How to make evidence based neuropsychology a daily occurrence.

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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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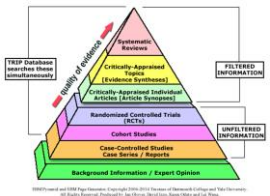

The levels-of-evidence framework and the underlying principles of evidence-based practice may be the most widely-debated, and peer-reviewed, set of quality guidelines in the history of health-care.

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

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Frontal Screening for dementia using INECO Frontal Screening (IFS)

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Financial Disclosure

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Employee of: St Vincent's Hospital Melbourne
Consultant for: nil
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Honoraria from: nil

Frontal screening for bvFTD with INECO: a diagnostic CAT

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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.

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

TERESA TORRALVA,[1,2] MARÍA ROCA,[1,2] EZEQUIEL GLEICHGERRCHT,[1] PABLO LÓPEZ,[1,3] AND FACUNDO MANES[1,2]

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(RECEIVED January 1, 2009; FINAL REVISION June 30, 2009; ACCEPTED June 30, 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=20) 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, Dysexecutivism, Frontotemporal dementia, Alzheimer disease, Differential diagnosis

Dementia v controls
96.2% sensitivity, 91.5% specificity

bvFTD v AD
72.0% sensitivity, 81.3% specificity

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

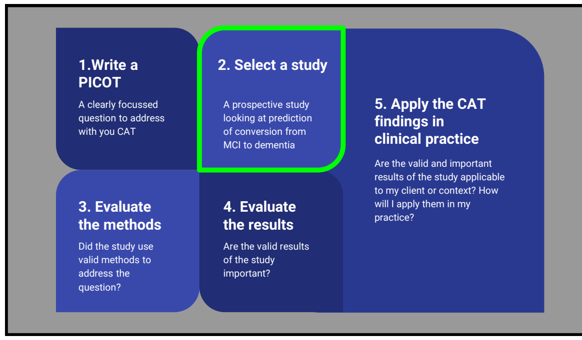
3. Evaluate the methods
Did the study use valid methods to address the question?

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?

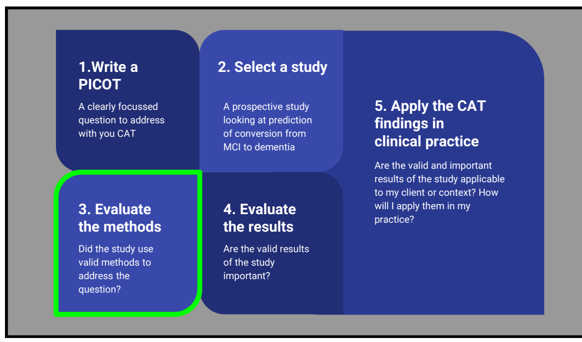
Diagnostic CAT

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

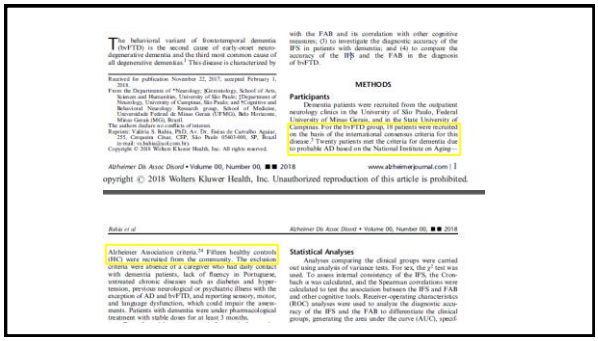


cebm.net/2014/06/critical-appraisal

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

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.[7] Twenty patients met the criteria for dementia due to probable AD based on the National Institute on Aging

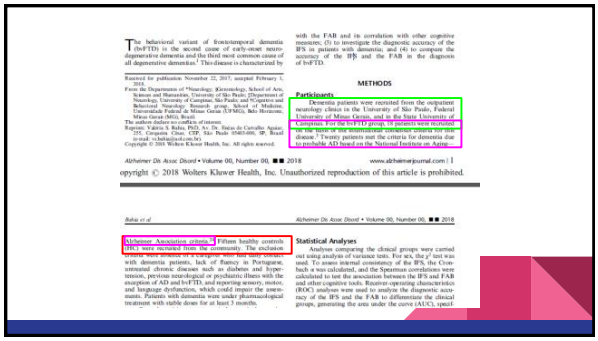
Alzheimer Association criteria.[8] Fifteen healthy controls (HC) were recruited from the community. The exclusion criteria were absence of a caregiver who had daily contact with dementia patients, lack of fluency in Portuguese, untreated chronic diseases such as diabetes and hypertension, previous neurological 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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Bahia et al Alzheimer Dis Assoc Disord • Volume 00, Number 00, ■■ 2018

Alzheimer Association criteria.[8] Fifteen healthy controls (HC) were recruited from the community. The exclusion

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.

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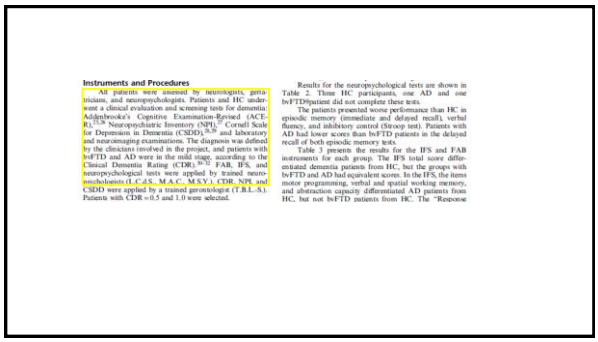
Was the reference standard (dx criteria) applied regardless of the index (INECO) test result?

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),[15,16] Neuropsychiatric Inventory (NPI),[17] Cornell Scale for Depression in Dementia (CSDD),[18–20] 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).[20–22] FAB, IFS, and neuropsychological tests were applied by trained neuropsychologists (L.C.d.S., M.A.C., M.S.V.). 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 bvFTD patient 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.

