional librarian for assistance with search strings. Search terms included those related to MS, fatigue, and psychological interventions (**Table A1** in Appendix). As preliminary searches indicated few papers published in this area, we made no restrictions on language, year of publication, or publication type in our search. In addition, we also used Web of Science to search publications which cited our included studies and we undertook a hand-search of the reference lists of a relevant systematic review (36).

Inclusion Criteria

Articles were included if they: (a) included participants with MS who were aged 18 years or older; (b) included participants who had self-reported neurologist-diagnosed MS, or doctor-diagnosed MS, or recruitment of PwMS from MS society, clinic, and hospital; (c) assessed interventions involving psychological therapy, CBT (including self-management), stress reduction techniques, meditation, mindfulness, relaxation, guided imagery, progressive muscle relaxation, or educational counseling; (d) had a comparison group (baseline (within group) or standard-care or non-active/active-control group) or single psychological intervention group; (e) included an outcome measure for fatigue assessed using a validated tool; (f) were written in English; and (g) were full text article. In addition, we deviated from our original protocol and made *a posteriori* decision to include pilot studies in this review given that small studies can contribute meaningful information to meta-analyses.

We excluded papers not written in English, and studies with multi-component interventions that did not isolate the psychological therapy in design or analysis, literature reviews (including systematic reviews and meta-analyses), case reports, case series, or reported qualitative findings only. We contacted primary authors and co-authors when the methods described did not enable us to determine whether the inclusion criteria were met.

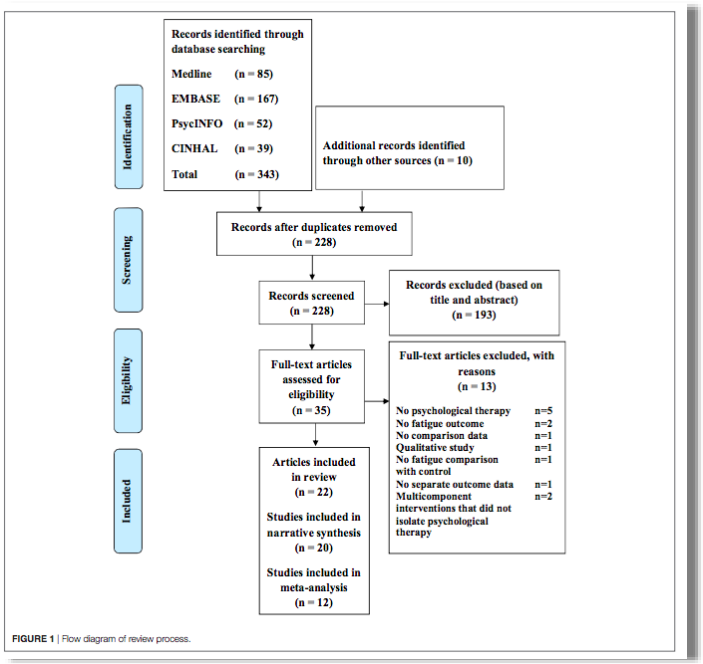

FIGURE 1 | Flow diagram of review process.

Were the criteria used to select articles for inclusion appropriate?

Yes.

Were the included studies sufficiently valid for the type of question asked?

[Intervention Review]

Exercise for depression

Gary M Cooney[1], Kerry Dwan[2], Carolyn A Greig[3], Debbie A Lawlor[4], Jane Rimer[5], Fiona R Waugh[6], Marion McMurdo[7], Gillian E Mead[8]

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Contact address: Gillian E Mead, Centre for Clinical Brain Sciences, University of Edinburgh, Room S1642, Royal Infirmary, Little France Crescent, Edinburgh, EH16 4SA, UK. gillian.e.mead@ed.ac.uk, gmead@staffmail.ed.ac.uk.

Editorial group: Cochrane Common Mental Disorders Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 9, 2013.

Citation: Cooney GM, Dwan K, Greig CA, Lawlor DA, Rimer J, Waugh FR, McMurdo M, Mead GE. Exercise for depression. *Cochrane Database of Systematic Reviews* 2013, Issue 9. Art. No.: CD004366. DOI: 10.1002/14651858.CD004366.pub6.

Exercise for depression

$g = -0.62$ (-0.81, -0.42)

Too good to be true?

-0.62 (-0.81,-0.42)

-0.18 (-0.47,0.11)

Were the included studies sufficiently valid for the type of question asked?

Yes (ish).

