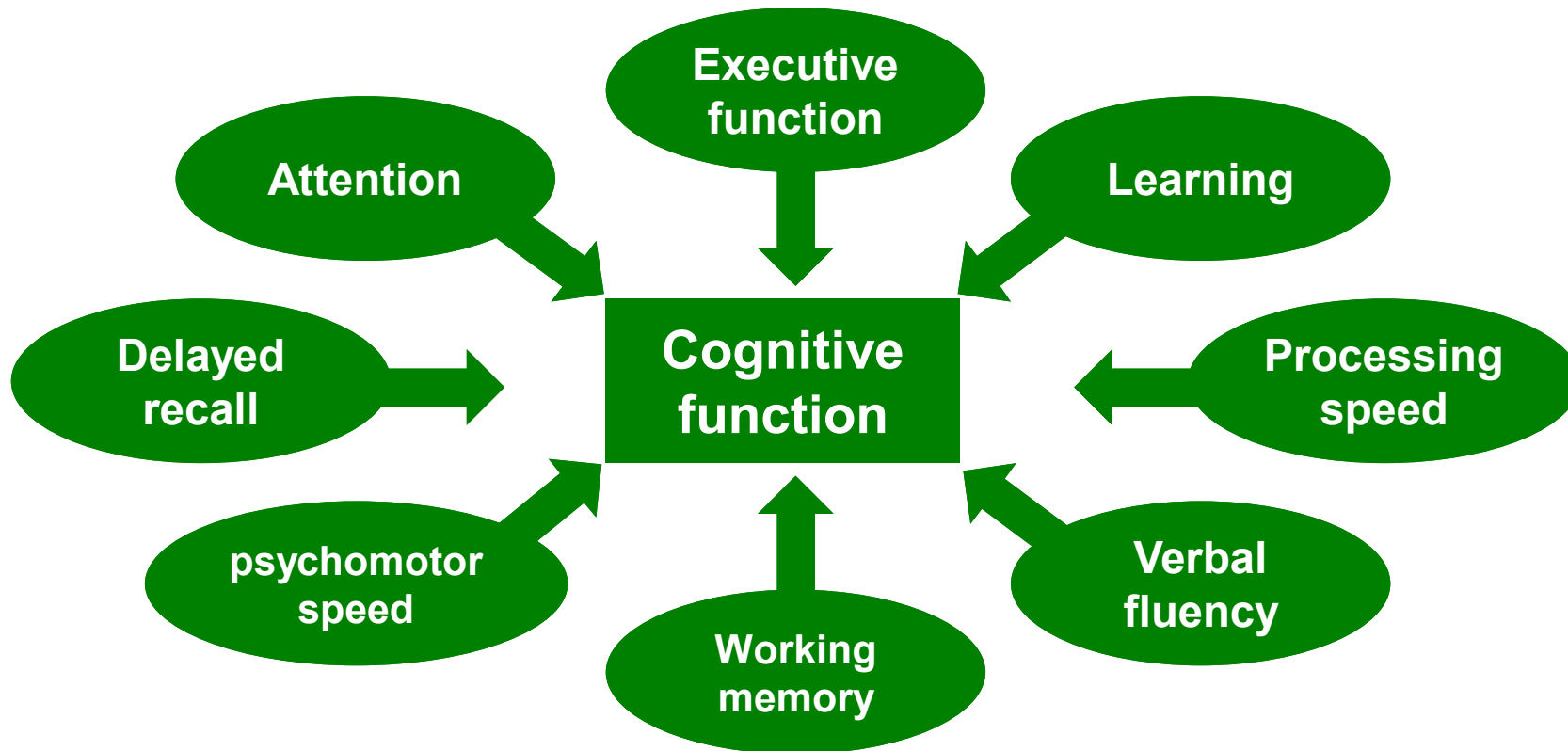
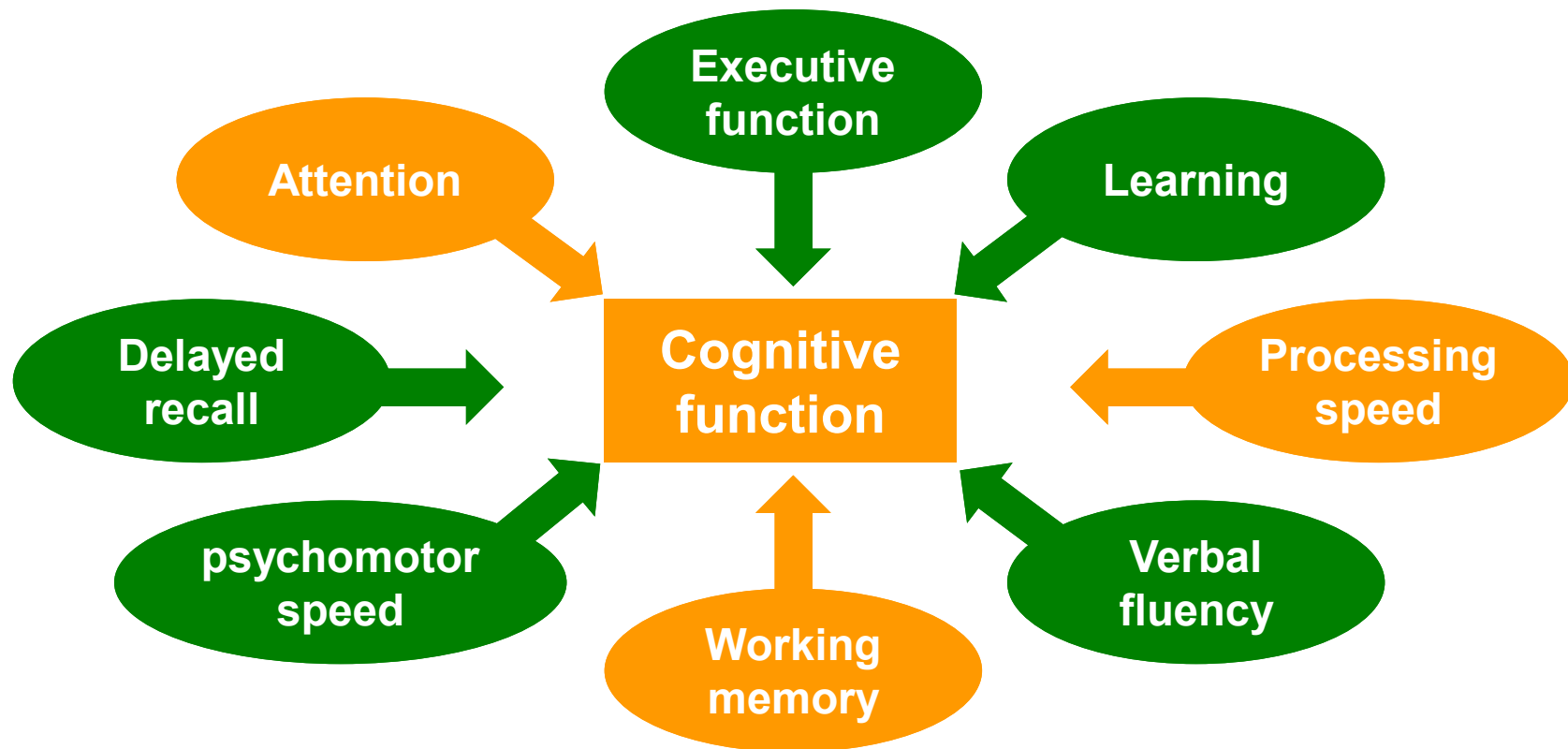

