Advances in the Diagnosis and Prevention of Neurocognitive Impairment in HIV-Infected Persons

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Advances in Diagnosis

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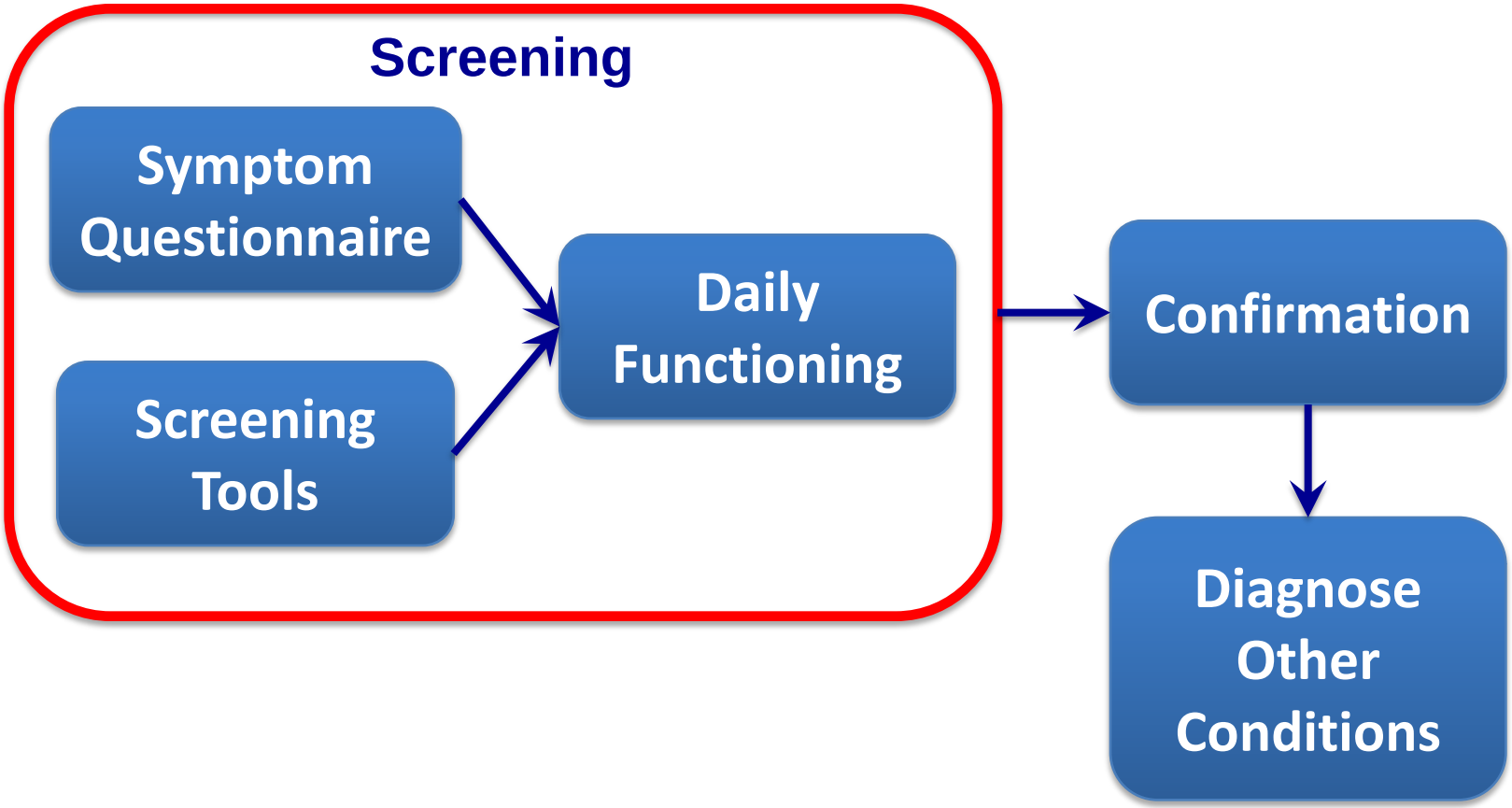
Basic Approach to Screening and Diagnosis



Importance of Standardized Procedures

- "…standardized procedures should be followed whenever possible, both to collect the needed information and to interpret that information to make three types of determination"
  - Presence and severity of neurocognitive impairment
  - Presence and severity of functional decline
  - Degree to which cognitive impairment or functional decline are likely to have been influenced by comorbid conditions

Antinori et al, Neurology 2007, 69: 1789-99

Assessment, Diagnosis, and Treatment of HIV-Associated Neurocognitive Disorder: A Consensus Report of the Mind Exchange Program

The Mind Exchange Working Group

Many practical clinical questions regarding the management of human immunodeficiency virus (HIV)–associated neurocognitive disorder (HAND) remain unanswered. We sought to identify and develop practical answers to key clinical questions in HAND management. Sixty-six specialists from 30 countries provided input into the program, which was overseen by a steering committee. Fourteen questions were rated as being of greatest clinical importance. Answers were drafted by an expert group based on a comprehensive literature review. Sixty-three experts convened to determine consensus and level of evidence for the answers. Consensus was reached on all answers. For instance, good practice suggests that all HIV patients should be screened for HAND early in disease using standardized tools. Follow-up frequency depends on whether HAND is already present or whether clinical data suggest risk for developing HAND. Worsening neurocognitive impairment may trigger consideration of antiretroviral modification when other causes have been excluded. The Mind Exchange program provides practical guidance in the diagnosis, monitoring, and treatment of HAND.

Keywords. AIDS dementia complex; HIV-associated dementia (HAD); HIV-associated neurocognitive disorder (HAND); HIV encephalopathy; neurocognitive impairment.

The Mind Exchange Working Group
Clinical Infectious Diseases 2013, 56(7): 1004–17

Which patients should be screened for HAND, and when? How often should patients be screened?

- **Assess all patients with HIV** (CEBM 5)
  - Can assist in treatment and management decisions, provide reassurance, and detect cognitive, behavioral and mood changes before symptoms arise or are acknowledged (CEBM 2b)
  - There is no rationale for screening only symptomatic patients (CEBM 2b)
- **Screen patients early in disease using a sensitive tool** (CEBM 5)
  - Screen within 6 months of diagnosis (CEBM 5)
- **Screen patients before initiation ART, if possible** (CEBM 5)
- **Screen every 6–12 months in higher-risk patients or every 12–24 months in lower-risk patients** (CEBM 5)

Clinical Infectious Diseases 2013; 56(7):1004-17

Impact on Clinical Resources can be Reduced by Targeting Higher Risk Patients

Evidence-supported risk factors	Risk Factor/Comorbidity for HAND and/or Non-HIV-Related NCI	Can Assist Identification of Patients: With Current HAND	At Risk of Developing HAND in Future	At Risk of Non-HIV-Related NCI	CEBM Levels (See Question Details for References)
Readily assessable in clinic					
Disease factors	Low nadir CD4+ T-cell count	X	X		CEBM 1b
	High plasma HIV RNA; high CSF HIV RNA	X	X		CEBM 2b
	Low current CD4 (pre-cART)	X	X		CEBM 2b
	Presence of past HIV-related CNS diseases	X	X		CEBM 1b
	Longer HIV duration	X	X		CEBM 2b
Treatment factors	Low cART adherence	X	X		CEBM 1b
	Episodes of cART interruption	X	X		CEBM 2a
	Nonoptimal cART regimen	X	X		CEBM 2a
	Short cART duration (related to treatment failure)	X	X		CEBM 1b
Comorbidities	Positive HCV serostatus with high HCV RNA	X	X	X	CEBM 1b
	History of acute CV event			X	CEBM 1b
	CV risk factors (hyperlipidemia, elevated blood pressure, chronic diabetes, and diabetes type II)			X	CEBM 1/2b
	Anemia and thrombocytopenia	X	X	X	CEBM 1/2b
Demographic factors	Older age	X	X	X	CEBM 1b
	Low level of educational achievement	X	X	X	CEBM 2b
	Ethnicity	X	X	X	CEBM 2b
	Sex (female, as associated with lower socioeconomic status in some countries)	X	X	X	CEBM 3a
	Lack of access to standard care; poverty	X	X	X	CEBM 3b
Other neurological and psychiatric factors	Neuropsychiatric disorders, eg, MDD, anxiety, PTSD, psychosis, bipolar disorder (current or history of)	X	X	X	CEBM 2b
	Illicit drug/alcohol abuse/dependence (current or history of)	X	X	X	CEBM 2a
	Syphilis or systemic infection	X	X	X	CEBM 2b
	Alzheimer's disease			X	Use APA (in press)
	Cerebrovascular disease			X	Use APA (in press)
	Traumatic brain injury and seizure	X	X	X	CEBM 2b
	Vitamin or hormone deficiency			X	Use APA (in press)
	Prior HCV coinfection*			X	CEBM 2b
Complex cART factors	Lower CPE	X	X		CEBM 2a
	cART neurotoxicity			X	CEBM 3b
Difficult to assess in clinic					
Biomarkers	Abnormal CSF neopterin	X			CEBM 2a
	Abnormal plasma HIV DNA	X			CEBM 2b
	Abnormal NFL	X			CEBM 2a
	Abnormal MCP-1	X			CEBM 2a
	Abnormal serum osteopontin	X			CEBM 4

- **Lower nadir or current CD4+ T-cells**
- **Higher HIV RNA**
- **Poor adherence**
- **Anemia**
- **Older age**
- **Vascular disease risk factors**

Clinical Infectious Diseases 2013; 56(7):1004-17

Screening for HIV-related neurocognitive impairment in clinical practice: Challenges and opportunities

T.J. Barber[a]*, D. Bradshaw[a,b], D. Hughes[c], L. Leonidou[a,d], A. Margetts[e], D. Ratcliffe[e], S. Thornton[e], A. Pozniak[a], D. Asboe[a], S. Mandalia[c], M. Boffito[a], N. Davies[f], B. Gazzard[a] and J. Catalan[e]

- "…we should not shy away from utilising different tests to understand the cognitive function of our HIV-infected patients but instituting widespread screening outside of clinical trials cannot currently be recommended."