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?

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

Alzheimer Dis Assoc Disord • Volume 00, Number 00, ■■ 2018 — *Accuracy of the INECO Frontal Screening*

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		
		+ve	-ve	Totals
Diagnostic Test Result IFS	+ve	a12	b8	20
	-ve	c6	d12	18
		18	20	38

What are the results?

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

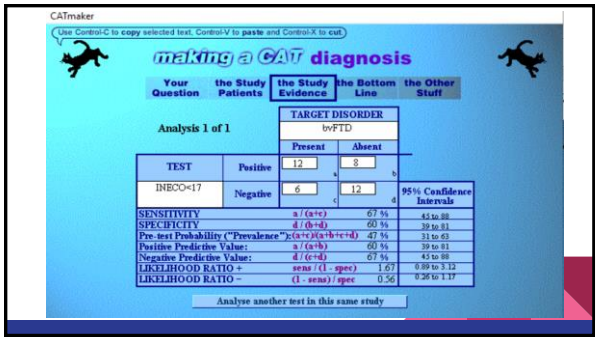
NPV = proportion of people with a negative test who don't have the disease

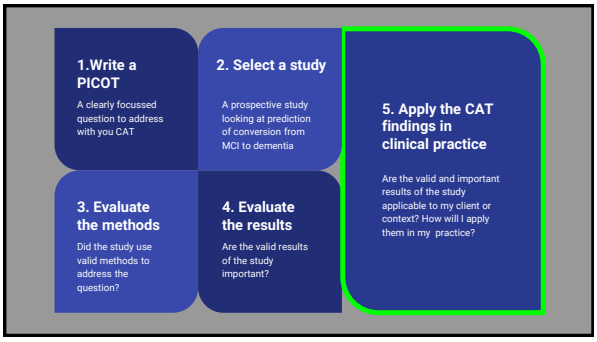
= 12/(6+12)

= 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)

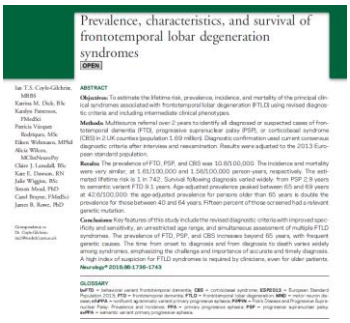




Is the diagnostic test available, affordable, accurate, and precise in your setting?

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
Kandiya Patterson, FMedSci
Patricia Vázquez Rodríguez, MSc
Eileen Wehmann, MPhil
Alicia Wilcox, MClinNeuroPsy
Claire J. Lansdall, BSc
Kate E. Dawson, RN
Jake Wiggins, BSc
Simon Mead, PhD
Carol Brayne, FMedSci
James B. Rowe, PhD

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 neuroimaging. Results were adjusted to the 2013 European standard population.

Results: The prevalence of FTD, PSP, and CBS was 10.8/10,000. 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® 2015;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; **PPPA** = 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]

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 intracellular inclusions of tau, TDP-43 or fused in sarcoma protein. 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 diagnostic certainty over time. Carer education and support remain of paramount importance.

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

⇩

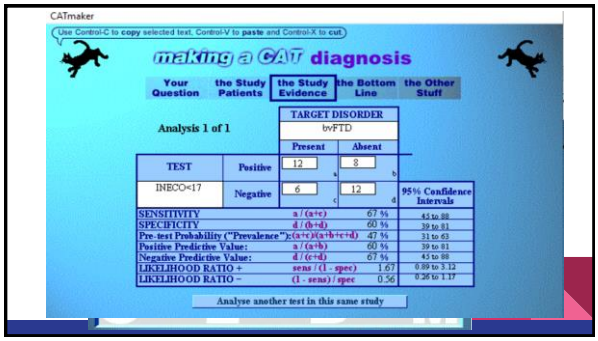
If 80% of all dementias are AD
then total dementia cases = 47%

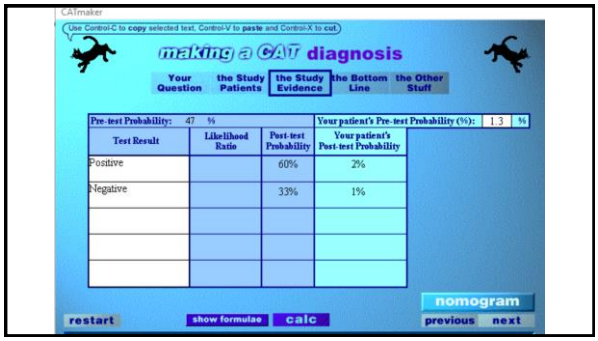
⇩

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?

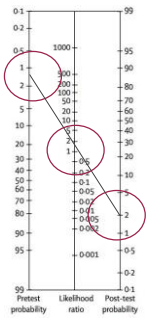
Yes.





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)

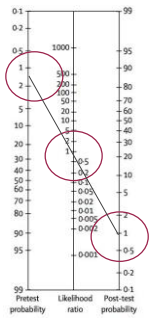


Post-test probability = 2%

(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!

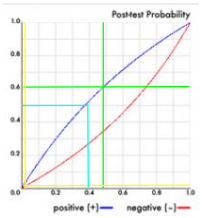
Given a positive test result on INECO (score<17) , the likelihood that Sue has bvFTD

2%

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

1%

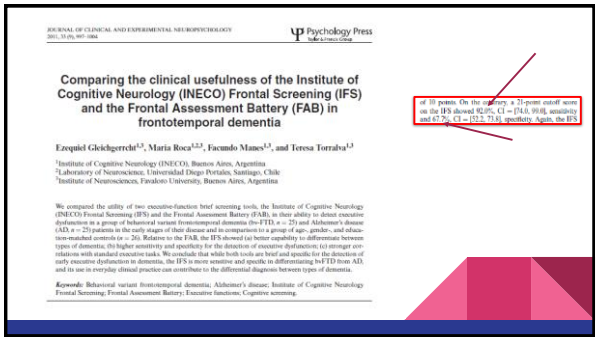
A graphical representation...