Screening or not screening, that is the question



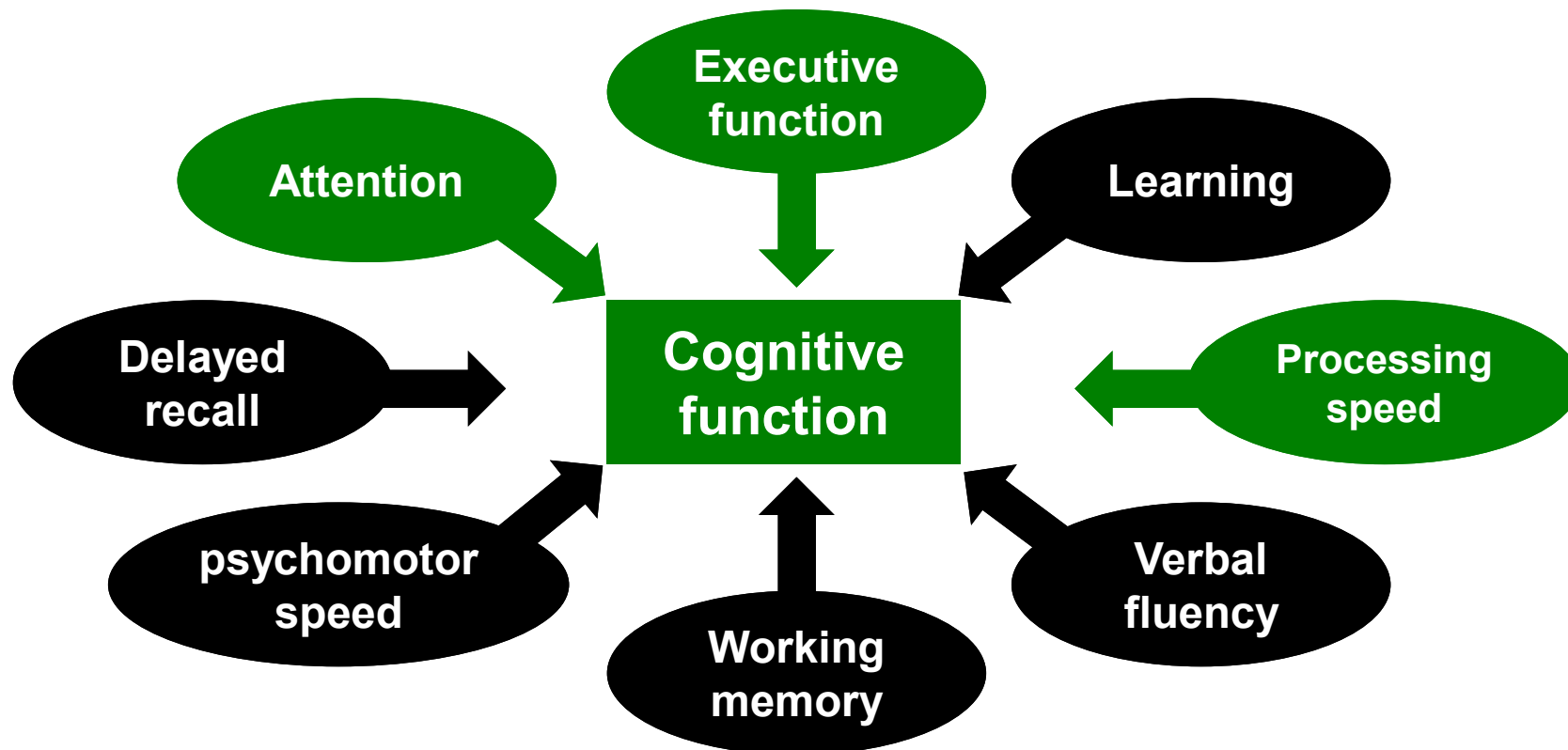
HAND diagnosis is based in the functional assessment of several neurocognitive domains