AIDS Care, 2014 26(2): 160-168

A SMARTPHONE APP TO SCREEN FOR HIV-RELATED NEUROCOGNITIVE IMPAIRMENT

- Developed a smartphone-based screening tool, NeuroScreen, that includes an easy-to-use graphical user interface with 10 automated neurocognitive tests
- 50 HIV+ individuals were administered a gold-standard neurocognitive test battery and NeuroScreen, which briefly assesses individuals across 6 cognitive abilities on a large format smartphone (13.5 cm diagonal)
- High level of acceptability by both patients and providers
- **94% sensitivity to detect NCI; 64% specificity**
- Moderate to high correlations between individual NeuroScreen tests and paper-and-pencil tests (e.g., vs. global T-score $r = 0.61$, $p < 0.01$)

Robbins et al, Journal MTM 2014, 3:1:2336

CSF Viral Escape Occurs in Approximately 10% of Treated Patients

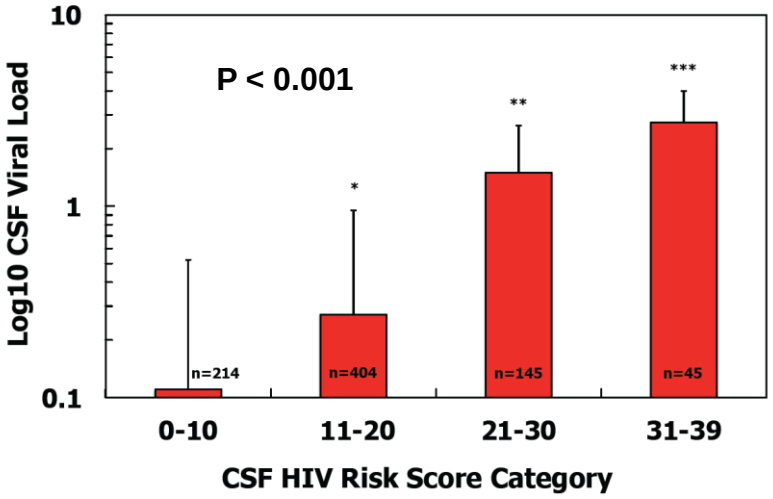
First Author	Sample Size	Percent with CSF VE	ART Correlates
Rawson[1]	142	**21%**	↓ CPE
Cusini[2]	60	**6.7%**	↓ CPE
Edén[3]	69	**11%**	Not ZDV
Perez-Valero[4]	1,264	**4.4%**	PI/r Use ATV Use
Pinnetti[5]	303	**10.6%**	ATV/r Use ABC+3TC Use
Edén[6]	373	**10%**	Not Noted
Weighted Median		**10.3%**	

[1]Rawson et al, Journal of Infection (2012) 65, 239e245; [2]Cusini et al, J Acquir Immune Defic Syndr 2013,62:28–35; [3]Eden et al, J Infect Dis 2010, 2010; 202(12):1819–1825; [4]Perez-Valero et al, J Intl AIDS Soc 2012, 15(Suppl 4):18189; [5]Pinnetti et al, CROI 2014, Abstract 443; [6]Eden et al, CROI 2014, Abstract 445

Published case series/reports of CSF Viral Escape:
Canestri et al, CID 2010; Peluso et al, AIDS 2012; Khoury et al, J Neurovirol 2013

The CSF Risk Score

- Cross-sectional analysis of 1,053 adults receiving combination ART assessed between 2004 and 2007
- Multivariable logistic regression model to identify correlates of CSF HIV RNA > 50 copies/mL
- Internal validation by 5-fold cross-validation and bootstrapping
- CSF HIV Risk Score developed by weighting regression units for retained variables as integer points

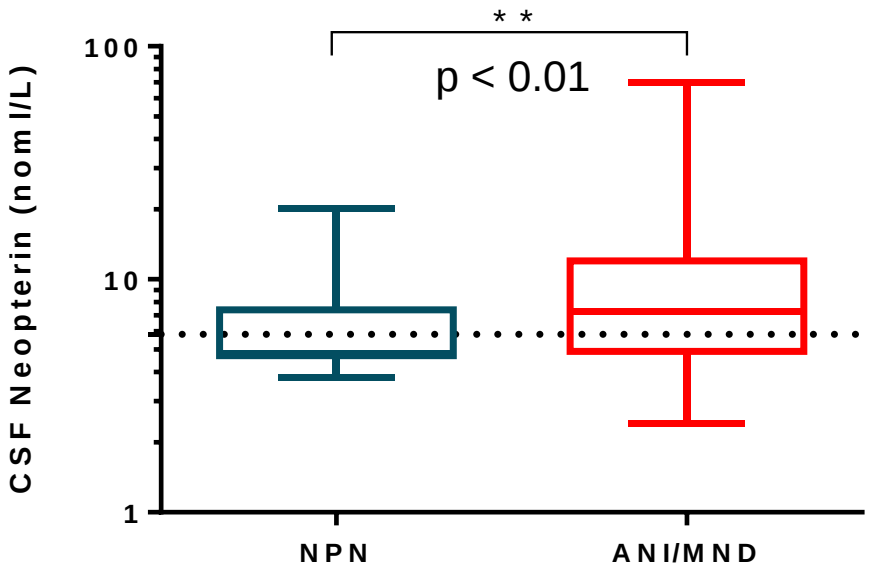


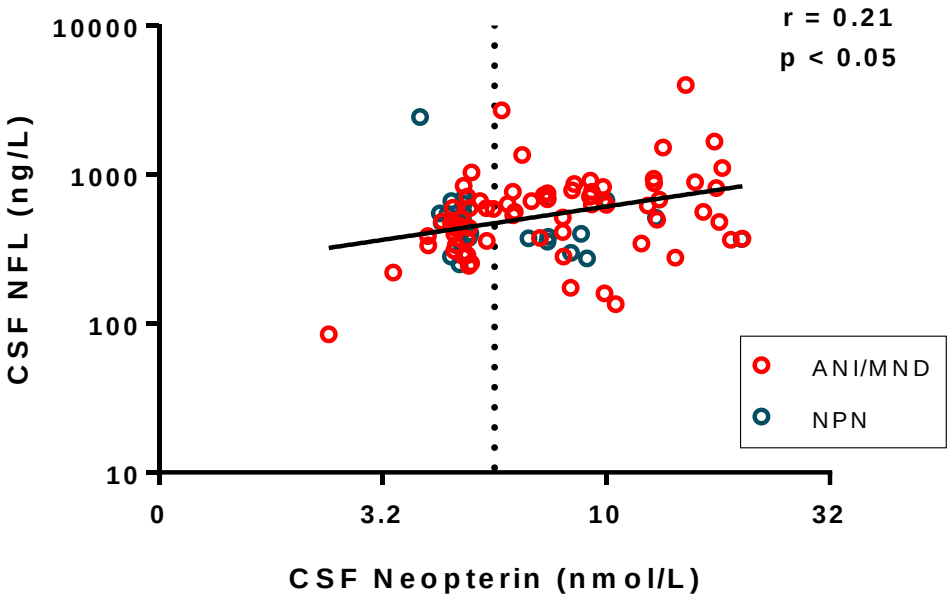
Hammond et al, CROI 2014, Abstract 509

Condition	Value	Odds Ratio	Risk Score
Race	White	1.00	0
	Black	1.81	3
	Other	2.39	4
Current MDD	No	1.00	0
	Yes	2.25	4
4-Day Adherence	≥ 95%	1.00	0
	85-94%	1.79	3
	< 85%	1.82	3
CPE Value		0.77	
	≥ 10		0
	5 – 9		6
	< 5		9
Plasma HIV RNA		4.88	
(copies/mL)	< 50		0
	50 – 199		2
	200-9999		10
	> 10,000		18
ART Duration		0.99	
(months)	> 36		0
	24 – 36		2
	13 – 24		3
	7 – 12		3
	< 6		4

ANI and MND is Associated with Higher Neopterin but not NFL

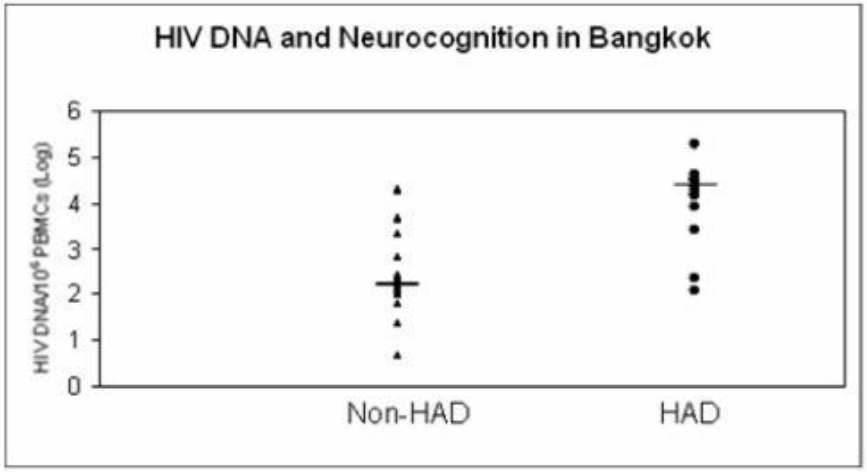
- Cross-sectional analysis of 100 HIV+ subjects taking suppressive ART without significant neuropsychiatric confounds
- Subjects were classified as NP-normal (NPN, n=79) or NP-impaired (ANI, n = 38; MND, n=33)