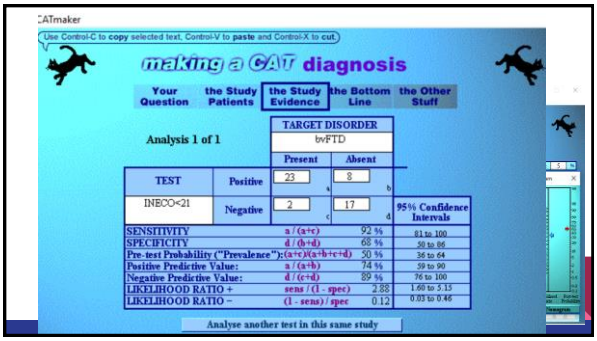


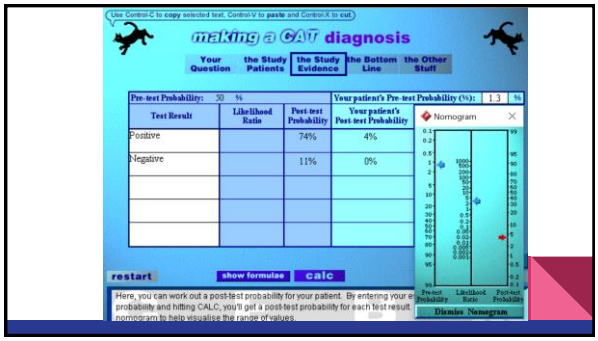
Study prevalence = 18/38 = .47

Setting (Memory clinic) prevalence = 0.013

?base-rate to reach 0.5 decision threshold







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

Original Article

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

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

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.

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Predicting who will develop dementia

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Financial Disclosure

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Consultant for: nil
Stockholder in: nil
Research support from: nil
Honoraria from: nil

Predicting who will develop dementia

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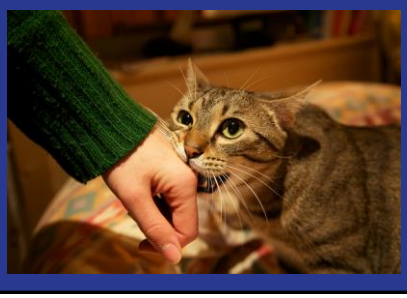
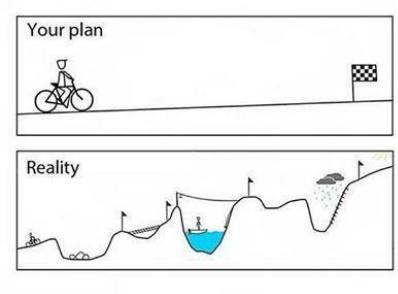


Michael the commercial pilot

Should he go back to work?

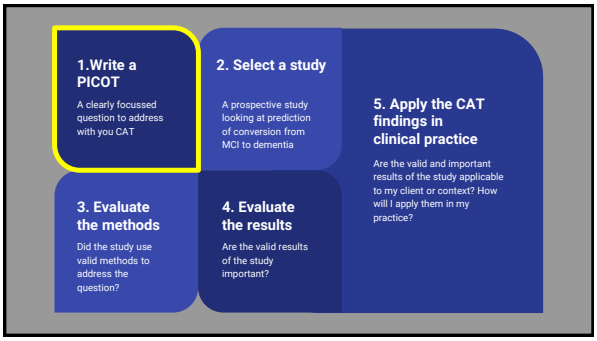
Diagnostic CAT

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)



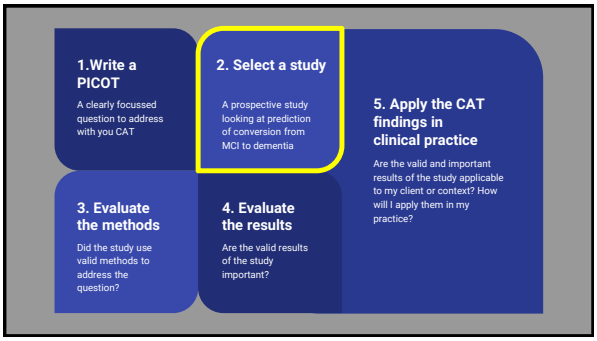
Mary, 69, is forgetting things

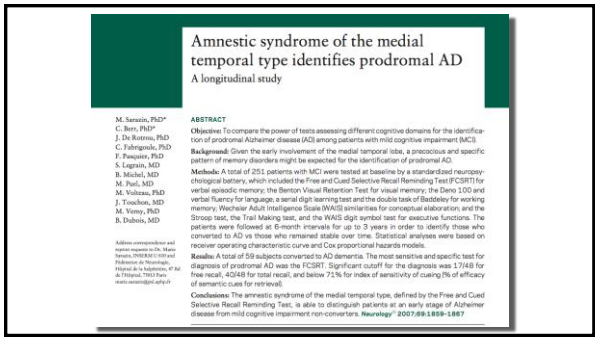
(but not much)



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

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ABSTRACT

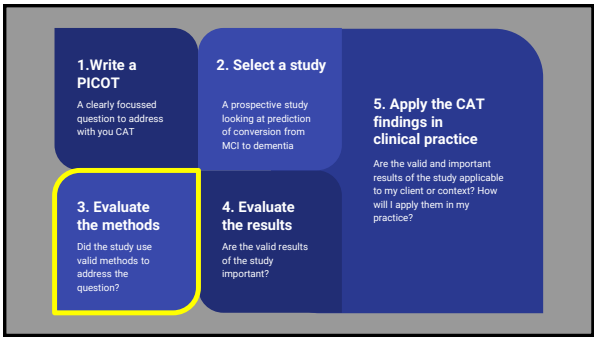
Objective: To compare the power of tests assessing different cognitive domains for the identification of prodromal Alzheimer disease (AD) among patients with mild cognitive impairment (MCI).