If the function in two or more of those domains is impair, global cognitive function is considered impair



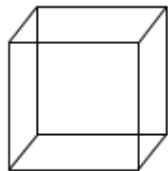
A potential first approach for screening is to select a few tests with high sensitivity detecting HAND



The HIV dementia Scale (HDS)

HIV Dementia Scale

Max Score	Score	Memory-Registration
4	()	Give four words to recall (dog, hat, green, peach) - 1 second to say each. Then ask the patient all 4 after you have said them.)
4	()	Attention¹ Anti-saccadic eye movements: 20 (twenty) commands. ____ errors of 20 trials. less than or equal to 3 errors = 4; 4 errors = 3; 5 errors = 2; 6 errors = 1; > 6 errors = 0)
6	()	Psychomotor Speed Ask patient to write the alphabet in upper case letters horizontally across the page (use back of this form) and record time: ____ seconds. less than or equal to 21 sec = 6; 21.1 - 24 sec = 5; 24.1 - 27 sec = 4; 27.1 - 30 sec = 3; 30.1 - 33 sec = 2; 33.1 - 36 sec = 1; > 36 sec = 0)
4	()	Memory - Recall Ask for 4 words from Registration above. Give 1 point for each correct. For words not recalled, prompt with a "semantic" clue, as follows: animal (dog); piece of clothing (hat), color (green), fruit (peach). Give 1/2 point for each correct after prompting.
2	()	Construction Copy the cube below, record time: ____ seconds. (< 25 sec = 2; 25 - 35 sec = 1; > 35 sec = 0)



Total Score: ____/16

Validity of the HDS as a screening diagnostic tool

N	GOAL STANDARD	Cutoff (16)	SENSITIVITY	ESPECIFICITY	REF
46	HAD ANI / MND	≤ 10	57% 93%	84% 38%	Bottiggi et al 2007
135 182 (CONTROL)	ANI / MND	≤ 10 Control group	17,2% 70%	93,5% 73,3%	Morgan et al 2008
200	ANI / MND	≤ 14	Complaining 83% Non complaining 88%	Complaining 63% Non-complaining 82%	Simioni et al 2010

The International HIV dementia Scale (HDS)

International HIV Dementia Scale (IHDS)

Memory-Registration: Give four words to recall (dog, hat, bean, red) – 1 second to say each. Then ask the patient all four words after you have said them.

Repeat words if the patient does not recall them all immediately. Tell the patient you will ask for recall of the words again a bit later.

1. Motor speed.

Have the patient tap the first two fingers of the non-dominant hand as widely and as quickly as possible.

4 = 15 in 5 seconds

3 = 11-14 in 5 seconds

2 = 7-10 in 5 seconds

1 = 3-6 in 5 seconds

0 = 0-2 in 5 seconds

2. Psychomotor speed.

Have the patient perform the following movements with the non-dominant hand as quickly as possible:

- Clench hand in fist on flat surface.
- Put hand flat on surface with palm down.
- Put hand perpendicular to flat surface on the side of the 5th digit.
- Demonstrate and have patient perform twice for practice.

4 = 4 sequences in 10 seconds

3 = 3 sequences in 10 seconds

2 = 2 sequences in 10 seconds

1 = 1 sequence in 10 seconds

0 = unable to perform

3. Memory-recall.

Ask the patient to recall the four words. For words not recalled, prompt with a semantic clue as follows: animal (dog); piece of clothing (hat); vegetable (bean); color (red).

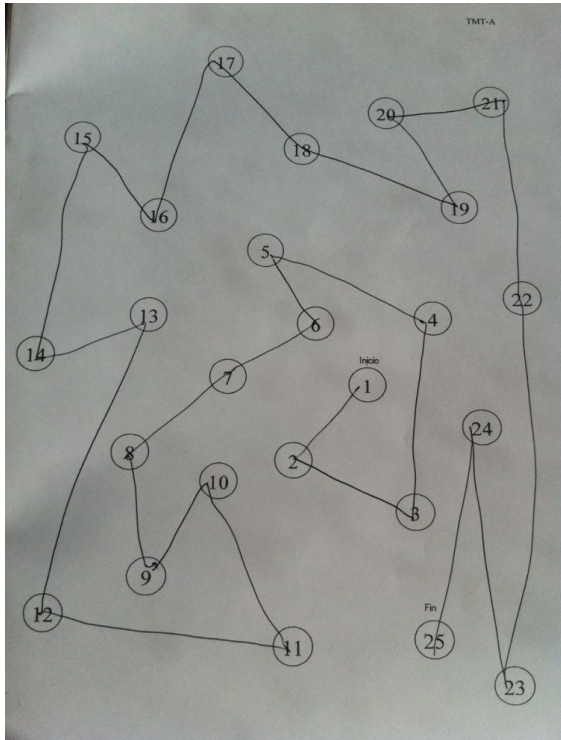
Give 1 point for each word spontaneously recalled. Give 0.5 points for each correct answer after prompting

Maximum – 4 points.