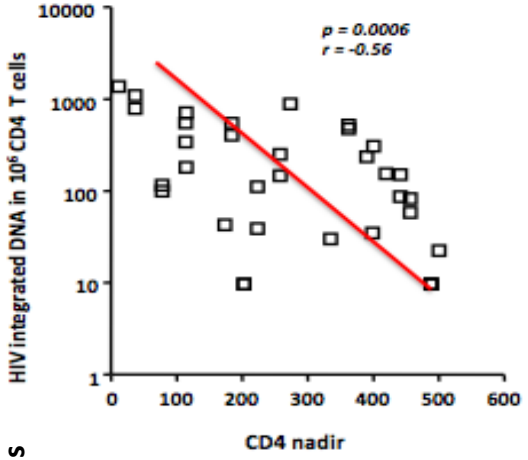


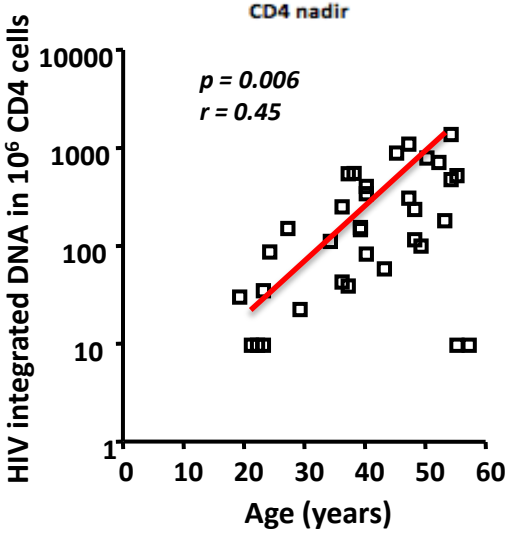
Edén et al, CROI 2014, Abstract

Higher HIV DNA Content is Associated with Older Age, Lower CD4 Nadirs, CMV, and Neurocognitive Impairment



Shiramizu et al, Int J Med Sci 2006, 6;4(1):13-8





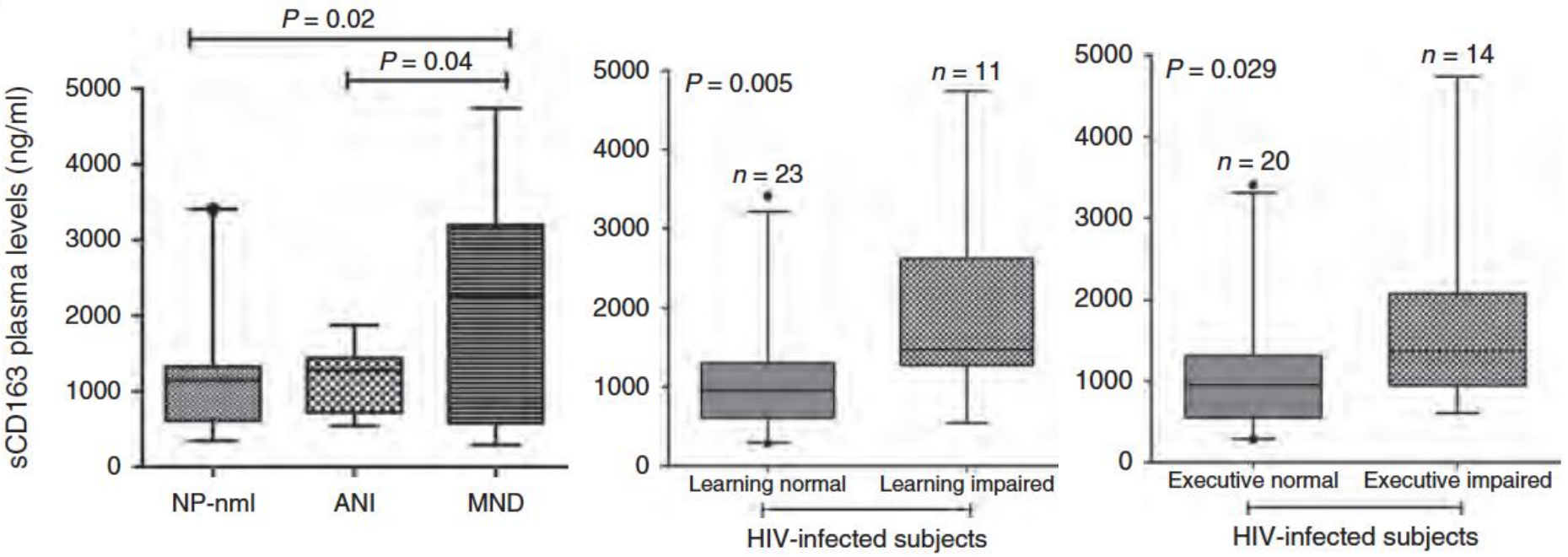
Boulassel, Routy et al. J Clin Virol 2012, 53: 29– 32
Graphs Courtesy Jean-Pierre Routy, McGill Univ.

Multivariable Regression of HIV DNA in PBMCs

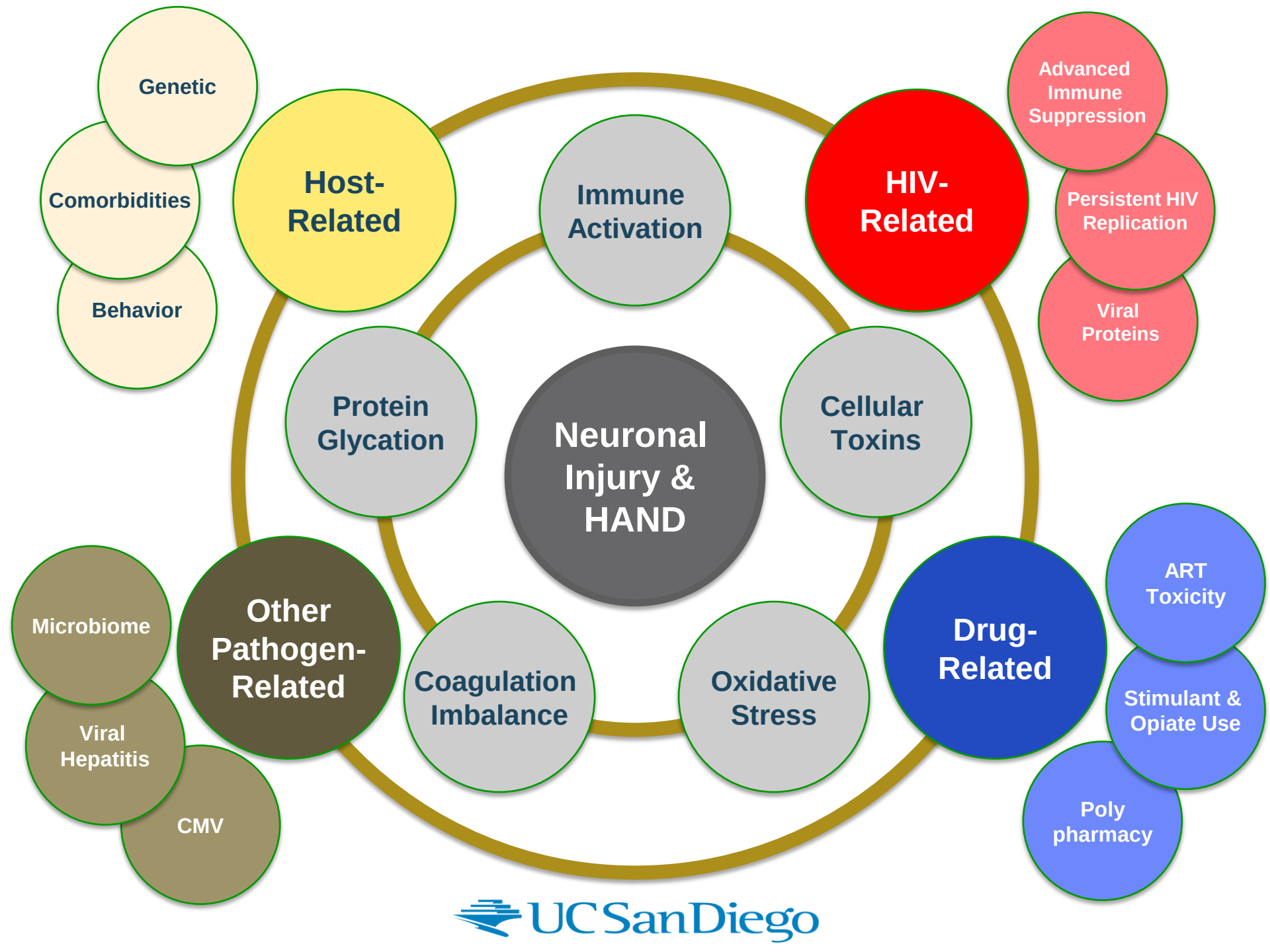
	Multivariate Regression, All Samples	
Variable	Estimate (95% CI)	P
Presence of CMV in PBMCs	.28 (.001–.56)	.049
Presence of CMV in semen	…	
Longer interval since HIV infection (mo)	.01 (–.00003 to .02)	.051
HIV RNA load (log_{10} copies/mL)	…	
$CD4^+$ T-cell count (cells/mm^3)	…	
100% match with detection probe	.83 (.39–1.27)	<.001

Gianella et al, J Infect Dis 2013, 207: 898–902

Soluble CD163 in Plasma is Associated with Impaired Learning and Executive Functioning



Burdo et al, AIDS 2013, 27:1387–1395


Genetic
Comorbidities
Behavior
Host-Related
Immune Activation
HIV-Related
Advanced Immune Suppression
Persistent HIV Replication
Viral Proteins
Protein Glycation
Neuronal Injury & HAND
Cellular Toxins
Microbiome
Viral Hepatitis
CMV
Other Pathogen-Related
Coagulation Imbalance
Oxidative Stress
Drug-Related
ART Toxicity
Stimulant & Opiate Use
Poly pharmacy
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How should I approach screening for comorbidities that may influence the accuracy of the HAND diagnosis?

- **Infections other than HIV**
  - Syphilis, opportunistic infections and other HIV-related CNS disorders (CEBM 2b)
  - HCV co-infection and associated liver disease may worsen HAND (CEBM 2b, 5)
- **Prescription drugs** (CEBM 2b)
  - Drugs with anticholinergic properties
  - Polypharmacy/drug interactions
- **Psychiatric illnesses and substance abuse** (CEBM 1b)
  - Particularly major depression, anxiety, and post-traumatic stress disorder

Clinical Infectious Diseases 2013; 56(7):1004-17

How should I approach screening for comorbidities that may influence the accuracy of the HAND diagnosis?

