

Workshop. Practical Training on diagnosis and  
management of clinical CNS problems in  
HIV-positive individuals

**Screening**

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# Clinical Guidelines Recommendations

## EACS 2017

Self-complain or relatives complaining

Without:

- Severe psychiatric condition\*
- Drug or alcohol abuse\*
- Neurologic sequelae
- Current neurological disease\*

Self-reported symptoms

- The three questions

Exclude/treat depression

## GESIDA 2013

Self-complain

Medical criteria:

- AIDS
- Low CD4
- Off ART
- HCV/HIV
- Age >50
- Uneducated

Neurocognitive Screen

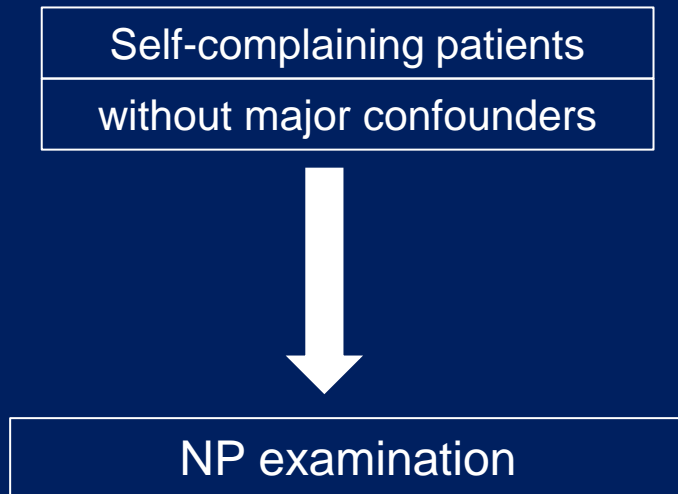
- BNCS

Exclude/treat comorbidities\*

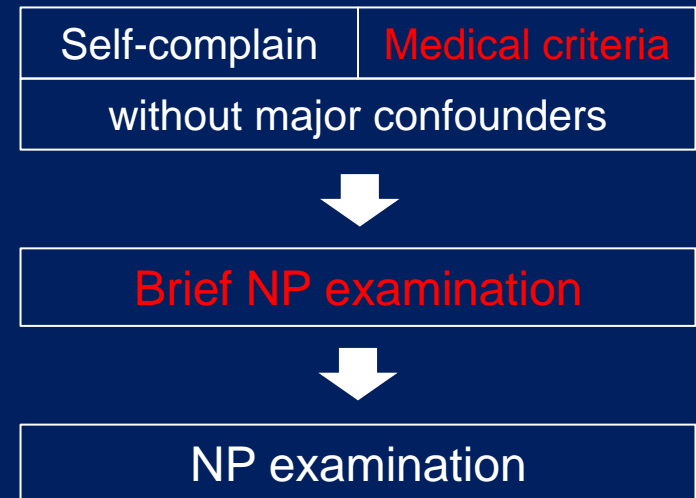
NP examination

# Differences Between Clinical Guidelines

## EACS 2017



## GESIDA 2013



# Are Medical Criteria Useful?

	N=140
Neurocognitive impairment (Frascati criteria). N (%)	36 (25,7)
Male. N (%)	32 (22,9)
Age. Median (IQR)	46.33 (8,2)
Caucasian ethnicity . N (%)	125 (89,3)
Years of education. Mean (SD)	9,55 (6,01)
AIDS. N (%)	90 (64,3)
Time since HIV diagnosis (months). Mean (SD)	184,75 (79,46)
Time virologically suppressed (months). Mean (SD)	75,39 (41,96)
CD4 nadir (c/mm3). Mean (SD)	162 (123,94)
Current CD4 (cells/mm3). Mean (SD)	624,43 (304,28)
Active HCV infection. N (%)	30 (21,4)
Intravenous drug use mode of HIV transmission. N(%)	42 (30)

Screening tool	HDS		BNCS		PHYSICIAN IMPRESSION	
	Cut off	≤10	≤14	NPZ3≤-0,33	Altered test*	YES/NO
Sensitivity		0,22	0,56	0,69	0,53	0,39
Specificity		0,62	0,28	0,73	0,91	0,90
Likelihood ratio positive		0,57	0,79	2,58	6,1	3,9
Likelihood ratio negative		1,27	1,54	0,42	0,52	0,67
Positive predictive value		0,18	0,24	0,47	0,68	0,54
Negative predictive value		0,67	0,62	0,87	0,85	0,83



vs.