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 Déno 1.00 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 1.7/48 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**

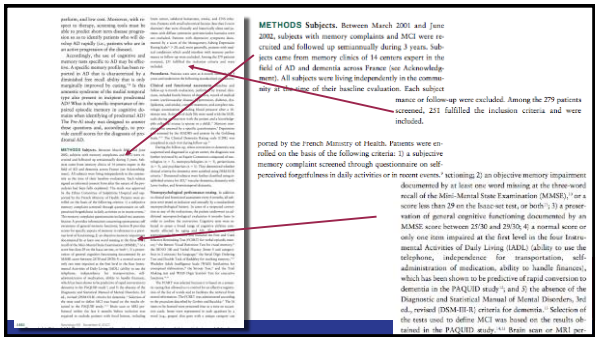


https://www.cebm.net/category/ebm-resources/tools/

Or

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

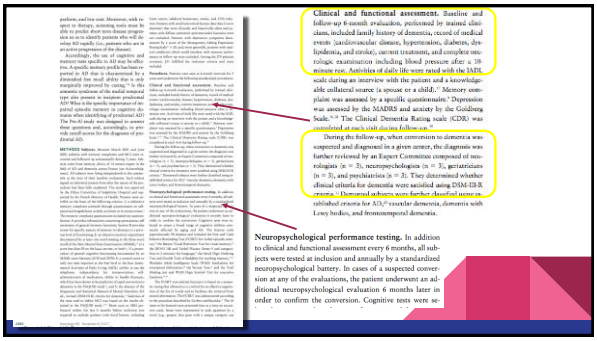
Was the diagnostic test evaluated in a representative spectrum of patients (like those in whom it would be used in practice)?



maybe

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

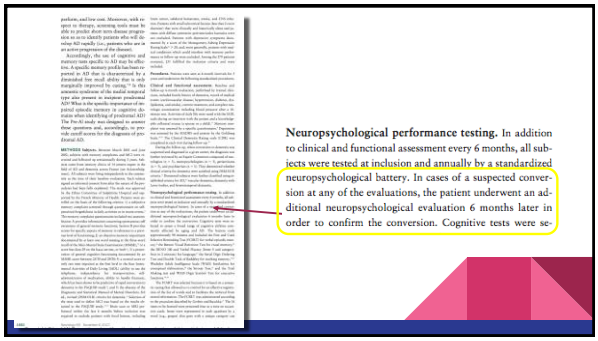
Was the reference standard applied regardless of the index test result?



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?



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?

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

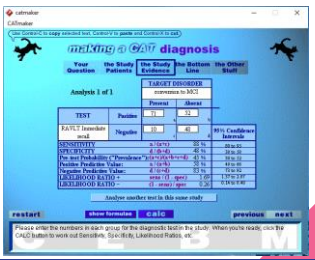
Are the valid and important results of the study applicable to my client or context? How will I apply them in my practice?

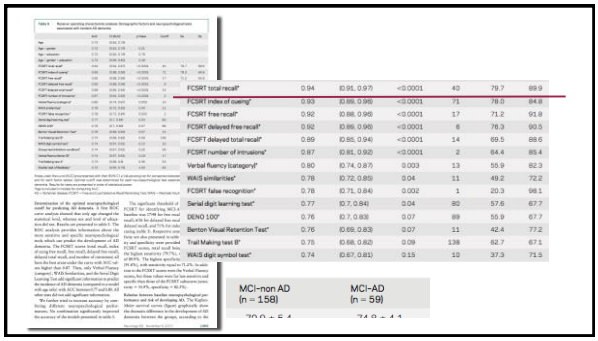
Are the test characteristics presented?

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?

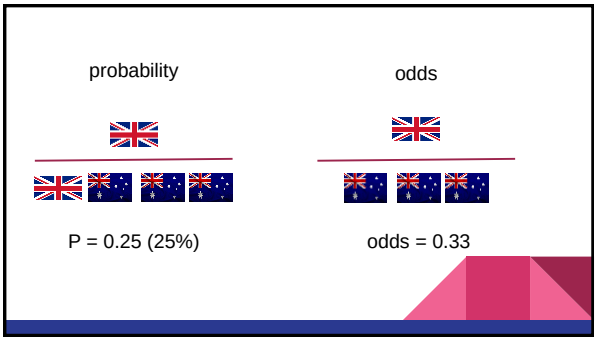




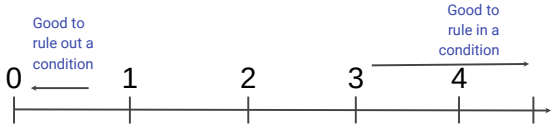
FCSRT total recall*	0.94	(0.91, 0.97)	<0.0001	40	79.7	89.9
FCSRT index of cueing*	0.93	(0.88, 0.98)	<0.0001	71	78.0	84.8
FCSRT free recall*	0.92	(0.88, 0.96)	<0.0001	17	71.2	91.8
FCSRT delayed free recall*	0.92	(0.89, 0.96)	<0.0001	6	76.3	90.5
FCSFT delayed total recall*	0.89	(0.85, 0.94)	<0.0001	14	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	87.7
DEMO 100*	0.76	(0.7, 0.83)	0.07	89	55.9	87.7
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	82.7	67.1
WAIS digit symbol test*	0.74	(0.67, 0.81)	0.15	10	37.3	71.5