- **Cerebrovascular disease and metabolic syndrome** (CEBM 1b)
  - Particularly in patients who have long-standing HIV disease
- **Other chronic neurological disorders**
  - Traumatic brain injury (CEBM 1b), seizures (CEBM 2b), and Alzheimer's disease (CEBM 1b)
- **Vitamin or hormone deficiency** (CEBM 2b)
  - Red cell folate (CEBM 5), vitamin B12 (CEBM 2a), testosterone (CEBM 1b) and thyroid function (CEBM 2b)

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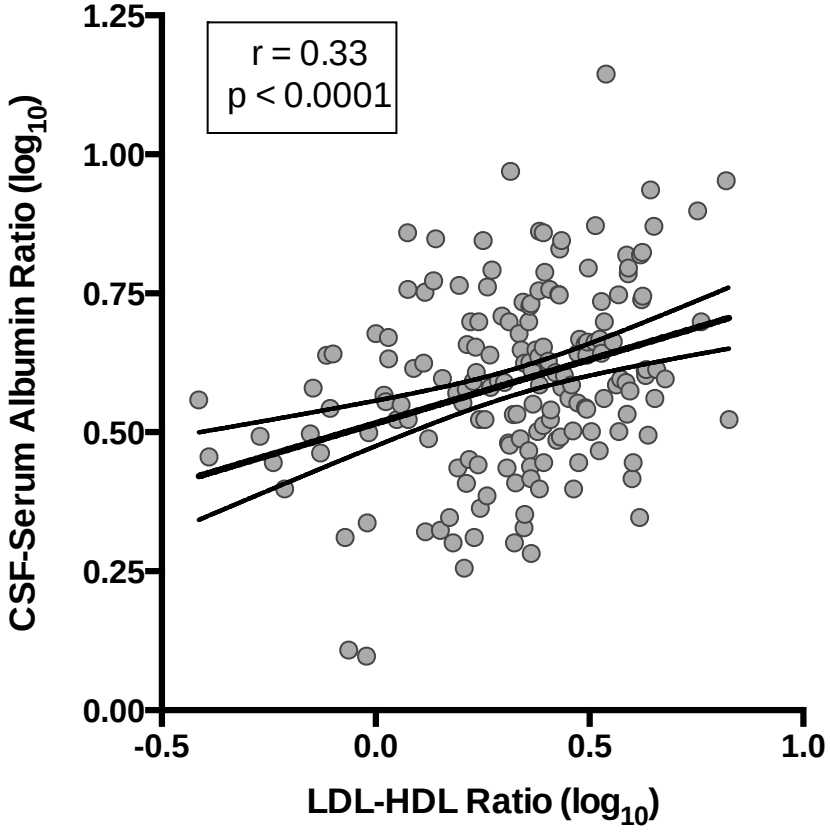
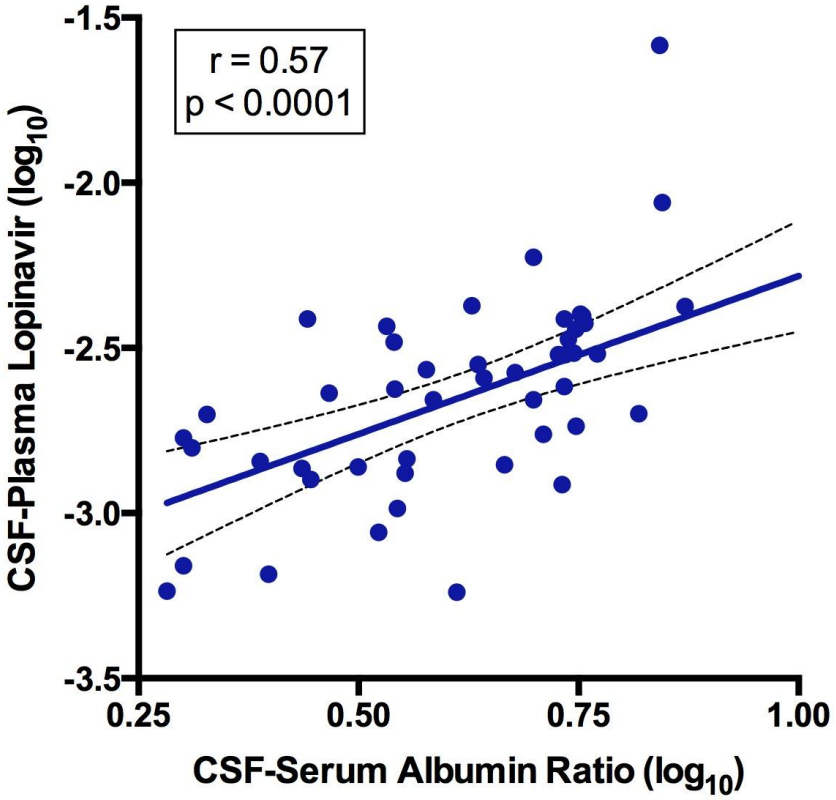
Clinical Infectious Diseases 2013; 56(7):1004-17

Lipid Profiles are Associated with BBB Permeability, Which is Associated with Drug Distribution into CSF





Advances in Prevention (and Treatment)

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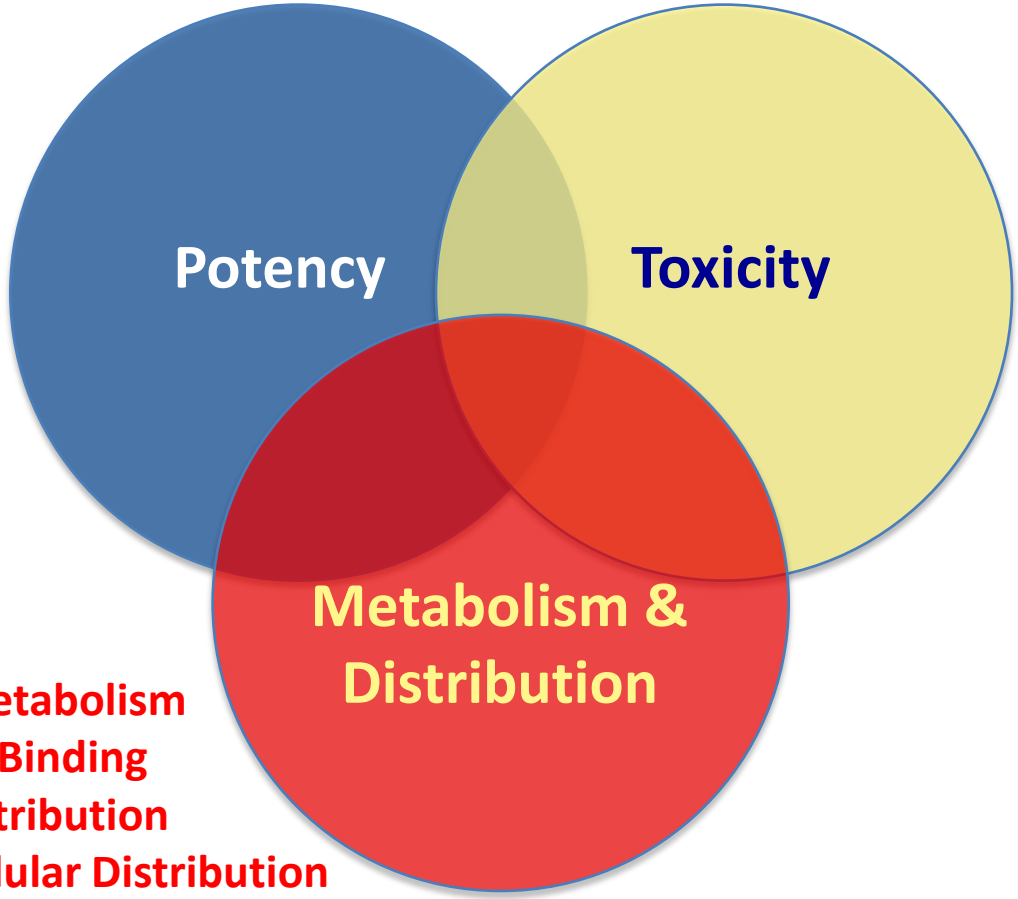
Multiple Characteristics Influence ART Effectiveness in the Central Nervous System

- **Suppression of HIV Replication**
  - Lymphocytes
  - Monocytes & Macrophages
- **Immune Recovery**



- **Neurotoxicity**
  - Central NS
  - Peripheral NS
- **Hepatotoxicity**
- **Renal Toxicity**
- **Metabolic & Vascular Disorders**

- **Slow Metabolism**
- **Protein Binding**
- **CNS Distribution**
- **Intracellular Distribution**
- **Molecular Transporters**

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Ideal **Characteristics of Analyses of CNS Effectiveness of ART**

- Studies should be randomized and longitudinal
- Power and duration should be sufficient
- Assessments should be standardized and comprehensive
- Drug regimen potency and toxicity should be similar
  - For those that focus on CPE, regimens should have the same number of drugs

