



Key clinical research: Neurologic studies

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Aims “Neuro Study”

- To assess neurocognitive co-morbidities and associated depression symptoms in HIV infected individuals.
 - To assess the trajectory of neurocognitive morbidity over two years of follow up on ART
 - To define the level of compartmentalized virus in the CSF and examine associations with dementia, stratified by HIV subtype.

Neurocognitive performance and normative comparison data in HIV+ and HIV- individuals in Rakai, Uganda

HIV+ participants

- ❖ N= 400 HIV positive
- ❖ Education 5 years
- Age M 35 years

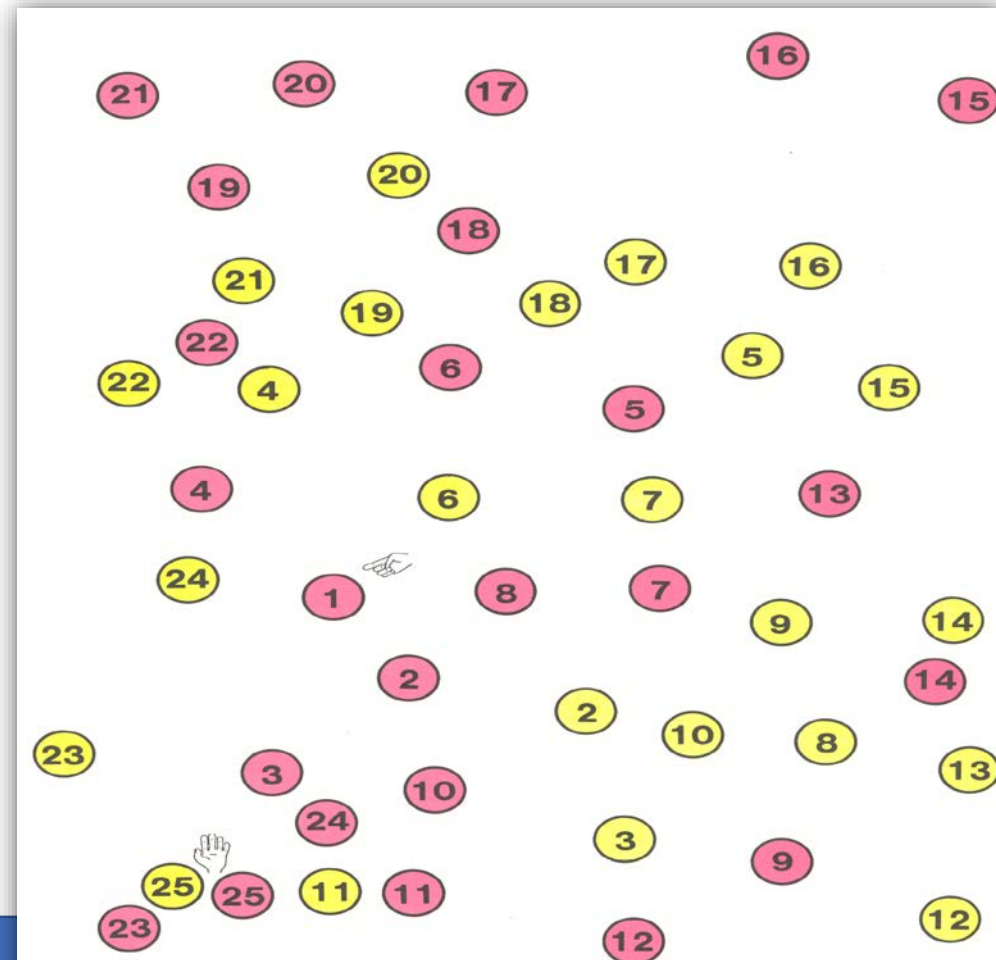
Matched HIV – 400
Controls

Symbol Digit

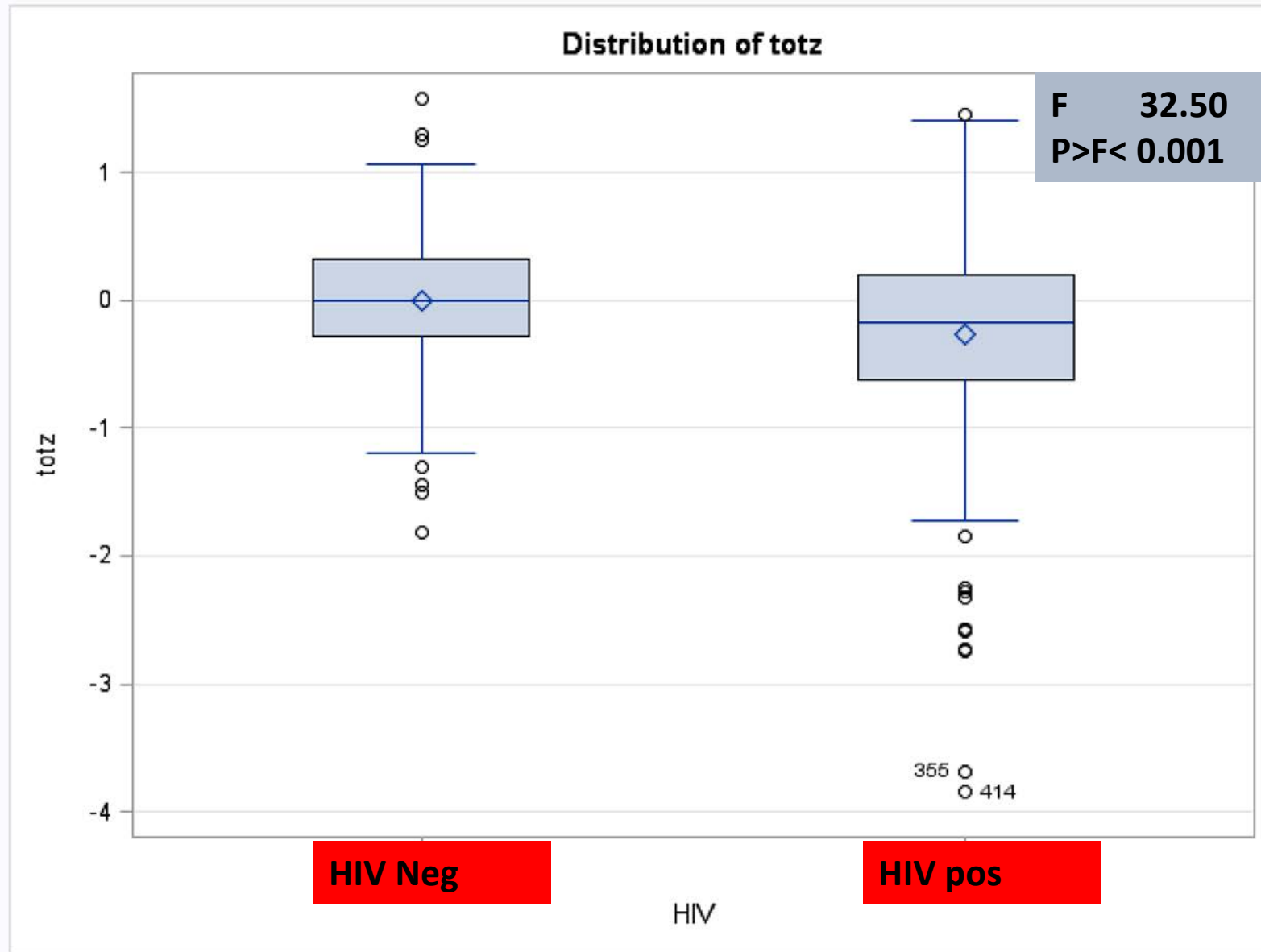
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Color Trail 1



HIV Negative and HIV Positive neurocognitive performance



Neurocognitive performance was lower for HIV positive individuals

HAND: HIV Associated Neurocognitive Disorders

HIV+ only: Pre- and Post-ART Cognitive Function

	Baseline (n=312)	Follow-Up (n=312)	p
Normal	130 (44%)	141 (49%)	< 0.001
ANI	20 (7%)	39 (13%)	
MND	103 (35%)	97 (33%)	
Dementia	39 (13%)	15 (5%)	