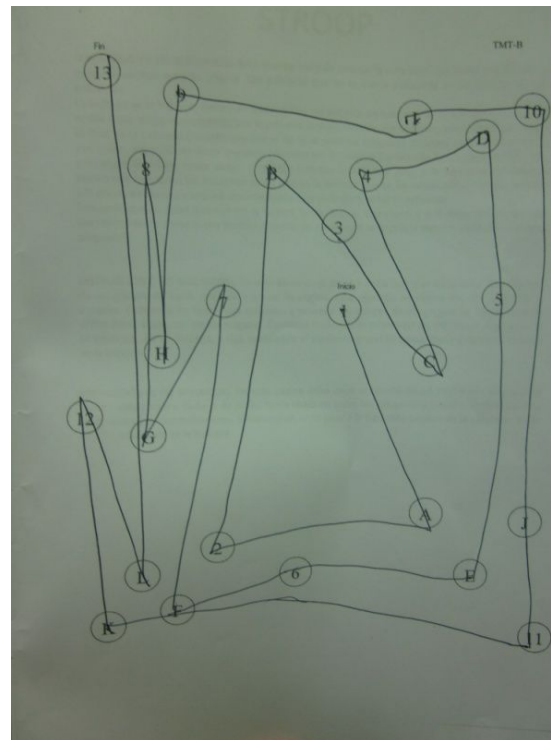
Validity of the IHDS as a screening diagnostic tool

N	Gold Standard NPZ-6	Cutoff (12)	Sensitivity	Specificity	REF
66 (US)	ANI / MND or 1 test \leq -2DS	≤ 10	80%	57%	Sacktor et al 2005
81 (UG)			80%	55%	

Brief neurocognitive screen - BNCS



TRAIL MAKING TEST A
(Atención/Velocidad
Procesamiento)



TRAIL MAKING TEST B
(Funciones ejecutivas)



CLAVE DE NÚMERO
(WAIS-III) (Velocidad de
procesamiento)

Validity of the BNCS as a screening diagnostic tool

N	Gold Standard NPZ-5	Cutoff	Sensitivity	Specificity	REF
301	ANI / MND or 1 test \leq -2DS	2 Test \leq -1DS or 1 Test \leq -2DS	23.6%	98.3%	Ellis et al 2005
		1 Test \leq -1DS	44%	88%	
		NPZ-3 \leq -0.33	65%	72%	

The NEU Screen

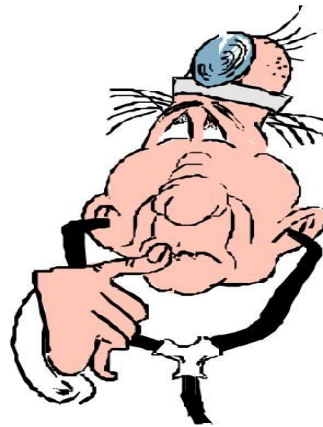
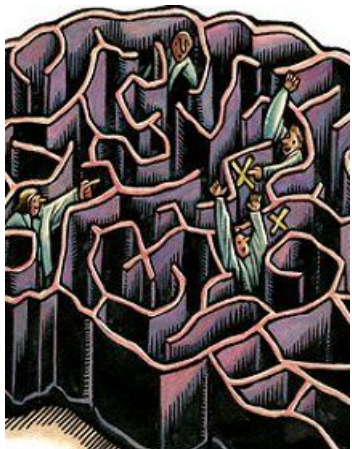
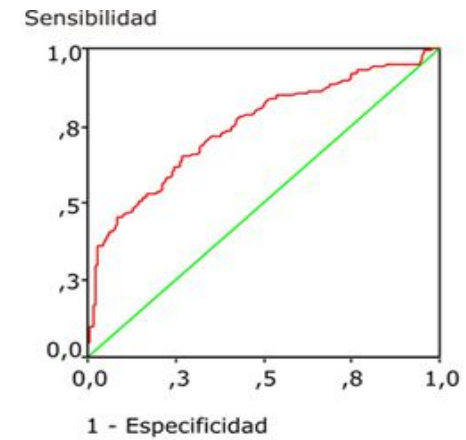
TABLE 3. Characteristics of the NEU Screen

Neurocognitive Area	Score (Test)	Computerized	Instrumental	Paper-Based	Approximate Application Time
Information processing speed	Total time (TMT-A)			X	2'
Executive functioning	Total time (TMT-B)			X	3'
Verbal fluency	Total score (COWAT)			X	4'
Total	3 scores			3 scores	8–10 min
Sensitivity (95% CI)	74.5% (60% to 85.2%)			Positive predictive value (95% CI)	79.1% (64.6% to 89%)
Specificity (95% CI)	81.8% (68.6% to 90.4%)			Negative predictive value (95% CI)	77.5% (64.4% to 87%)

CI, confidence interval.

	<60 years	≥60 years
S	74.01	90.91
E	72.12	92.31
VPP	73.18	90.91
VPN	72.12	92.31

NP screening tools have several problems ...