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

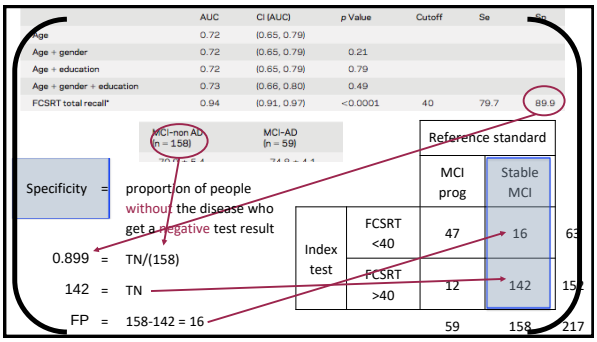
LR = odds of having the condition (compared to not having it



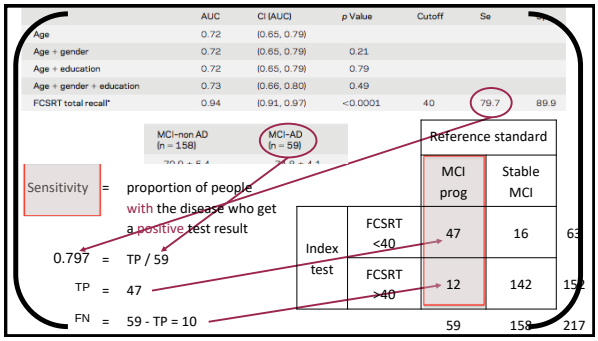
What's useful in LRs

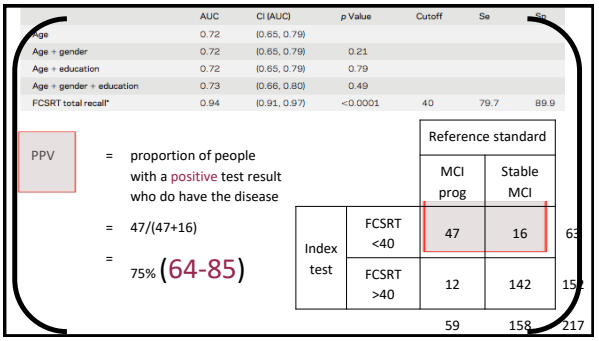


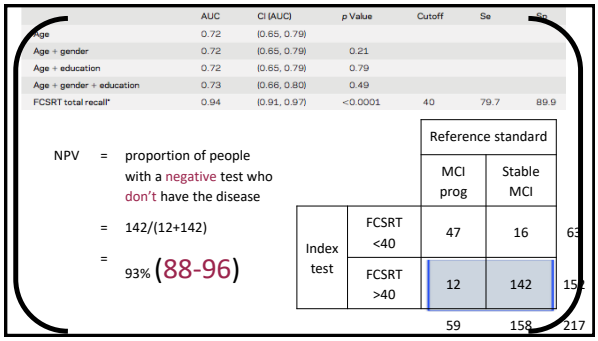
throw your test in the bin

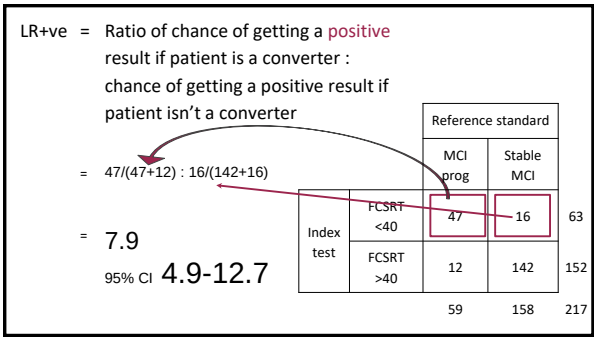


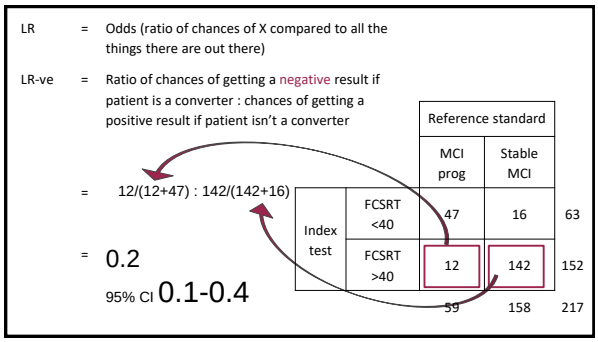
	AUC	CI (AUC)	*p* Value	Cutoff	Se	Sp
Age	0.72	(0.65, 0.79)				
Age + gender	0.72	(0.65, 0.79)	0.21			
Age + education	0.72	(0.65, 0.79)	0.79			
Age + gender + education	0.73	(0.66, 0.80)	0.49			
FCSRT total recall*	0.94	(0.91, 0.97)	<0.0001	40	79.7	89.9

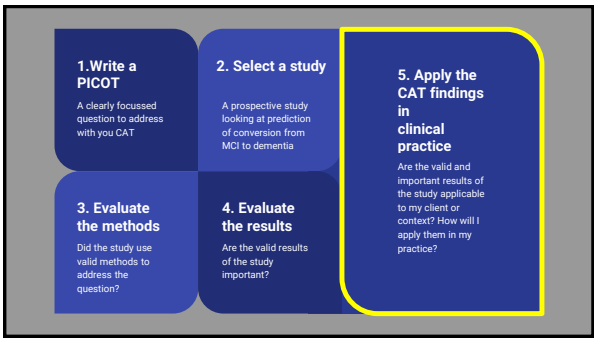

AUC CI (AUC) p Value Cutoff Se
Age 0.72 (0.65, 0.79)
Age + gender 0.72 (0.65, 0.79) 0.21
Age + education 0.72 (0.65, 0.79) 0.79
Age + gender + education 0.73 (0.66, 0.80) 0.49
FCSRT total recall* 0.94 (0.91, 0.97) <0.0001 40 79.7 89.9
MCI–non AD (n = 158)
MCI–AD (n = 59)
Sensitivity = proportion of people with the disease who get a positive test result
0.797 = TP / 59
TP = 47
FN = 59 - TP = 10
Reference standard
MCI prog
Stable MCI
Index test
FCSRT <40
47
16
63
FCSRT >40
12
142
152
59
158
217