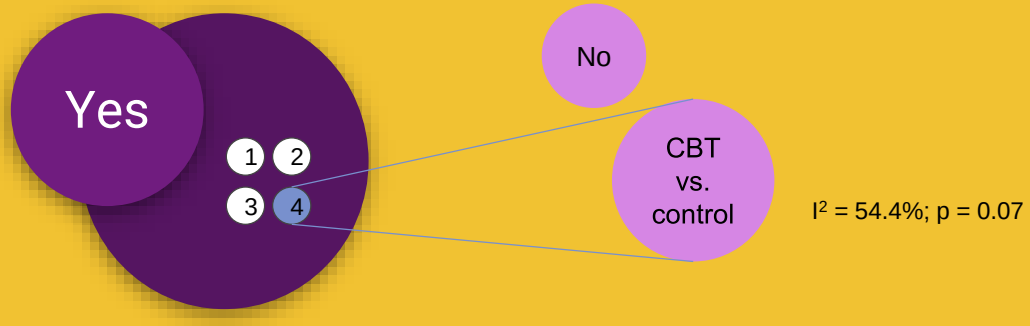
Quality Appraisal

Two authors (Aung Zaw Zaw Phyo and Thibaut Demaneuf) evaluated the quality of included studies using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for

TABLE 1 | Quality of evidence rating for included studies based on the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies.

Reference	Selection bias	Study design	Confounders	Blinding	Data collection method	Withdrawals and dropouts	Global rating
Alsaleh and Shahrbanoo (39)	Moderate	Strong	Weak	Moderate	Strong	Weak	Weak
Anderson et al. (51)	Moderate	Weak	Weak	Moderate	Strong	Strong	Weak
Bogosian et al. (40)	Strong	Strong	Strong	Moderate	Strong	Moderate	Strong
Carletto et al. (52)	Strong	Strong	Strong	Moderate	Strong	Strong	Strong
Dayapoglu and Tan (33)	Moderate	Moderate	Weak	Moderate	Strong	Weak	Weak
Ehde et al. (41)	Strong	Strong	Strong	Moderate	Strong	Strong	Strong
Fischer et al. (42)	Strong	Strong	Strong	Moderate	Strong	Moderate	Strong
Grossman et al. (53)	Strong	Strong	Strong	Moderate	Strong	Strong	Strong
Jongen et al. (56, 57)	Moderate	Weak	Weak	Moderate	Strong	Strong	Weak
Kiropoulos et al. (43)	Strong	Strong	Strong	Moderate	Strong	Strong	Strong
Kos et al. (44)	Moderate	Strong	Strong	Moderate	Strong	Strong	Strong
Mackay et al. (34)	Weak	Strong	Strong	Weak	Strong	Weak	Weak
Mohr et al. (45)	Strong	Strong	Strong	Moderate	Strong	Strong	Strong
Moss-Morris et al. (46)	Moderate	Strong	Strong	Moderate	Strong	Strong	Strong
Nazari et al. (35)	Moderate	Strong	Strong	Moderate	Strong	Weak	Moderate
Spitzer and Pakenham (54)	Moderate	Weak	Weak	Moderate	Strong	Strong	Weak
Thomas et al. (47, 48)	Weak	Strong	Strong	Moderate	Strong	Strong	Moderate
van Kessel et al. (49)	Strong	Strong	Strong	Moderate	Strong	Strong	Strong
van Kessel et al. (55)	Moderate	Strong	Strong	Weak	Strong	Moderate	Moderate
Vazirinejad et al. (50)	Moderate	Strong	Strong	Moderate	Strong	Weak	Moderate

Were the results similar from study to study?



1.Write a PICOT

A clearly focussed question to address with you CAT

2. Select a study

A Cochrane review, systematic review or RCT

3. Evaluate the methods

Did the study use valid methods to address the question?

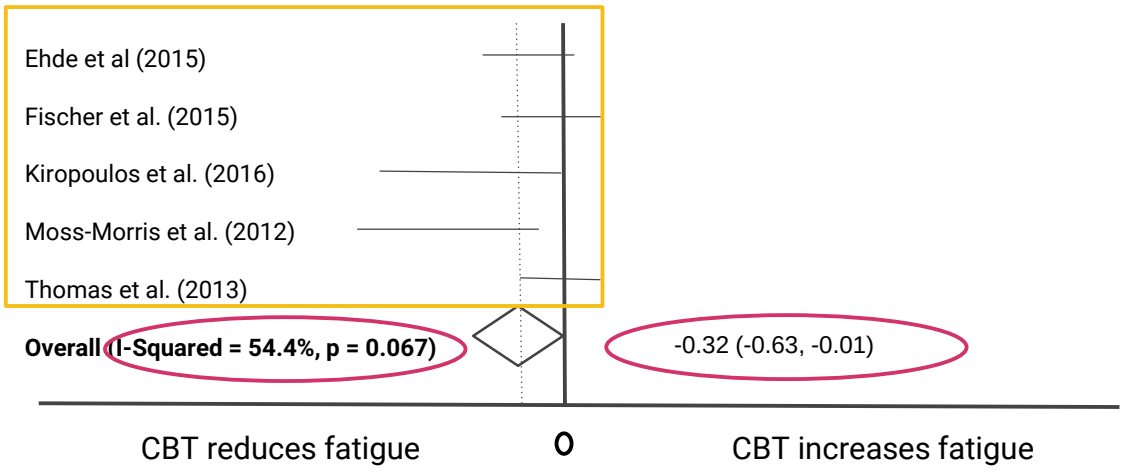
4. Evaluate the results

Are the valid results of the study important?

