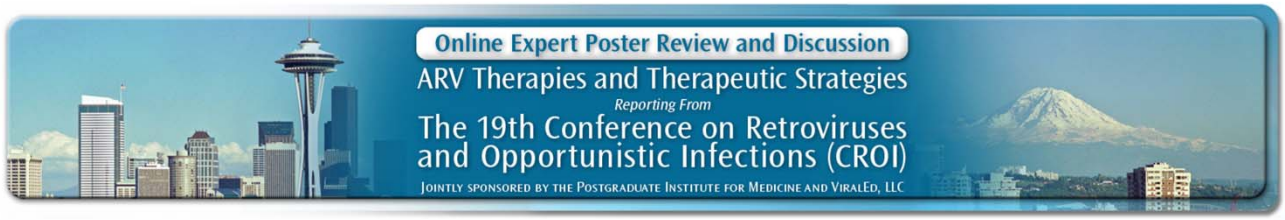

Asymptomatic HIV-associated Neurocognitive Disorder (ANI) Increases Risk for Future Symptomatic Decline: A CHARTER Longitudinal Study

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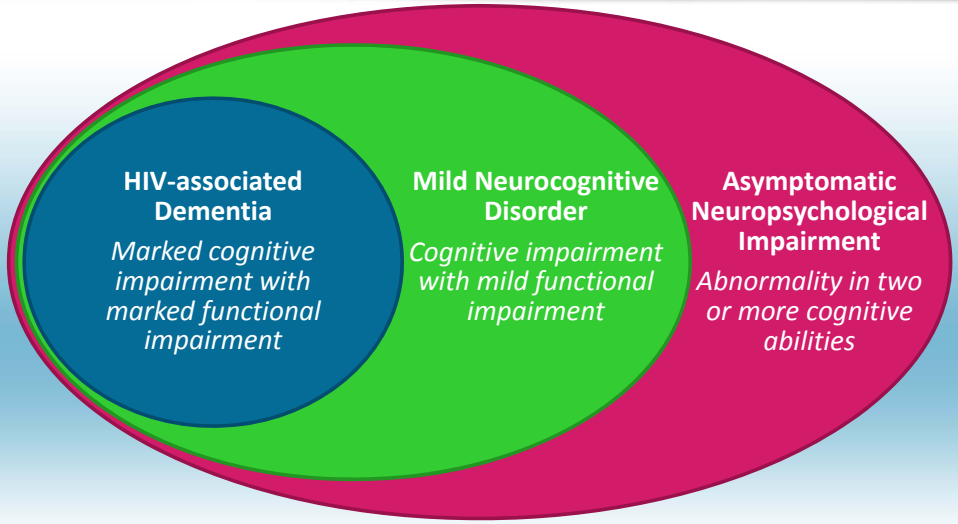
Abstract # 77

Background and Aim

- Despite combination ARV therapy (CART) HIV-associated neurocognitive disorders (HAND) have been reported in 30% - 50% HV+ person
- Asymptomatic neurocognitive impairment (ANI) is the most common HAND diagnosis (eg., 33% of 1555 CHARTER cases)*
- Concerns re ANI: since ANI does not affect everyday function, is it relevant? Does it have concurrent or predictive validity?
- **Aim:** To determine if ANI confers risk of progression to symptomatic HAND

*Heaton et al., 2010

HIV Associated Neurocognitive Disorder (HAND): Frascati Criteria



Antinori, et al, Neurology 2007

Participants

- 347 longitudinal CHARTER participants with up to 90 months of follow-up (media 45.2 months)
  - **226 NML Cases:** No neurocognitive impairment and no self-reported or observed declines in everyday functioning
  - **121 ANI Cases:** Neurocognitively impaired, but no self-reported or observed declines in everyday functioning
- Participants completed neuromedical, laboratory, neurocognitive, and both self-report and performance-based measures of everyday functioning approximately every 6 months

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Baseline Comparison of ANI and NML: Background Characteristics