HIV Dementia **BUT** unchanged HAND at 2 years

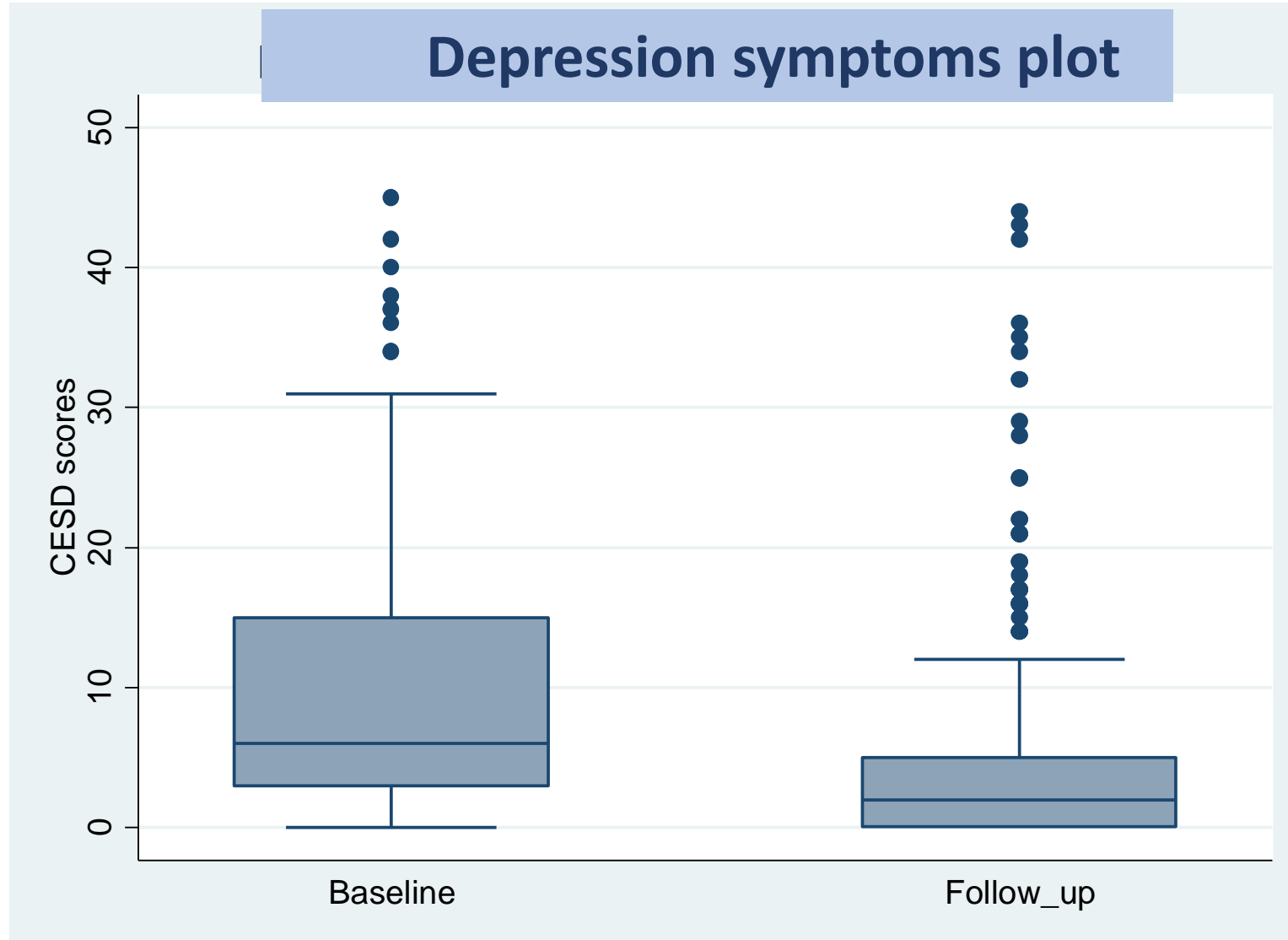


Baseline Demographic Characteristics by Immunosuppression

	CD4 Category	
	<200 cells/ μ L (n=150)	350-500 cells/ μ L (n=183)
Age, Mean (SD)	33.8 (7.3)	36.8 (9.3)
Baseline Viral load >1000	148 (98.7%)	163 (89%)
Men	89 (59.4%)	81 (44.3)
Women	61 (40.6%)	102 (55.7%)
Initiated ART	147 (98%)	165 (90%)