AUC CI (AUC) p Value Cutoff Se
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
PPV = proportion of people with a positive test result who do have the disease
= 47/(47+16)
= 75% (64-85)
Reference standard
MCI prog
Stable MCI
Index test
FCSRT <40
47
16
63
FCSRT >40
12
142
152
59
158
217


AUC CI (AUC) p Value Cutoff Se
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
NPV = proportion of people with a negative test who don't have the disease
= 142/(12+142)
= 93% (88-96)
Reference standard
MCI prog
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
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
Stable MCI
Index test
FCSRT <40
47
16
63
FCSRT >40
12
142
152
59
158
217


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?

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?

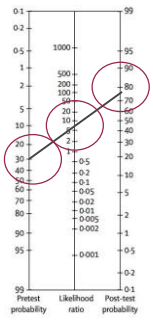
Will the resulting post-test probabilities affect your management and help your patient?

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



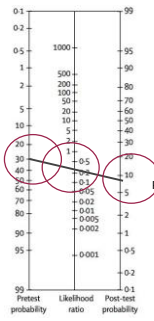
Post-test p = 77%

(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)

FCSRT helps

But we could do better

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

LR+ FCSRT = 7.9

LR+ Fluency = 3.2

	AUC	CI (AUC)	p Value	Cutoff	Se	Sp
	0.72	(0.65, 0.79)				
	0.72	(0.65, 0.79)	0.21			
	0.72	(0.65, 0.79)	0.79			
Age + gender + education	0.73	(0.66, 0.80)	0.49			
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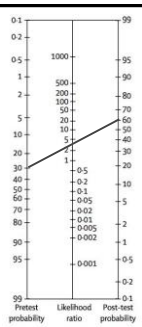
FCSRT number of intrusions*	0.87	(0.81, 0.92)	<0.0001	2	64.4	85.4
Verbal fluency (category)*	0.80	(0.74, 0.87)	0.003	13	55.9	82.3

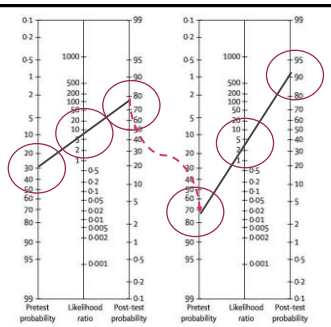
LR +ve = Odds that will convert to dementia if you get a positive test result

= 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

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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

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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

CBT for treating fatigue in MS

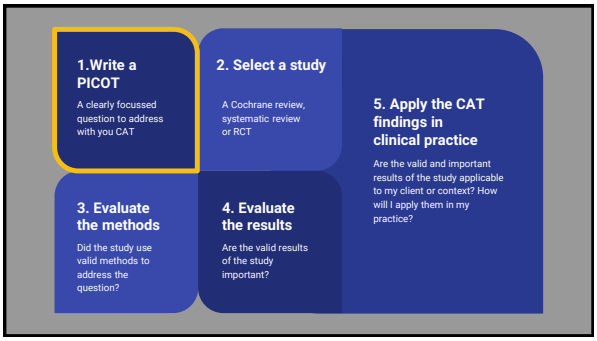
A Treatment CAT

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

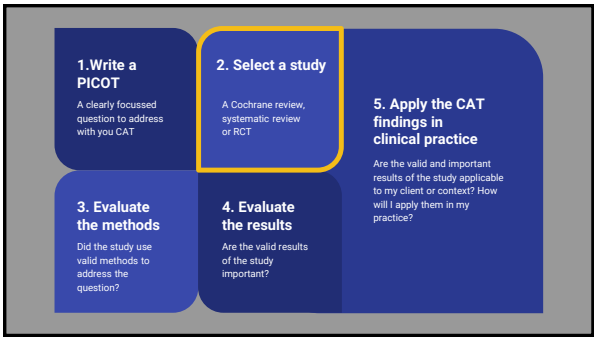
Quality is key

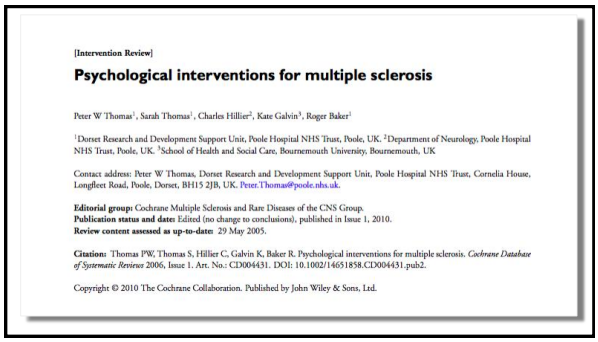
Don't believe everything you read

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]

[1]Dorset Research and Development Support Unit, Poole Hospital NHS Trust, Poole, UK. [2]Department of Neurology, Poole Hospital NHS Trust, Poole, UK. [3]School of Health and Social Care, Bournemouth University, Bournemouth, UK

Contact address: Peter W Thomas, Dorset Research and Development Support Unit, Poole Hospital NHS Trust, Cornelia House, Longfleet Road, Poole, Dorset, BH15 2JB, UK. Peter.Thomas@poole.nhs.uk.