Recent Reports Have Mixed Findings

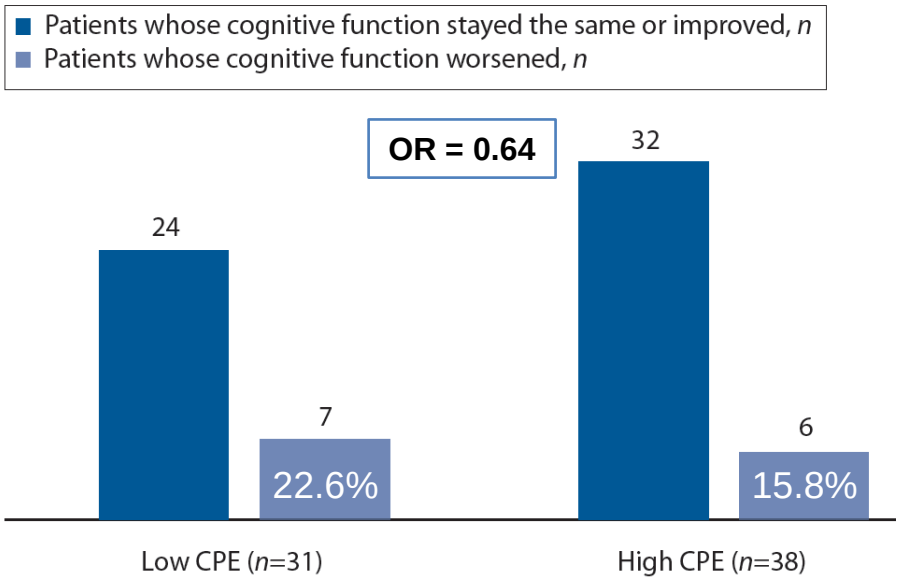
		N	NP	Duration	Principal Finding	Notes
Ciccarelli[1]	C-S	101	C	-	Beneficial	2010 version stronger than 2008 version
Ciccarelli[2]	C-S	215	C	-	Beneficial	Adjusted CPE using GSS
Casado[3]	C-S	69	B	-	Trend toward benefit	Beneficial when CD4 < 200
Vassallo[4]	L	96	C	22 months	Beneficial	~25% were not virologically suppressed
Cross[6]	L	69	C	~1 year	No association	Binary transformation only
Ellis[5]	RCT	49	C	16 weeks	No association	Beneficial in subgroup
Wilson[7]	C-S	118	B	-	Detrimental on 2 tests	Binary transformation only Substance users only
Kahouadji[8]	C-S	93	B	-	Detrimental on 1 test	Methodological flaws
Caniglia[9]	L	61,938	N	-	Detrimental	Absolute risk 1.1% vs. 0.9%

C-S = Cross-sectional, L = Longitudinal, RCT = Randomized clinical trial, C = Comprehensive, B = Brief, N = None, GSS = Genotype Susceptibility Score

[1]Ciccarelli et al, Antiviral Therapy 2013, 18: 153-160; [2]Ciccarelli et al, 20th CROI 2013, Abstract 405; [3]Casado et al, J Neurovirol 2014, 20: 54-61; [4]Vassallo et al, AIDS 2014, 28(4):493-501; [5]Ellis et al, Clin Infect Dis. 2014;58(7):1015-22; [6]Cross et al, S Afr Med J 2013;103(10):758-762; [7]Wilson et al, J Clin Experim Neuropsych 2013, 35:915-25, *[8]Kahouadji et al, HIV Medicine 2013, 14: 311-5.*

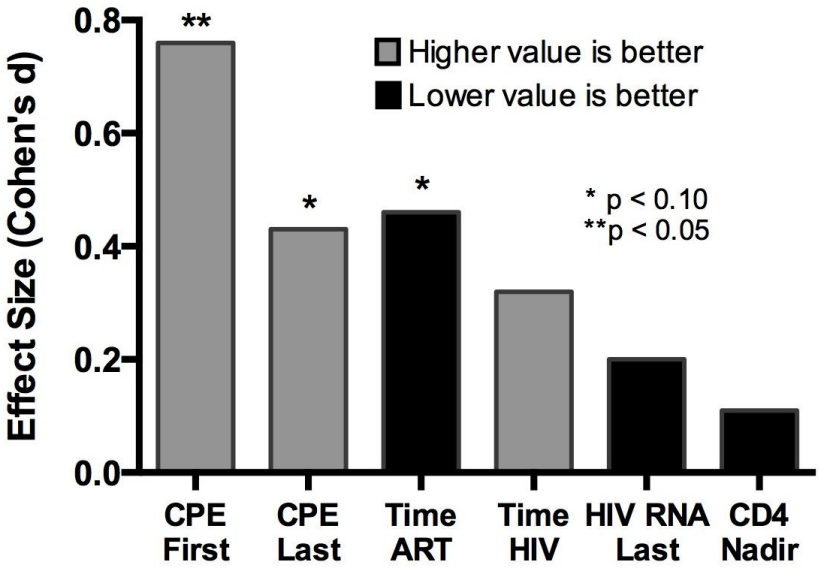
Two Uncontrolled Longitudinal Studies Found Similar Effect Sizes but Came to Different Conclusions

South Africa
(Subtype C)



Cross et al, S Afr Med J 2013;103(10):758-762
Odds ratio is calculated from data in the manuscript

France
(Subtype B)



Vassallo et al, AIDS 2014, 28(4):493-501
Graph is adapted from Table 2

Odds ratios from multivariable regression:

- Initial (first) CPE: 0.54
- End-of-follow-up (last) CPE: 0.65

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The relationship of CPE to HIV dementia

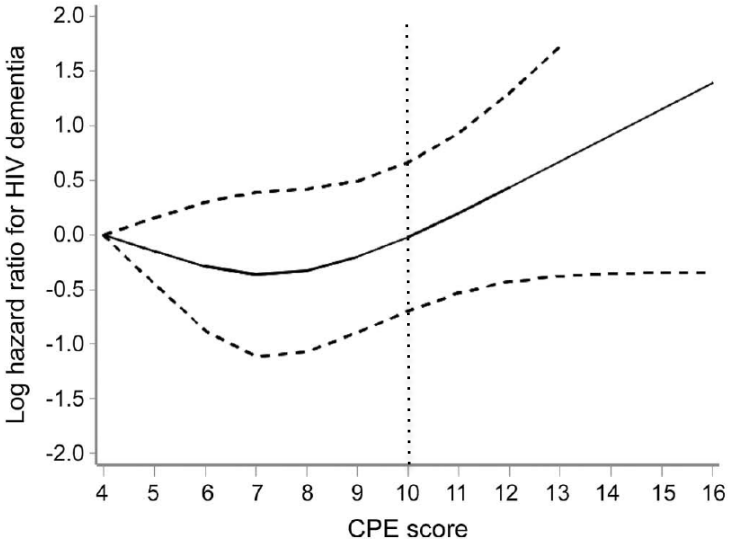
Slain by an ugly fact?

Design

- Data from 61,938 patients combined from 9 independent HIV cohorts from Europe and the U.S.
- Patients were evaluated prior to ART initiation between 1998 and 2013
- “Intent-to-treat” analysis
- CPE transformed into 3 categories
  - “Low”: ≤ 7
  - “Medium”: 8-9
  - “High”: ≥ 10

Findings

- 235 “HAD” events in 259,858 person-years of follow-up
  - 1 per 1106 person-years
- “High” CPE group had a 74% increased hazard ratio of “HAD”



Caniglia et al, Neurology 2014;83:1–8; Berger & Clifford, Neurology 2014;83:1–2

The relationship of CPE to HIV dementia

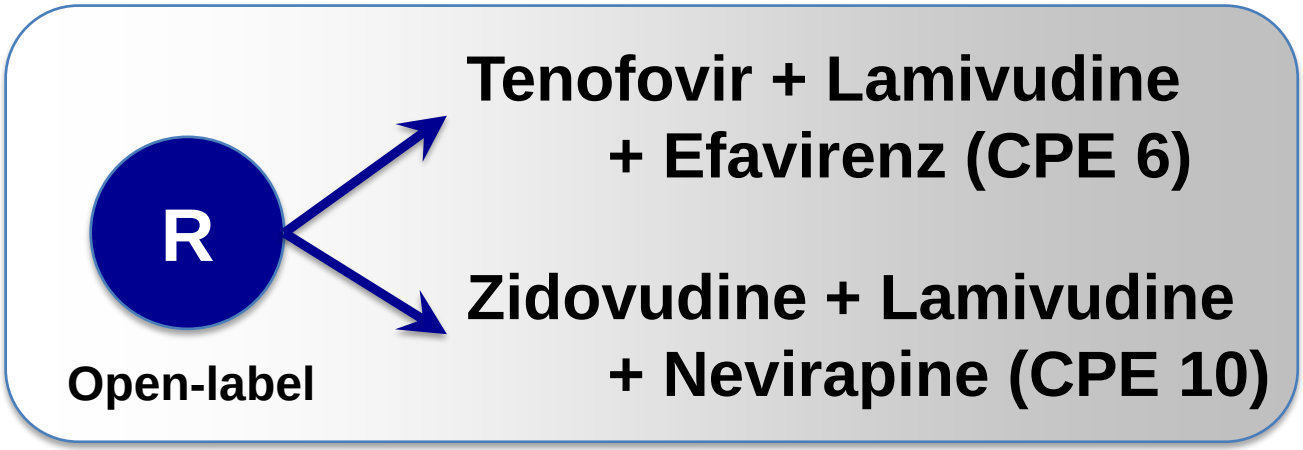
Slain by an ugly fact?