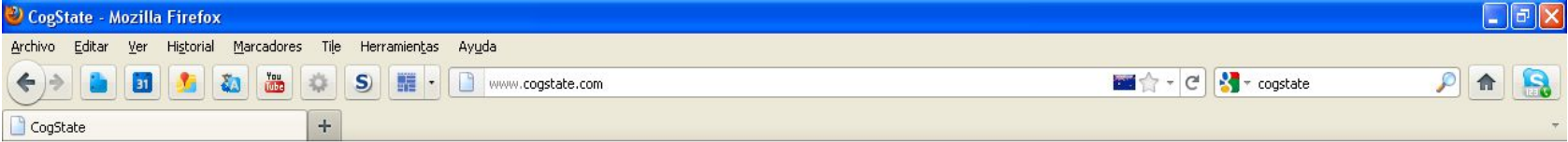




**For that reasons, different alternatives
have been proposed**



Computerized NP testing: The CogState



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Computerized NP testing Vs. standard testing

CogState 

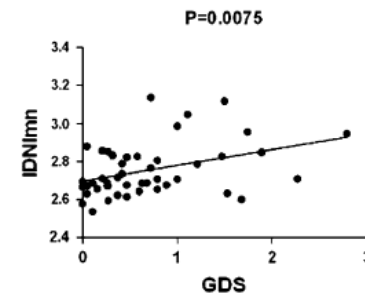
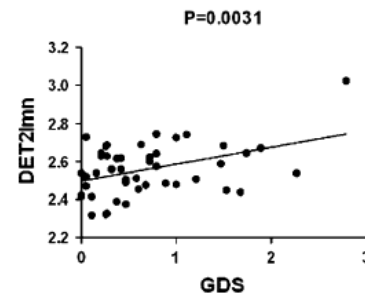
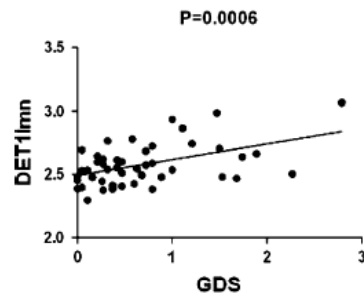
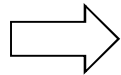
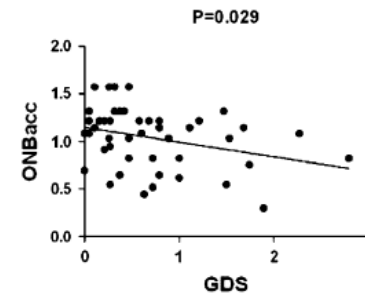
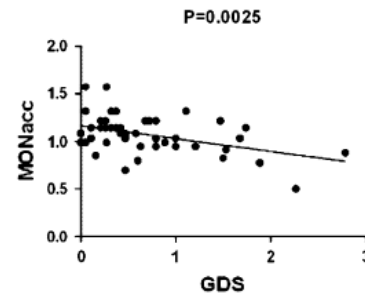


Vs.

Conventional
NP testing

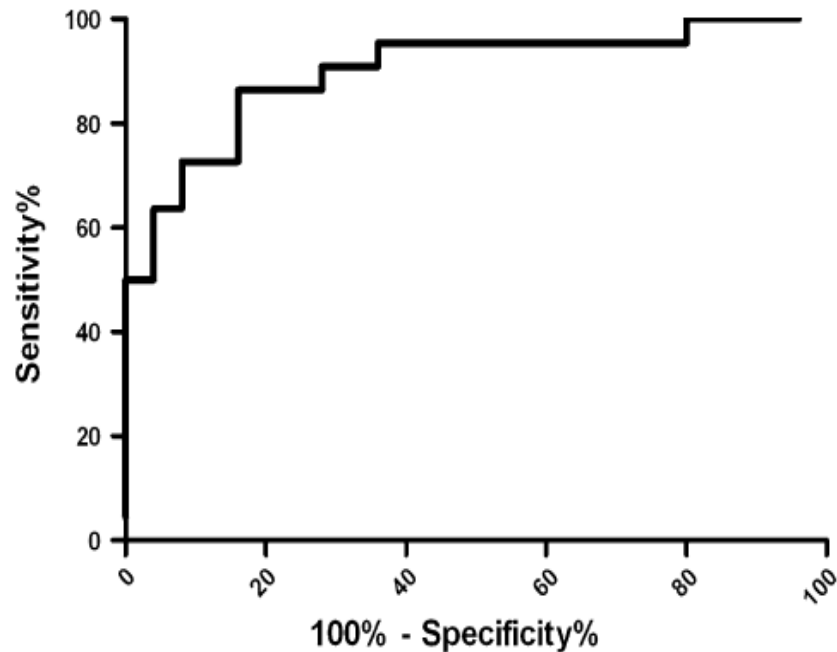


n = 46 (ANI/MND)



* Direct relation between specific test in each battery is poor but the relation between each test in the CogState and the GDS is good.