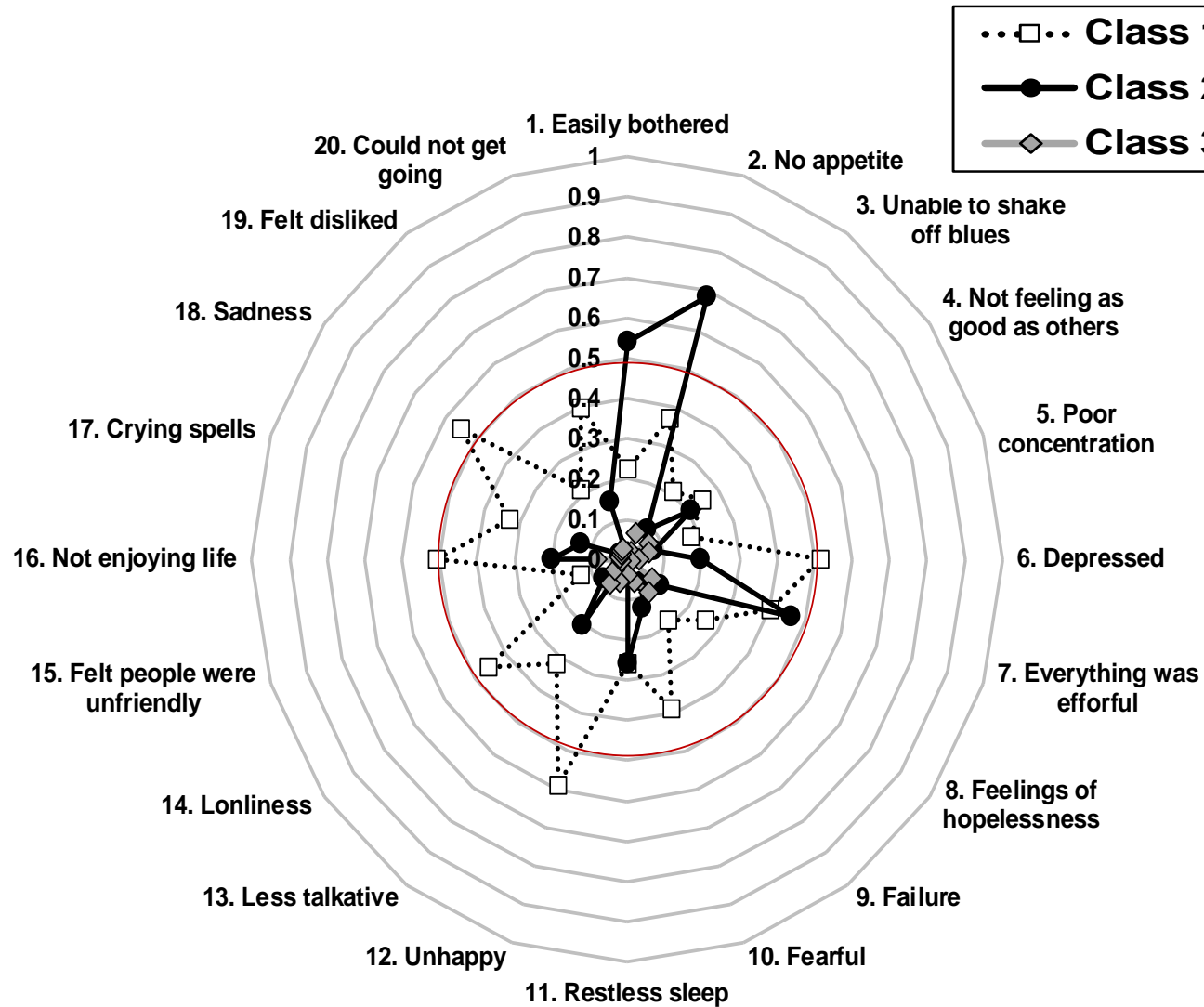


DEPRESSION SYMPTOMS IN HIV POSITIVE INDIVIDUALS AT BASELINE AND 2 YEAR FOLLOW UP



Mean (SD) CES-
Depression score
was **higher** at
baseline 9.6 than at
the 2 years 4.4 (7.4)
 $p < 0.01$