- **Did not use standardized assessments for diagnosing "HAD"**
  - "…diagnostic procedures that reflect standard clinical practice"
- **The categorical transformation of CPE is unusual**
  - Only 8.8% were in the "high CPE" group
  - No statistically significant association was found with CPE when analyzed continuously or as a 4-category variable
- **The between-group difference in absolute risk is not clinically meaningful:** 1 "HAD" case per > 4,000 person-years of follow-up
- **Does not account for factors that were associated with:**
  - **Changes in ART over time: 68% changed their initial regimen during observation**
  - "High" CPE regimens: more than 3 antiretroviral drugs, initiation of ART prior to 2004
  - Non-HIV causes of neurocognitive disease: psychiatric disease, substance use, co-infections

Caniglia et al, Neurology 2014;83:1–8; Berger & Clifford, Neurology 2014;83:1–2

Clinical Trial of CNS Penetrating ART to Prevent NeuroAIDS in China

249 HIV+ Adults
ART Naive, CD4 < 350/mm^3
Normal Neurocognitive Performance



Follow-up: 96 Weeks
Safety Assessments
Neurocognitive Testing, Functional Assessment
Pharmacogenetics
Immune Activation Biomarkers

Treatment Arms were Comparable at Baseline

	ZDV-3TC-NVP	TDF-3TC-EFV	p Value
Sample Size	127	122	-
Age (years)	32.9 (7.7)	31.9 (8.3)	0.19
Male Gender	124 (97%)	122 (100%)	0.12
AIDS Diagnosis	83 (66%)	81 (68%)	0.89
HIV RNA, Plasma (log_{10} c/mL)	4.2 (0.8)	4.2 (0.9)	0.95
CD4+ T-cells (/mm^3)	235.1 (89.8)	222.1 (83.6)	0.32
CD4+ T-cells < 200/mm^3	32%	32%	1.00
HCV Seropositive	3 (2%)	3 (2%)	1.00
HBV Core Antibody Positive	62 (49%)	58 (48%)	0.70
Hemoglobin (g/dL)	14.7 (1.1)	14.8 (1.2)	0.31
Serum Albumin (g/dL)	4.7 (0.3)	4.7 (0.4)	0.16
Global Deficit Score	0.12 (0.15)	0.14 (0.14)	0.15
Beck Depression Inventory	9.8 (7.6)	9.7 (8.3)	0.50

ZDV-3TC-NVP Was Associated with Substantially More Adverse Events

All Adverse Events

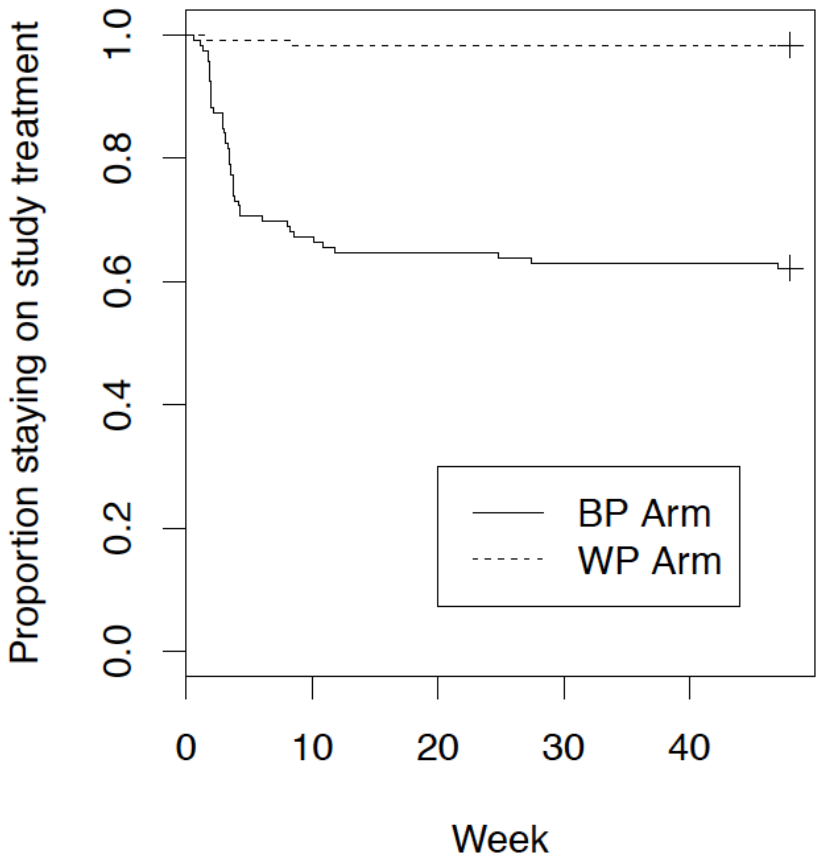
(Some subjects had more than one)

	ZDV-3TC-NVP	TDF-3TC-EFV	Total
Anemia	10	0	10
Hepatotoxicity	43	23	66
Leukopenia	24	5	29
Thrombocyto-penia	6	5	11
Rash	26	4	30
Fever	14	3	17
CNS/Psychiatric	0	1	1
Other	17	14	31
Total	140	55	195

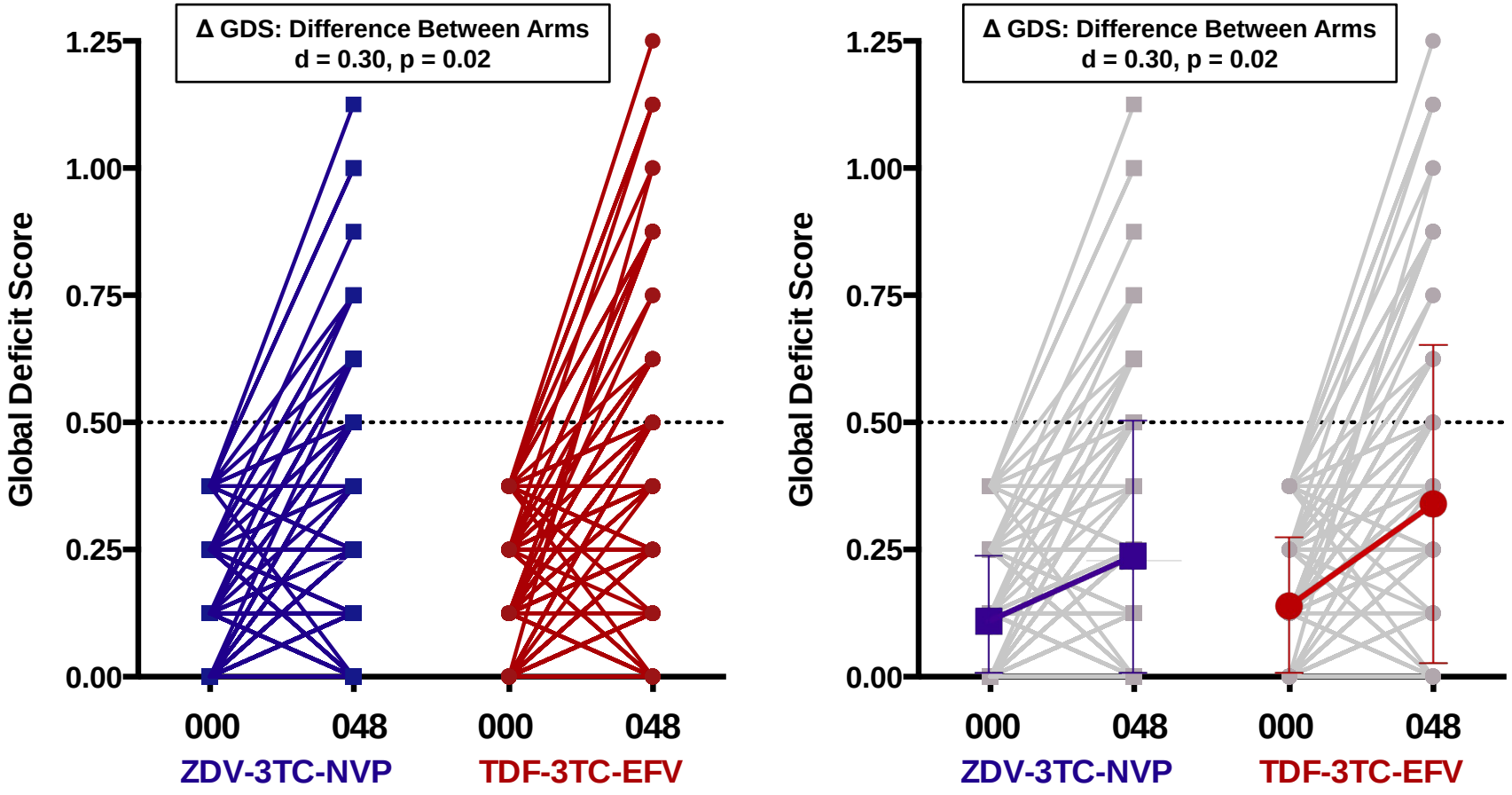
Discontinuation of Study Drug

ZDV-3TC-NVP: 46 (36%)

TDF-3TC-EFV: 2 (2%)