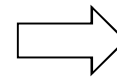
Computerized NP testing Vs. standard testing



AUC: 90% (95% CI: 0.81 – 0.99)

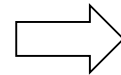
$p < 0.0001$

Limitations:

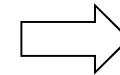


- Low number of subjects
- Lack of control group
- Absence of HAD

Another option as screening tools are the algorithms based on clinical factors



$$\begin{aligned}
 \text{4-year risk} &= 1 - \exp \left[- \exp \frac{\ln 4 - (22.9495 - 0.1564 \times \text{age} - 0.2029 \times \text{women} \right. \\
 &\quad \left. - 0.0593 \right. \\
 &\quad \left. \times \text{SBP} - 0.1285 \times \text{DBP} - 0.1907 \times \text{smk} - 0.1661 \times \text{parhm} - 0.0339 \times \text{BMI} \right. \\
 &\quad \left. + \frac{0.0016 \times \text{age} \times \text{DBP}}{0.8769} \right] = \\
 &= 1 - \exp \left[- \exp \frac{\ln 4 - (22.9495 - 0.1564 \times 60 - 0.2029 \times 1 - 0.0593 \times 128 \right. \\
 &\quad \left. - 0.1285 \times 85 - 0.1907 \times 1 - 0.1661 \times 2 - 0.0339 \times 32 + 0.0016 \times 60 \right. \\
 &\quad \left. \times 85 \right] = 0.5750 = 57.50\%
 \end{aligned}$$



CVD RISK CALCULATOR	
GENDER	Male ▾
Age (yrs)	45
Sys BP (mmHG)	130
SMOKER	No ▾
Total-C (mmol/l) ▾	5.5
HDL-C (mmol/l) ▾	3.3
DIABETES	No ▾
ECG LVH	No/Unsure ▾
ON BP MEDS	No ▾
10y ▾	<input type="button" value="Calculate"/> <input type="button" value="Clear"/>

A preliminary easy screening algorithm to detect HAND has been developed

Age :	<input type="text"/>	years
CD4:	<input type="text"/>	cells/mcL
CNS disease:	<input type="text"/>	"X"=yes / Blank:No
CART duration:	<input type="text"/>	months
NP = -14.99 NP Normal		

* Performed using the clinical data and NP results of 96 HIV+ subjects

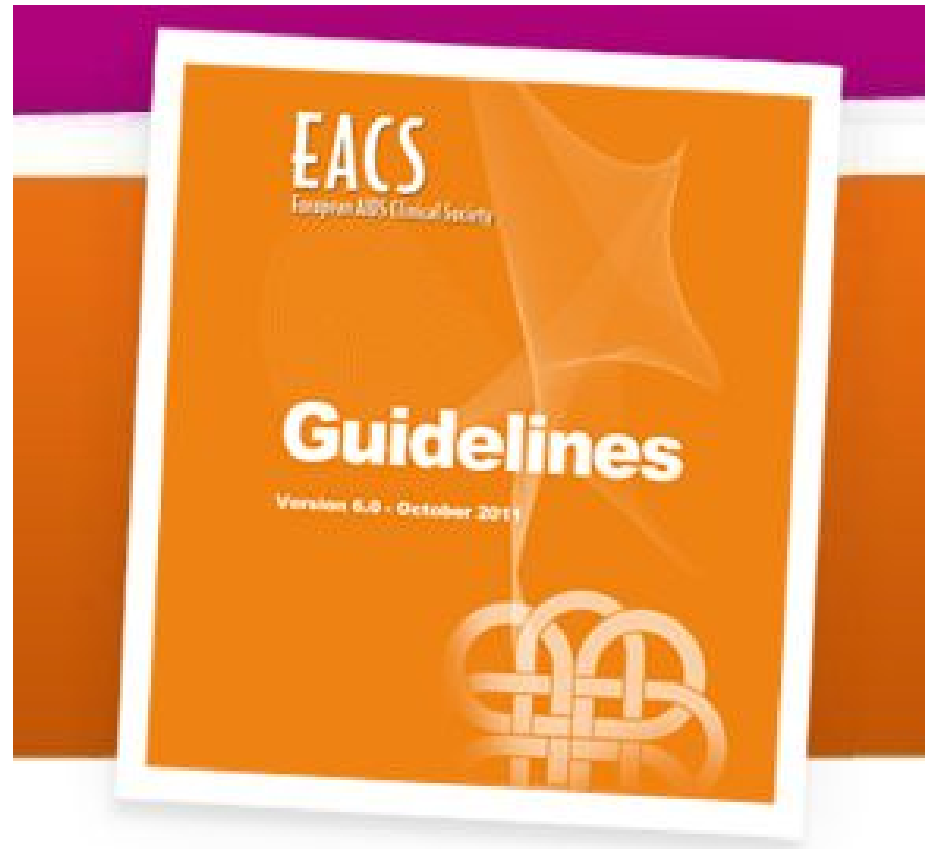
Cysique's algorithm results are promising, but only in her cohort

Tools		Global NP assessment	
		Positive	Negative
Screening algorithm	Positive	78%	30%
	Negative	22%	70%

This algorithm has its limitations:

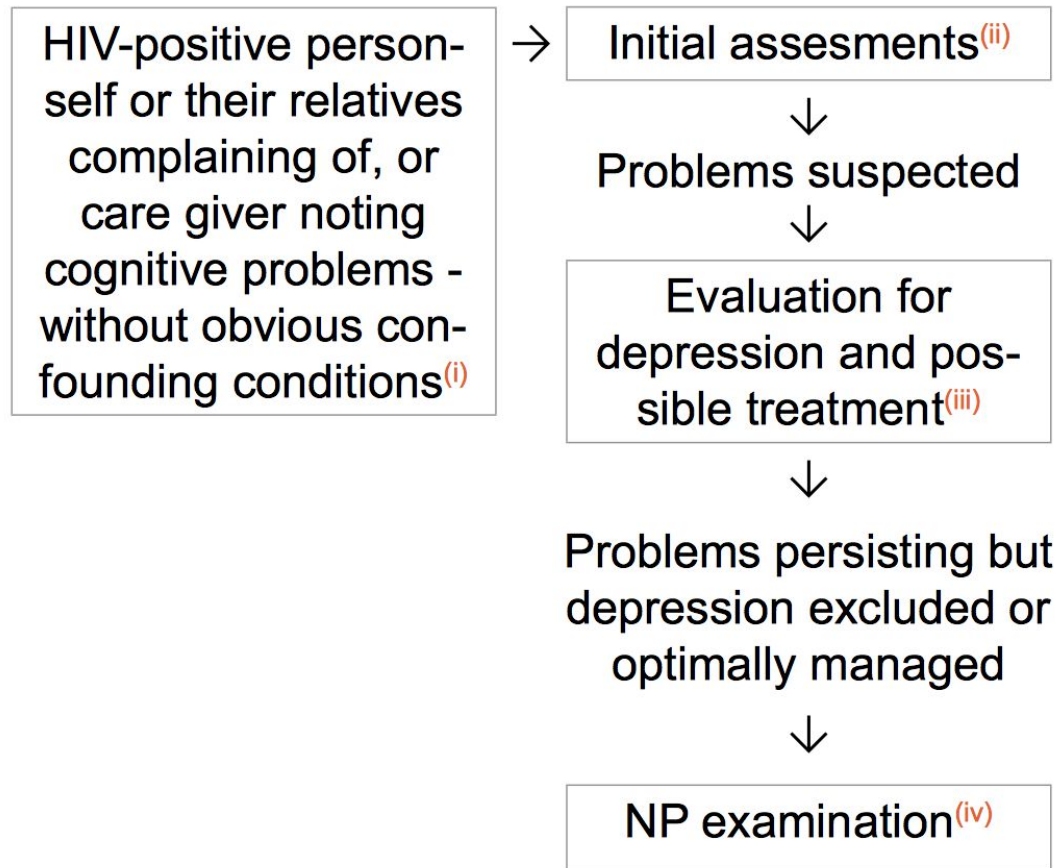
- ✓ It has only been validated in patients with AIDS
- ✓ It has only been validated in patients with HIV RNA < 50 cp/mL

The functional screening approach propose by the EACS guidelines



Available at <http://www.europeanaidsclinicalsociety.org/guid/index2.html?ml=1>

The functional screening approach propose by the EACS guidelines



EACS guidelines: The three questions

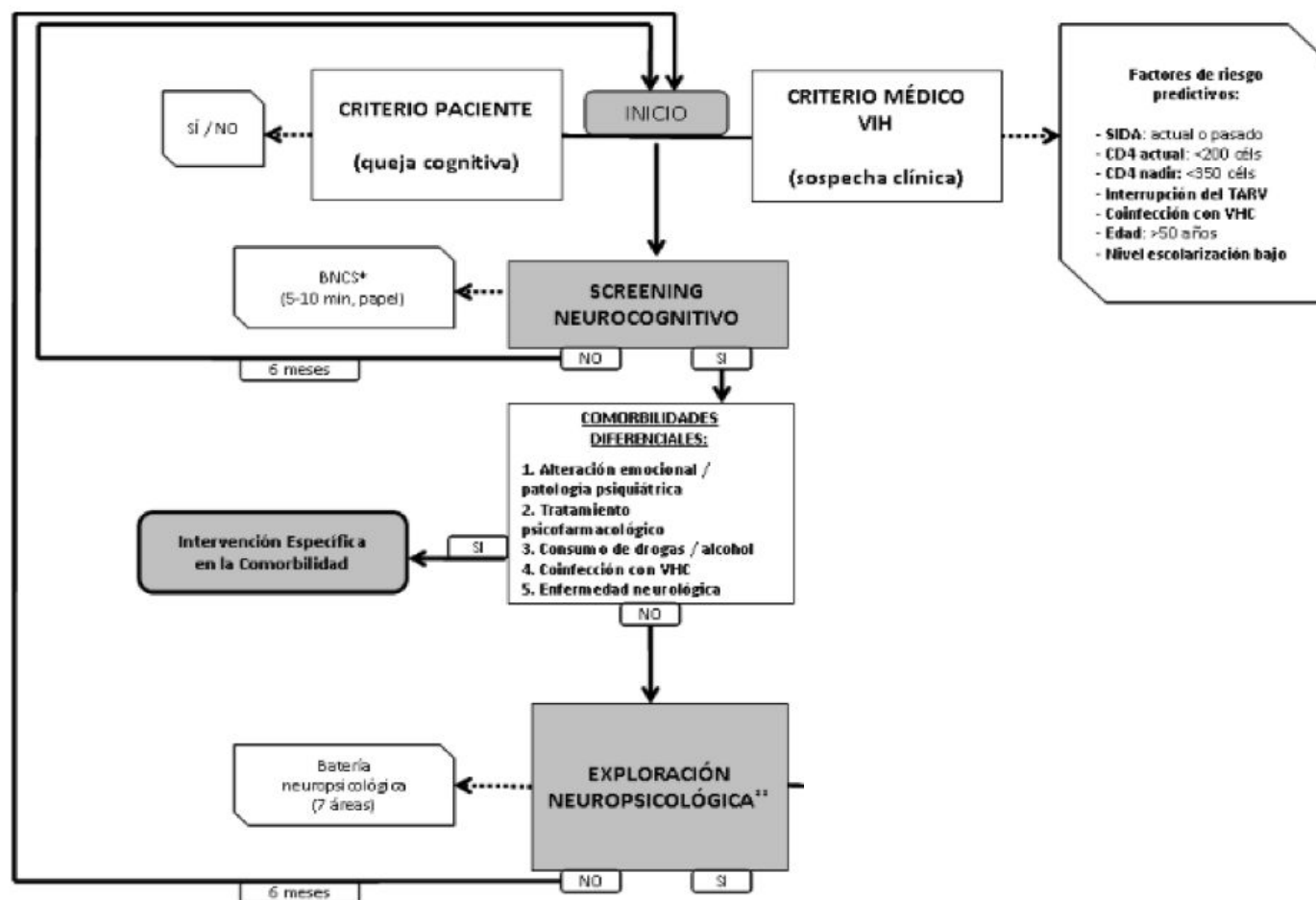
1. Do you experience **frequent memory loss** (e.g. do you forget the occurrence of special events even the more recent ones, appointments, etc.)?
2. Do you feel that you are **slower** when reasoning, planning activities, or solving problems?
3. Do you have **difficulties paying attention** (e.g. to a conversation, a book, or a movie)?