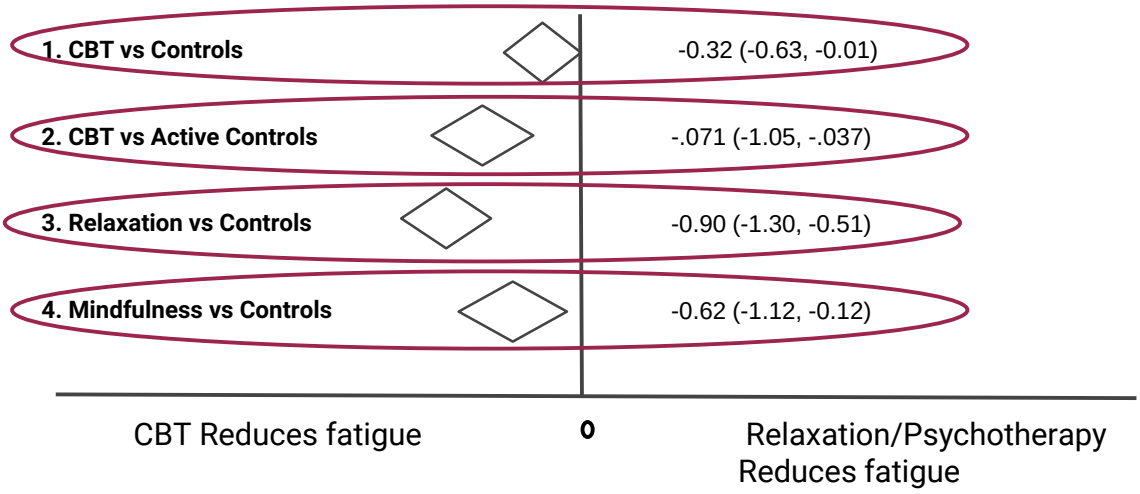
5. Apply the CAT findings in clinical practice

Are the valid and important results of the study applicable to my client or context? How will I apply them in my practice?

1. Comparison of CBT and controls on MS related fatigue



Effect sizes of interventions for MS related fatigue



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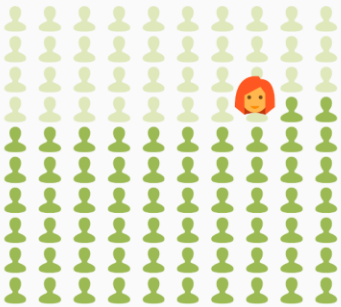
Back to Amy.



Miss CBT noticed more improvement in her fatigue than

62%

of people in the control group

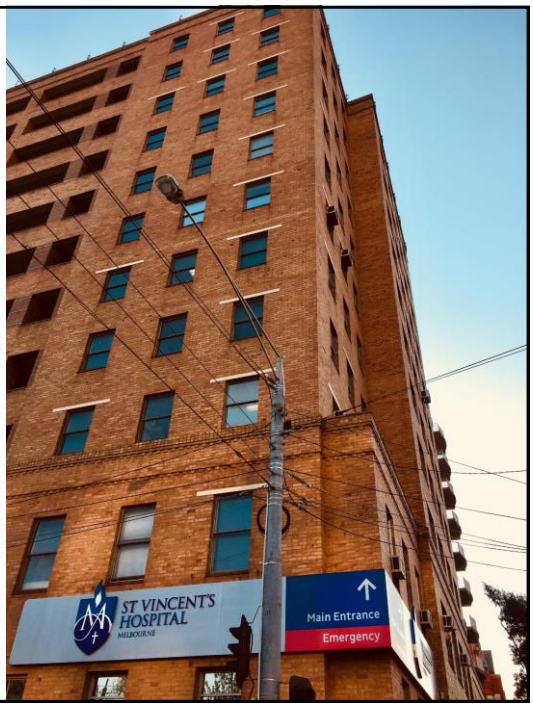
(See Coe, R. (2002) for conversion)

Quality is key

Don’t believe everything you read

Thanks!

Stephen Bowden
Catherine Meade
Brooke Davis
Leonie Simpson



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