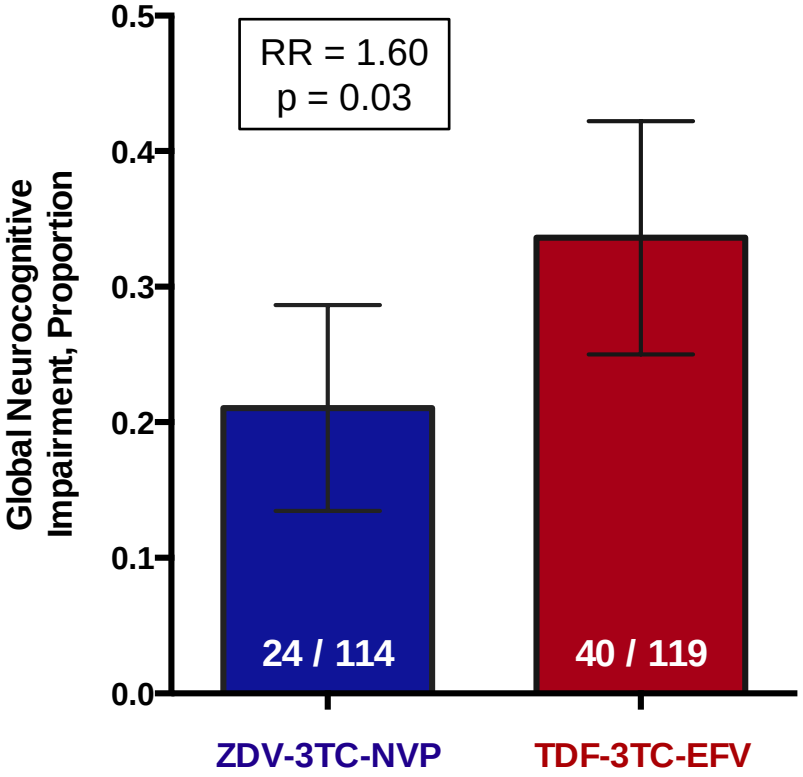


TDF-3TC-EFV Was Associated with More Neurocognitive Worsening

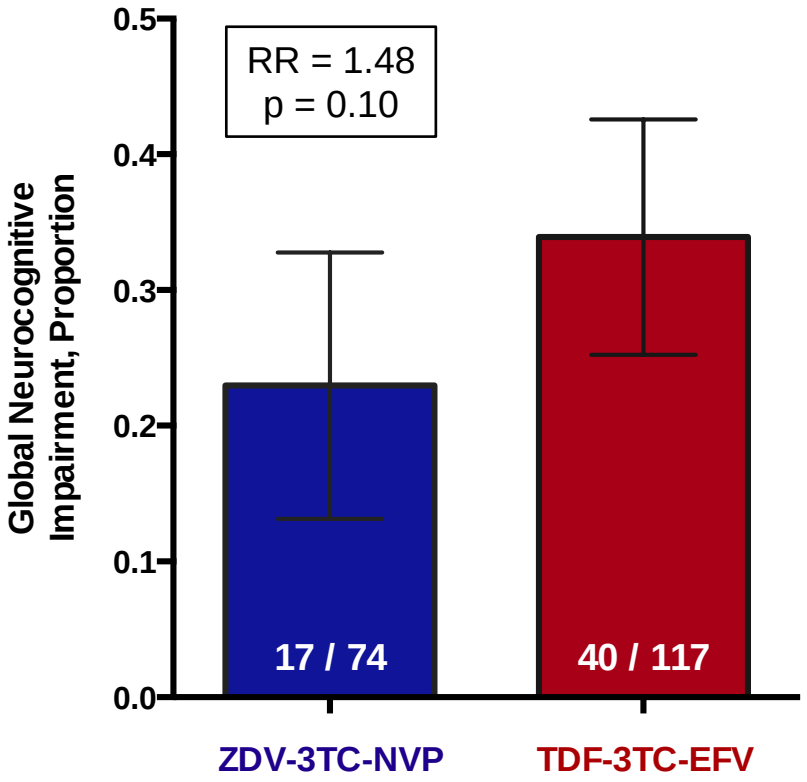


Intent-to-Treat, Completer Analysis, N = 239

TDF-3TC-EFV Was More Frequently Associated with Neurocognitive Impairment at 48 Weeks

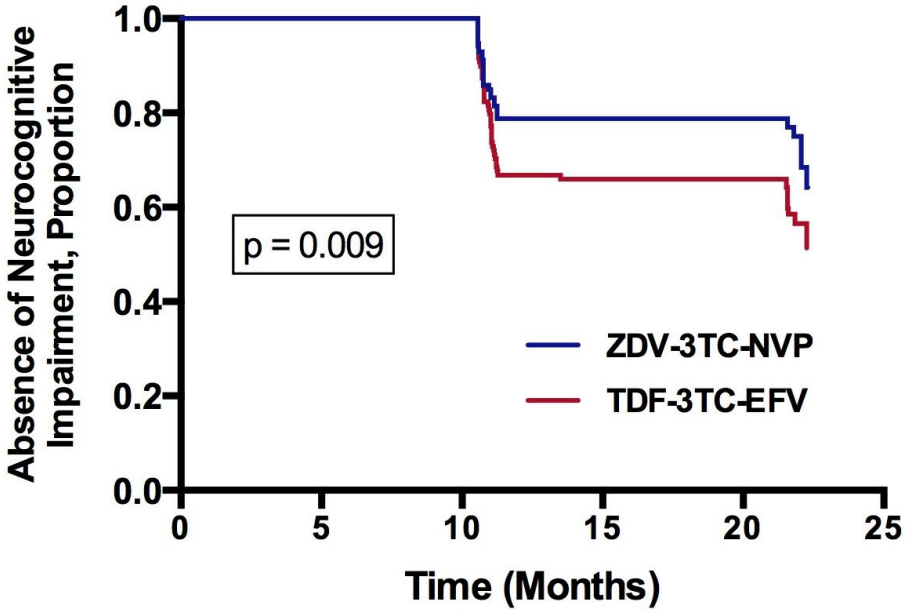


Intent-to-Treat, Completer Analysis N = 239

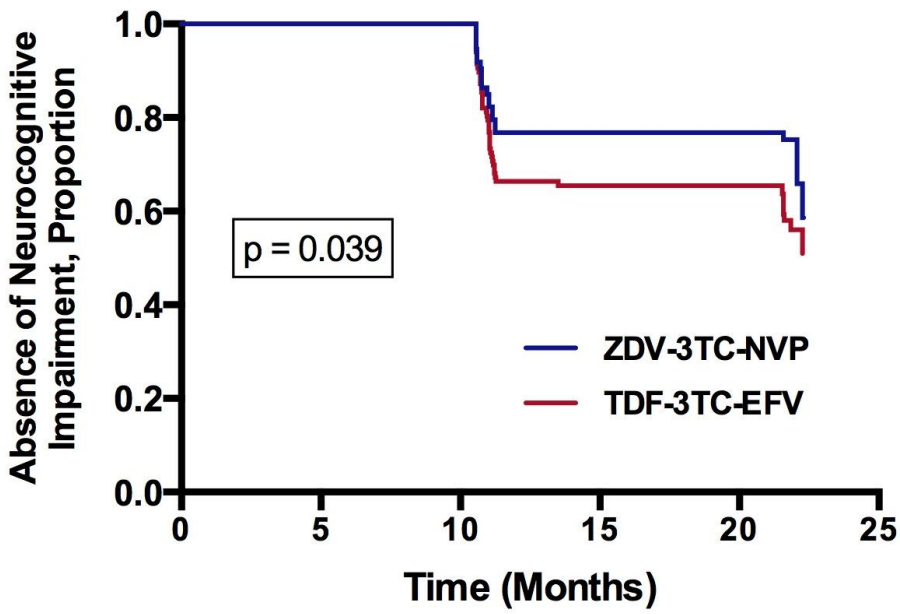


As Treated N = 191

TDF-3TC-EFV Was Associated with Shorter Time-to-Impairment



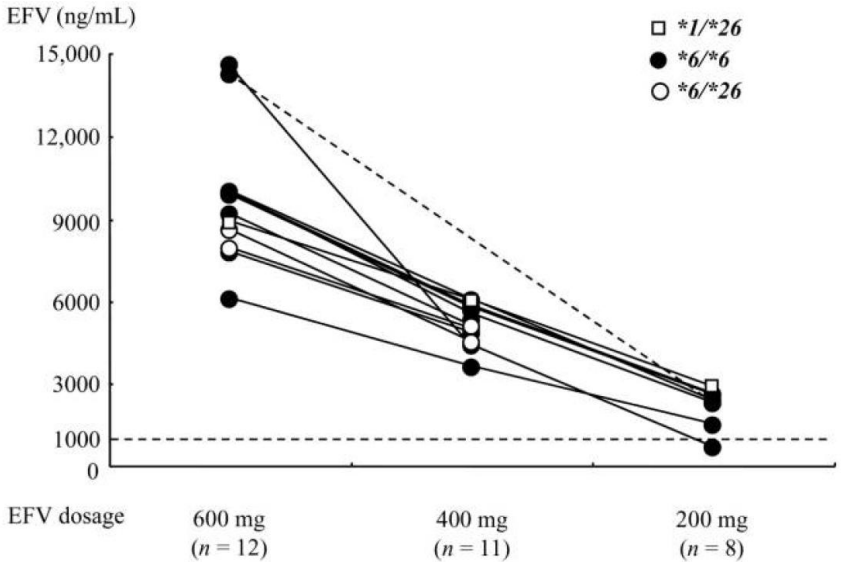
Intent-to-Treat, Completer Analysis N = 239



As Treated N = 191

The Lawrence Tree, Georgia O'Keeffe, 1929

Chronic Efavirenz Neurotoxicity May Improve with Dose Reduction



Symptom	No. (%) of subjects who reported symptom status during efavirenz treatment		
	Present[a] (n = 14)	Improved[b]	Disappeared[b]
Dizziness	8 (57)	8 (100)	4 (50)
Strange dreams	7 (50)[c]	7 (100)[c]	0 (0)
Depression	5 (36)	5 (100)	1 (20)
Irritability	5 (36)	5 (100)	1 (20)
Concentration problem	4 (29)	4 (100)	2 (50)
Sleep difficulty	3 (21)	3 (100)	0 (0)
Any of the above	10 (71)[c]	10 (100)[c]	4 (40)

UC San Diego

Gatanaga et al, Clinical Infectious Diseases 2007; 45:1230–7

DHHS Preferred Regimens (ART Naive)

TDF-FTC	EFV
	ATV/r
	DRV/r
	RAL
	EVG/c
	DTG
ABC-3TC	DTG

Last updated 30 October 2013; Available at http://www.aidsinfo.nih.gov/guidelines

DHHS Preferred Regimens (ART Naive)

TDF-FTC	EFV	• Short- and long-term neurotoxicity in some
	ATV/r	• CSF concentrations do not exceed inhibitory concentrations in some • May increase risk of CSF viral escape
	DRV/r	• CSF concentrations exceed 50% inhibitory concentrations in all
	RAL	• CSF concentrations exceed 50% inhibitory concentrations in all
	EVG/c	• No CSF pharmacokinetic data
	DTG	• CSF concentrations exceed 50% inhibitory concentrations in all • Fewer CNS side effects than EFV
ABC-3TC	DTG	• No CSF ABC pharmacokinetic data on daily dosing

Last updated 30 October 2013; Available at http://www.aidsinfo.nih.gov/guidelines

Guidelines to Consult in the Clinic

US DHHS

- Earlier initiation of ART may prevent subsequent brain dysfunction
- Does not discuss CPE or "CNS-active" ART

EACS

- Use "CNS-active" ART for patients with HIV-associated cognitive impairment, particularly with CSF viral escape

Mind Exchange

- **Without HAND:** No evidence supports use of higher CPE ART
- **With HAND:** Higher CPE ART generally asso-ciated with better neurocognitive functioning but evidence base is limited

BHIVA

- "CPE score should not influence therapeutic decisions in subjects with neurocognitive impairment commencing ART"

DHHS Guidelines: Available at http://www.aidsinfo.nih.gov/guidelines; Last updated 30 October 2013; EACS Guidelines: Available at http://eacsociety.org/Portals/0/Guidelines_Online_131014.pdf; Last updated October 2013; Mind Exchange: Clin Infect Dis. 2013;56(7):1004-17; BHIVA Guidelines: Available at http://www.bhiva.org/TreatmentofHIV1_2012.aspx; Last updated November 2013