Answer available: Never, hardly ever, **yes, definitively**

Clinical impression vs. BNCS (n=140)

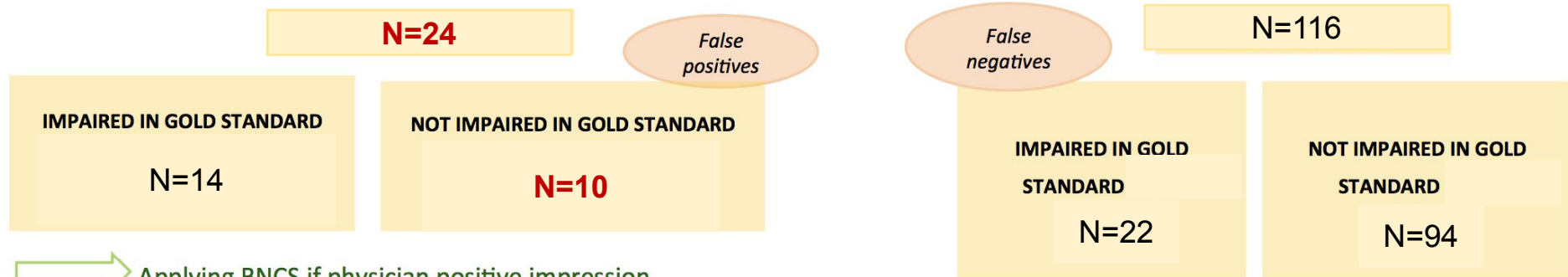
Screening tool	BNCS		PHYSICIAN IMPRESSION	
	Cut off	NPZ3 _≤ -0,33	Altered test*	
			YES/NO	
Sensitivity		0,69	0,53	0,39
Specificity		0,73	0,91	0,90
Likelihood ratio positive		2,58	6,1	3,9
Likelihood ratio negative		0,42	0,52	0,67
Positive predictive value		0,47	0,68	0,54
Negative predictive value		0,87	0,85	0,83

GESIDA guidelines: A mix of everything

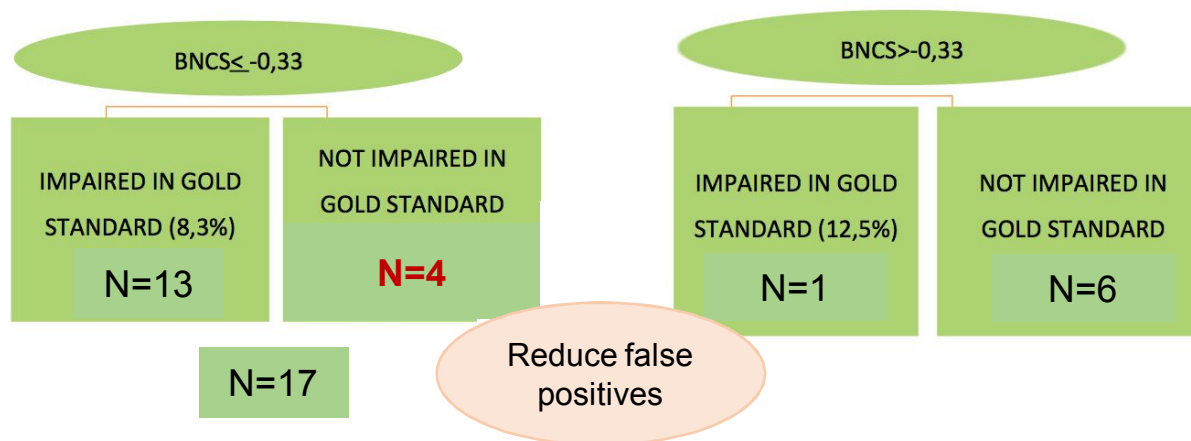


Analyzing the mix model (n=140)

→ Do you think your patient is neurocognitively impaired?



→ Applying BNCs if physician positive impression



Pacientes con deterioro que no serán evaluados
23 de 36 (63,9%)



DISCUSSION

