

# Recommended Earlier Initiation of Antiretroviral Therapy Based on Nadir CD4 Cell Count as a Risk Factor for HIV-related Neurocognitive Impairment

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## Background:

Nadir CD4 cell count has been proposed as a new potential risk factor for irreversible HIV-related neurocognitive impairment. Furthermore, benefits of HAART have been observed to be insufficient for neurocognitive reversal. We compared different nadir CD4 cell count cutoffs to study their possible clinical significance related to the initiation of HAART.

## Methods:

Observational, cross-sectional study, where 64 HIV-infected patients were compared according to 4 nadir CD4 cell count cutoffs:

>200 versus ≤200 (n=38) vs (n=26)	>250 versus ≤250 (n=30) vs (n=33)	>300 versus ≤300 (n=23) vs (n=36)	>350 versus ≤350 (n=16) vs (n=35)
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Demographic - Clinical Variable	Neuropsychological Variable	
	Function	Measure (Test)
Age (years), gender (% male), education (years), time since HIV diagnosis (years), time on treatment (years), CD4+ cell count (cells/mL), viral load (copies/mL), depression (BDI), and anxiety (STAI)	Attention/working memory (3)	Digit span forward, digit span backward and letters-numbers (WAIS-III)
	Information processing speed (2)	TMT-A and SDMT
	Verbal memory (1)	Long-term recall (CVLT)
	Learning (1)	A list (CVLT)
	Executive functioning (3)	TMT-B, interference (Stroop Test) and percentage of errors (WCST)
	Verbal fluency (2)	COWAT and animals test
	Motor function (4)	Dominant hand and non-dominant hand (ETT), dominant hand and non-dominant hand (GPT)

\*: BDI, Beck Depression Inventory; STAI, State-Trait Anxiety Inventory; WAIS-III, Wechsler Adult Intelligence Scale-III; TMT-A, Trail Making Test - Part A; SDMT, Symbol Digit Modalities Test; CVLT, California Verbal Learning Test; TMT-B, Trail Making Test - Part B; WCST, Wisconsin Card Sorting Test; COWAT, Controlled Oral Word Association Test; ETT, Electronic Tapping Test; GPT, Grooved Pegboard Test.

**Exclusion Criteria:** Patients reporting drug abuse, psychiatric treatment or neurological disorder were excluded.

**Data Analysis:** ANOVA, non-parametric and Chi Square tests were performed. Demographic and clinical variables were controlled.

## Results:

### 1) Percentage of patients showing neurocognitive impairment:

✓ Differences did not reach statistical significance, although the percentage of impaired patients tended to be higher while the nadir cutoff fell.

Nadir CD4 cutoff	% of impaired patients
Nadir >200 (n=38)	52.63%
Nadir ≤200 (n=26)	73.07%

Nadir CD4 cutoff	% of impaired patients
Nadir >250 (n=30)	53.33%
Nadir ≤250 (n=33)	66.66%

Nadir CD4 cutoff	% of impaired patients
Nadir >300 (n=23)	56.52%
Nadir ≤300 (n=36)	63.88%

Nadir CD4 cutoff	% of impaired patients
Nadir >350 (n=16)	62.5%
Nadir ≤350 (n=35)	57.14%

### 2) Differences regarding neurocognitive and motor functions (t scores):

✓ Differences in 2 areas, and a general tendency to show a netter neurocognitive functioning in the groups of patients with higher nadir counts was observed.

Nadir CD4 cutoff	Attention/Working Memory			Information Processing Speed		Verbal Memory	Learning	Executive Function			Verbal Fluency		Motor Function			
	Digit span forward	Digit span backward	Letters-numbers	TMT-A	SDMT	Long-term recall	A-list	TMT-B	Interference	Percentage of errors	COWAT	Animals	Dominant (ETT)	Non-domin. (ETT)	Dominant (GPT)	Non-domin. (GPT)
>200	51.53	54.11 *	53.83	55.15	51.03	50.53	49.58	55.88 *	52.05	55.71	43.14	53.51	45.81	45.60	53.16	53.36
≤200	48.52	49.68	51.81	52.25	48.65	49.62	48.85	51.29	49.96	49.68	42.88	54.04	44.19	47.46	54.12	54.58
>250	51.57	53.13	53.00	54.11	50.97	50.33	49.00	55.52	51.69	54.70	42.97	53.28	47.10	47.07	52.79	52.76
≤250	49.19	51.56	53.15	53.70	49.58	50.61	50.48	52.73	50.97	52.17	42.88	53.58	42.85	45.25	54.15	54.69
>300	51.83	53.30	53.22	54.67	51.65	49.57	49.48	55.67	51.30	55.74	41.43	52.09	47.13	46.91	53.83	53.39
≤300	50.00	52.63	53.50	54.09	49.64	50.83	50.00	53.53	51.55	51.57	44.29	55.03	42.97	44.67	53.94	54.59
>350	52.31	56.00	53.88	54.13	52.63	50.00	48.00	56.13	51.44	56.56	40.69	52.00	49.31	48.94	53.88	54.44
≤350	50.24	52.76	53.52	53.90	49.77	51.14	50.83	53.74	51.00	51.53	44.00	55.15	42.74	45.75	53.24	53.76

## Conclusions:

\*: p<0.05

Our results confirm the nadir CD4 cell count as a potential risk factor for HIV-related neurocognitive impairment. The prevalence of neurocognitive impairment is higher in those patients with lower nadir counts but, in addition, relevant differences are found when neurocognitive functioning is studied considering the nadir CD4 value. Earlier initiation of HAART therapy is recommended to achieve the major neurocognitive protection.