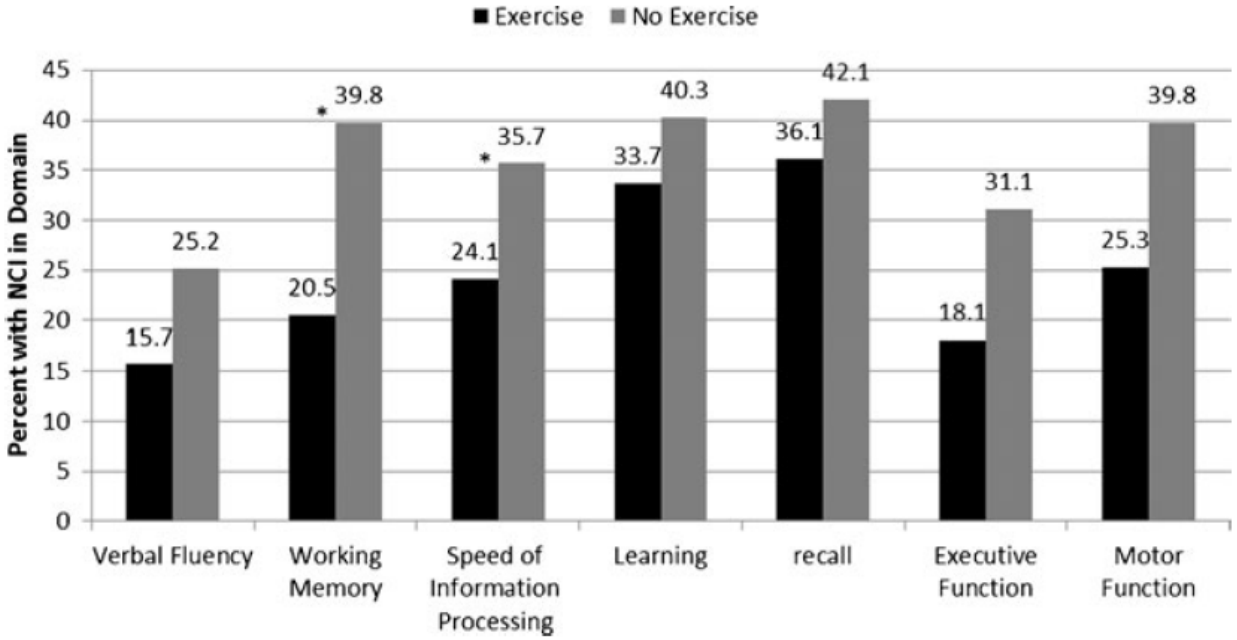
Older Americans: The Changing Face of HIV/AIDS in America

U.S. Senate Hearing, 18 Sept 2013

- Diet and exercise are currently the best intervention to prevent early onset of comorbidities & inflammation
- Early start of vigorous exercise
  - 250+ minutes a week of vigorous aerobic exercise
- Diet resembling a Mediterranean diet
  - Fish, chicken, vegetables, fruit, beans, nuts

Reported by NATAP.org, 21 September 2013

Exercise is Associated with Less Neurocognitive Impairment

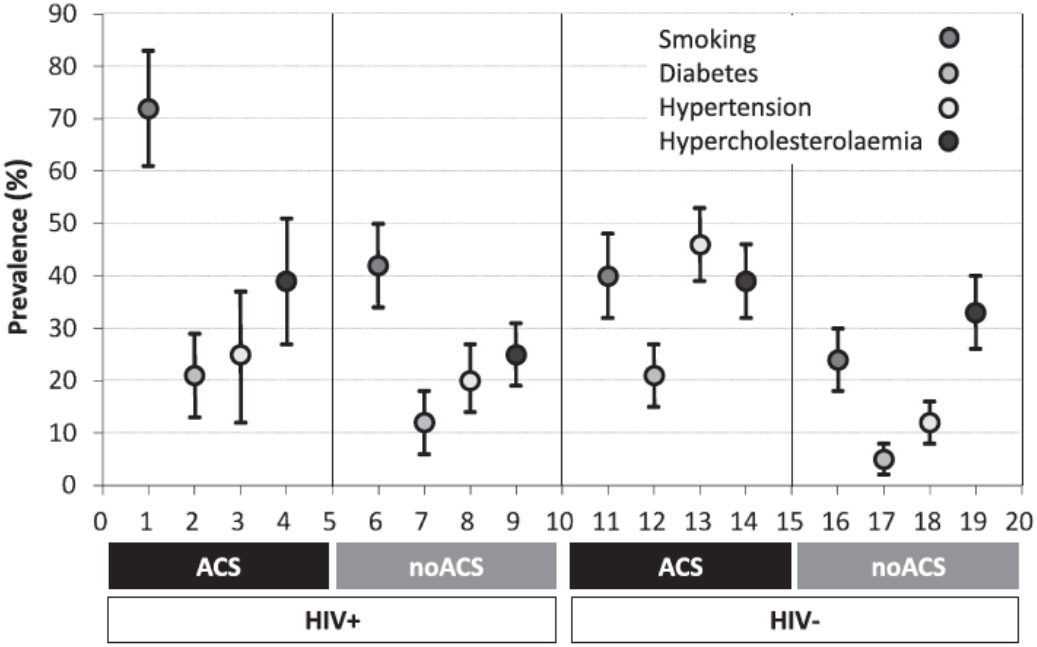


- 335 HIV+ adults enrolled in a cohort study completed a comprehensive neurocognitive battery and self-report of activity that increased heart rate in the last 72 hours
- Exercisers had lower odds of having global neurocognitive impairment (odds ratio = 0.38, $p < 0.05$) on multivariable analysis

Dufour et al, J Neurovirol 2013, DOI 10.1007/s13365-013-0184-8

Smoking May Play a Particularly Prominent Role for ACS in PLWH

- 569 adults in 2 parallel cohorts
- Risk factors for acute coronary syndrome
  - **PLWH:** Smoking and family history of CVD
  - **HIV seronegative:** Smoking, diabetes, and hypertension

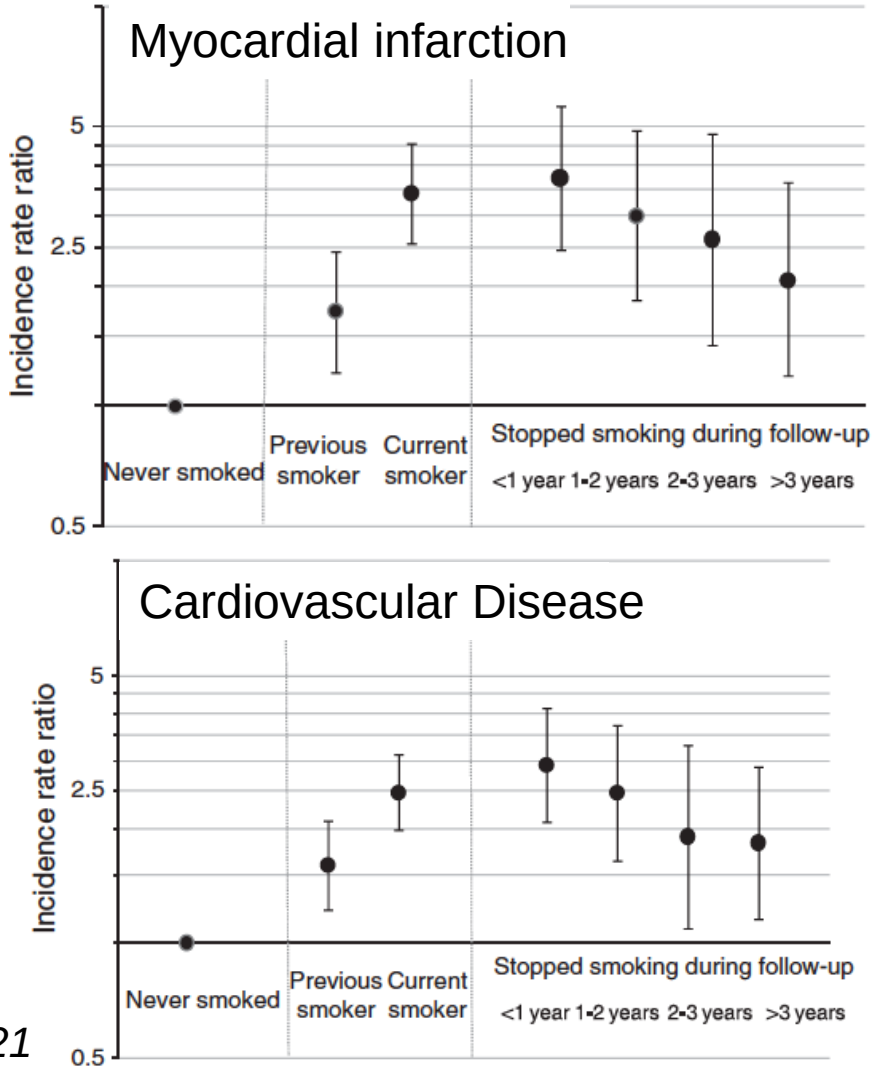


- Attributable risk for smoking was 54.4 vs. 30.6

Calvo-Sanchez et al, HIV Medicine (2013), 14: 40–48

Stopping Smoking Reduces Risk for Cardiovascular Events

- More than 27,000 patients had a total of 3,680 CVEs or mortality
- Adjusted incidence rate ratio in patients who stopped smoking decreased from 2.3 within the first year to 1.5 after > 3 years compared with those who never smoked



Petoumenos et al, HIV Medicine 2011, 12:412–421

Summary

- **Screening and diagnosis of HAND can be performed in the clinic using simple and inexpensive methods**
  - Tablet-based Neuroscreen may be a valuable tool
  - Opinions on the clinical value of screening vary
- **Opinions on management of HAND vary**
  - Initiation of suppressive ART is important
  - Some ART drugs appear to support neurocognitive health better than others
  - Management of other conditions that affect the CNS is critical, including metabolic and vascular disorders