# Are NP Screening Tools Useful?



BNCS

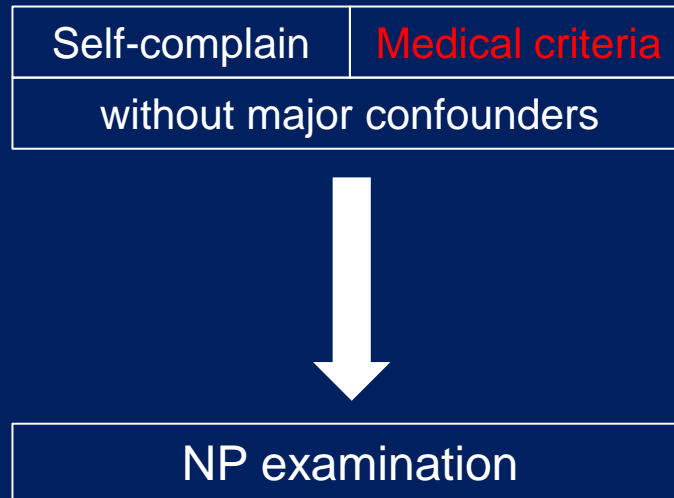


HDS

N	GOLD STANDARD (NPZ-5)	CUT-OFF	SENSIBILIITY	SPECIFICITY	REFERENCE
301	Frascati Criteria	2 test $\leq$ - 1SD or 1 test $\leq$ -2SD	23.6%	98.3 %	Ellis et al 2005
		1 test $\leq$ -1SD	44%	84 %	
		<b>NPZ3 <math>\leq</math> -0,33</b>	<b>65%</b>	<b>72 %</b>	
1580	Frascati Criteria	$\leq$ 10	27%	92%	Sakamoto et al 2012
Control		Control Group	69%	57%	

# The algorithm we are currently using in our NP clinic

## Hospital U. La Paz (Madrid)



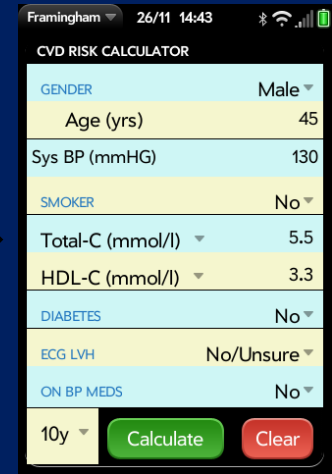
# How Can We Improve?

We need to develop algorithms based on clinical factors and diagnostic tests



$$4\text{-year risk} = 1 - \exp \left[ - \exp \left[ \frac{\ln 4 - (22.9495 - 0.1564 \times \text{age} - 0.2029 \times \text{women} - 0.0593 \times \text{SBP} - 0.1285 \times \text{DBP} - 0.1907 \times \text{smk} - 0.1661 \times \text{parhtn} - 0.0339 \times \text{BMI} + 0.0016 \times \text{age} \times \text{DBP})}{0.8769} \right] \right]$$

$$1 - \exp \left[ - \exp \left[ \frac{\ln 4 - (22.9495 - 0.1564 \times 60 - 0.2029 \times 1 - 0.0593 \times 128 - 0.1285 \times 85 - 0.1907 \times 1 - 0.1661 \times 2 - 0.0339 \times 32 + 0.0016 \times 60 \times 85)}{0.8769} \right] \right] = 0.5750 = 57.50\%$$



# An initial screening clinical algorithm has been proposed

## Results are promising but not good enough

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		

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

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

### 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



# Potential Elements of Improvement

- Brain MRI (conventional or 3T)
  - ✓ Number of white matter lesions (conventional)
  - ✓ DTI abnormalities (3T)
  - ✓ MRS abnormalities (3T)
- Biomarkers (blood or CSF?)
  - ✓ NFL, Neopterin, IP-10, MCP-1...
- HIV factors
  - ✓ Presence of “neurotropic” HIV clades
  - ✓ Detection of CSF compartmentalization / viral escape
- Others?