EFFECT OF ART ON DEPRESSION SYMPTOMATOLOGY



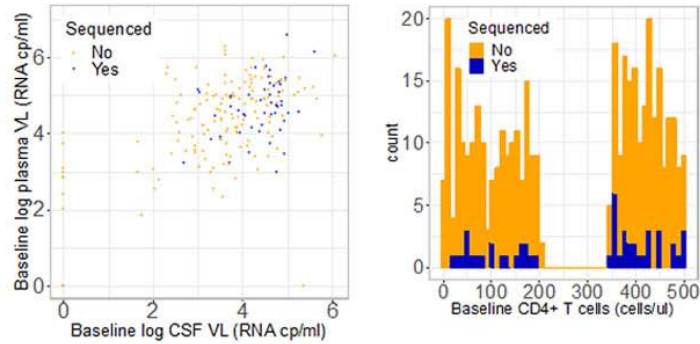
Take Home
Heterogeneity in ART –
related depressive symptom
improvement
Affect > Somatic

HAND and Mortality

	n (%)
Two-Year Mortality	
Alive	337 (84%)
Dead	17 (4%)
LTFU	45 (11%)

- Each one-stage increase in HAND severity was associated with a 58% increased odds of death at two years [OR 1.58, 95%CI (0.97, 2.57), p=0.06]

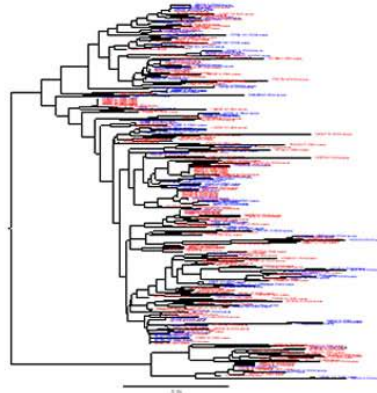
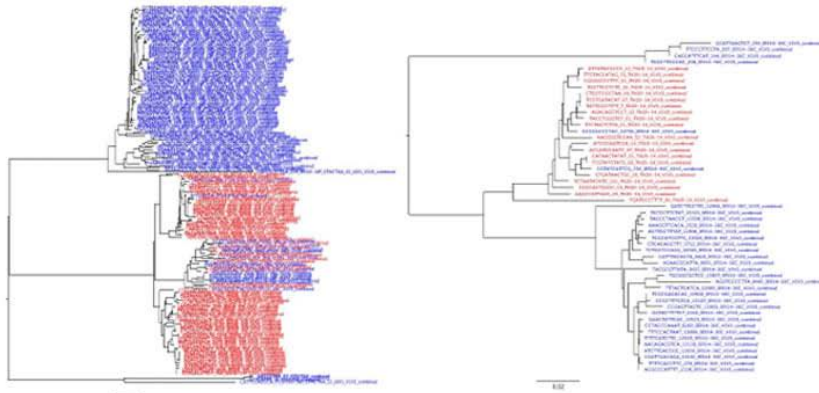
Is HIV-1 replication in the CNS associated with neurocognitive impairment?



HIV-1 populations in the CSF and plasma were analyzed by deep sequencing with Primer ID in 50 Individuals. Individuals analyzed by sequencing were representative of the overall cohort of HIV-infected people.

Compartmentalized:
produced by replication in the CNS

Equilibrated:
No evidence of replication in the CNS



	Subtype						Baseline			Follow-up			
	A	C	D	A/C	A/D	Unknown	Median plasma VL (RNA cp/ml)	Median CSF VL (RNA cp/ml)	Median baseline totalZ	Median CD4 count (cells/ul)	Median plasma VL (RNA cp/ml)	Median CSF VL (RNA cp/ml)	Median followup totalZ
Equilibrated (N=18)	5	1	4	1	3	4	6.45E+04	2.29E+04	-0.29	421	Udetectable	Udetectable	0.06
Compartmentalized (N=32)	12	0	10	1	2	7	5.31E+04	4.11E+04	-0.34	454	Udetectable	Udetectable	-0.19

64% evidence of CSF HIV compartmentalization affecting verbal learning

Resolving after ART initiation