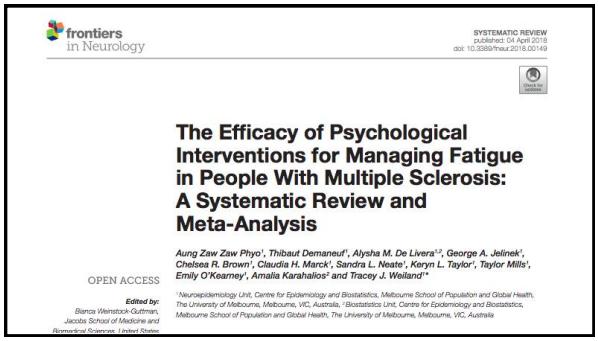
Editorial group: Cochrane Multiple Sclerosis and Rare Diseases of the CNS Group.
Publication status and date: Edited (no change to conclusions), published in Issue 1, 2010.
Review content assessed as up-to-date: 29 May 2005.

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]**

[1] Neuroepidemiology Unit, Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, Melbourne, VIC, Australia, [2] Biostatistics Unit, Centre for Epidemiology and Biostatistics, Melbourne School of Population and Global Health, The University of Melbourne, Melbourne, VIC, Australia

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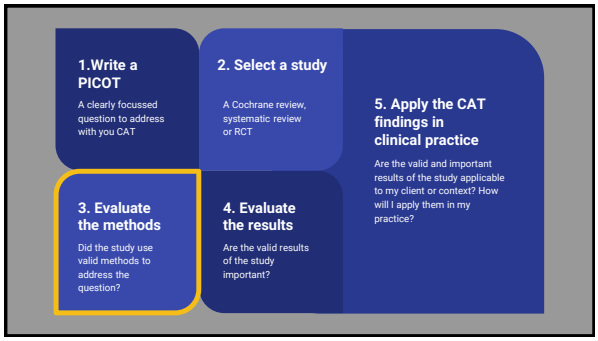
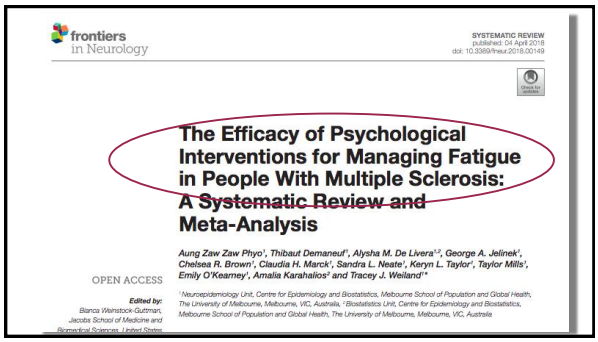
Jacobs School of Medicine and
Biomedical Sciences, United States



cebm.net/2014/06/critical-appraisal

Is the clinical question clearly stated?

Yes.



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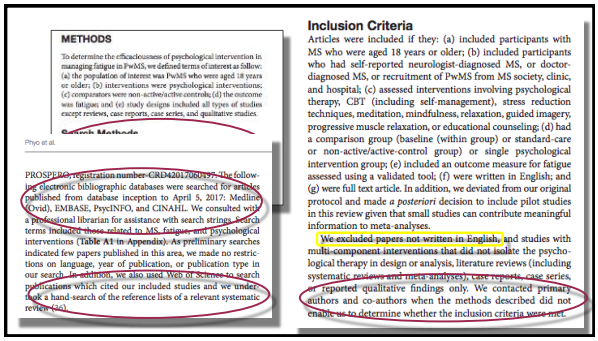
Is it unlikely that important, relevant studies were missed?

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

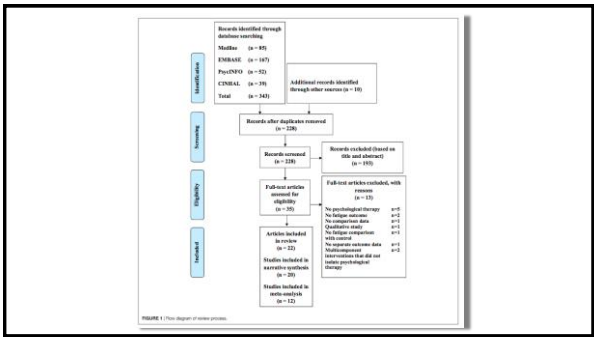
Phyo et al.

PROSPERO registration number CRD42017060959. 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 (46).

Inclusion Criteria

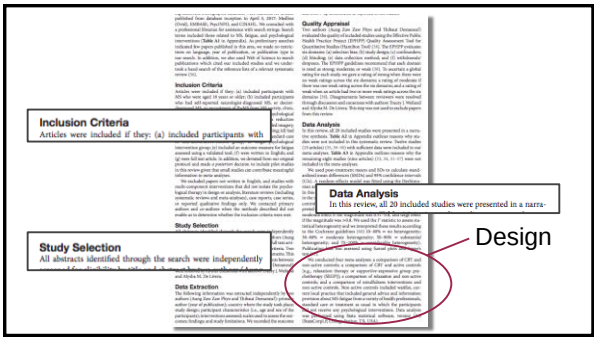
Articles were included if they: (a) included participants with MS who were aged 18 years or older; (b) included participants who had self-reported neurologist-diagnosed MS, or doctor-diagnosed MS, or recruitment of PwMS from MS society, clinic, and hospital; (c) assessed interventions involving psychological 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.



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]

[1]Division of Psychiatry, Royal Edinburgh Hospital, NHS Lothian, Edinburgh, UK. [2]Institute of Child Health, University of Liverpool, Liverpool, UK. [3]University of Birmingham, Birmingham, UK. [4]MRC Centre for Causal Analyses in Translational Epidemiology, School of Social and Community Medicine, University of Bristol, Bristol, UK. [5]University Hospitals Division, NHS Lothian, Edinburgh, UK. [6]General Surgery, NHS Fife, Victoria Hospital Kirkcaldy, Kirkcaldy, UK. [7]Centre for Cardiovascular and Lung Biology, Division of Medical Sciences, University of Dundee, Dundee, UK. [8]Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK

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).

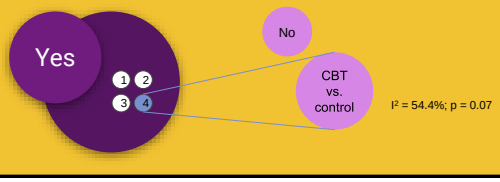
Quality Appraisal

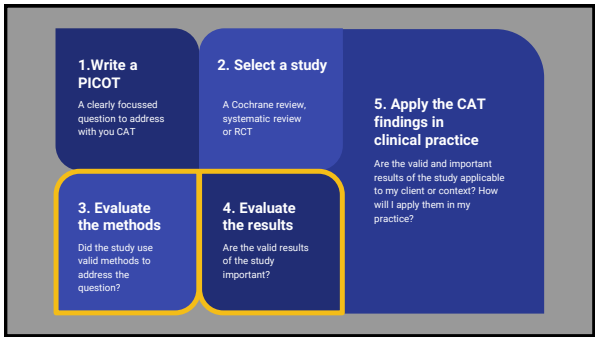
Two authors (Aung Zaw Zaw Phyo and Thibaut Demaneuf) evaluated the quality of included studies using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool for

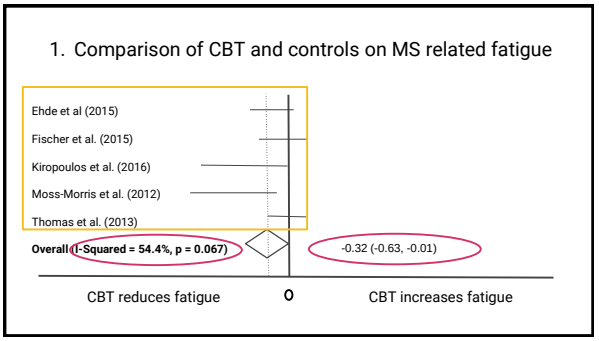
TABLE 1 | Quality of evidence rating for included studies based on the Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies.

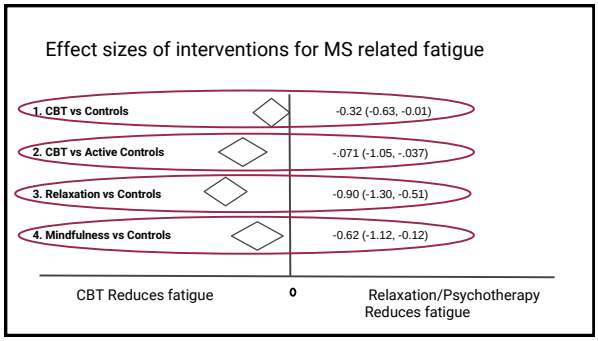
Reference	Selection bias	Study design	Confounders	Blinding	Data collection method	Withdrawals and dropouts	Global rating
Aisaieh and Shahrbanoo (36)	Moderate	Strong	Weak	Moderate	Strong	Weak	Weak
Anderson et al. (51)	Moderate	Weak	Weak	Moderate	Strong	Strong	Weak
Bogosian et al. (40)	Strong	Strong	Strong	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. (55, 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
Mose-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. (56)	Moderate	Strong	Strong	Weak	Strong	Moderate	Moderate
Vazinejad et al. (50)	Moderate	Strong	Strong	Moderate	Strong	Weak	Moderate

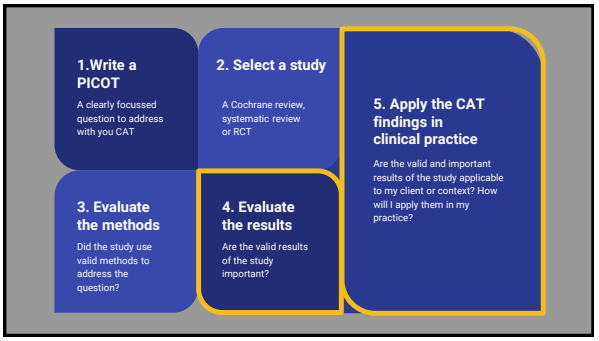
Were the results similar from study to study?




1.Write a PICOT
A clearly focussed question to address with you CAT
2. Select a study
A Cochrane review, systematic review or RCT
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?
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?


1. Comparison of CBT and controls on MS related fatigue
Ehde et al (2015)
Fischer et al. (2015)
Kiropoulos et al. (2016)
Moss-Morris et al. (2012)
Thomas et al. (2013)
Overall (I-Squared = 54.4%, p = 0.067)
-0.32 (-0.63, -0.01)
CBT reduces fatigue
0
CBT increases fatigue


Effect sizes of interventions for MS related fatigue
1. CBT vs Controls
-0.32 (-0.63, -0.01)
2. CBT vs Active Controls
-.071 (-1.05, -.037)
3. Relaxation vs Controls
-0.90 (-1.30, -0.51)
4. Mindfulness vs Controls
-0.62 (-1.12, -0.12)
CBT Reduces fatigue
0
Relaxation/Psychotherapy Reduces fatigue


1.Write a PICOT
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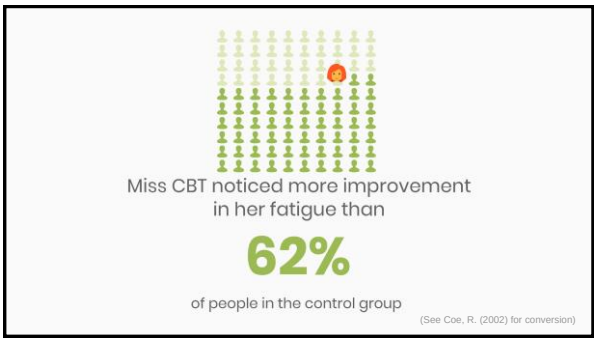
3. Evaluate the methods
Did the study use valid methods to address the question?
4. Evaluate the results
Are the valid results of the study important?

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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