	NML (n=226)	ANI (n=121)	*P*-value
Age	43.0 (8.6)	44.8 (8.0)	
Education	12.9 (2.4)	13.5 (2.2)	.04
% Male	81.9%	81.8%	
% Caucasian	45.6%	46.3%	
% Lifetime Substance Dx	71.2%	69.4%	
% with Comorbidity	22.6%	44.6%	<.0001

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Baseline Comparison of ANI and NML: Disease Characteristics

	NML (n=226)	ANI (n=121)	*P*-value
% AIDS	56.2%	62.8%	
Current CD4	459 [290-669]	425 [286-578]	
Nadir CD4	201 [61-370]	162 [38-273]	.03
% on ART	66.2%	72.7%	
Est. Duration HIV+ (months)	117.7 (75.0)	120.7 (81.6)	
% HCV+	20.4%	27.3	

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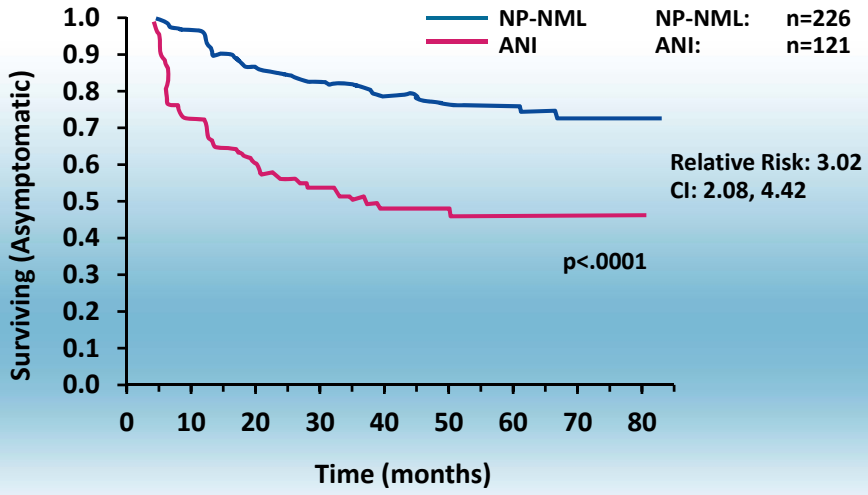
ANI Increases Risk for Symptomatic HAND: Self-report or Performance-based



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Baseline Predictors of Decline to Symptomatic HAND (SR or PB)

	No Decline (n=237)	Decline (n=110)	*P*-value
Background Factors			
Age	42.6 (8.7)	45.7 (7.4)	.002
Education	13.2 (2.3)	12.6 (2.2)	.007
% Male	86.9%	70.9%	.0003
% Lifetime Substance Dx	65.8%	80.9%	.004
% with Comorbidity	24.9%	41.8%	.001
Disease Factors			
% AIDS	54.4%	67.3%	.02
Nadir CD4	204 [56-378]	163 [55-277]	.03
% HCV+	18.1%	32.7%	.003

Ethnicity, on/off ART, current CD4, and estimated duration of HIV infection were non-significant

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Time-dependent Correlates of Decline to Symptomatic HAND

	Univariable		Multivariable	
Self-report	***P*-value**	**RR**	**95% CI**	***P*-value**
ANI vs. NML	.007	2.81	1.65, 4.76	.0001
Current MDD	.011	3.00	1.56, 5.77	.001
Performance-based	***P*-value**	**RR**	**95% CI**	***P*-value**
ANI vs. NML	<.00001	5.17	3.19, 8.39	<.00001
Current MDD	.0014	1.21	1.08, 1.35	.0006
SR or PB	***P*-value**	**RR**	**95% CI**	***P*-value**
ANI vs. NML	<.00001	3.41	2.33, 5.00	<.00001
Current MDD	.033	1.01	1.01, 5.77	.021

- ART treatment, regimen type, CNS penetration effectiveness score, plasma viral load, CSF viral load, and current substance use diagnoses were non-significant in univariable analyses

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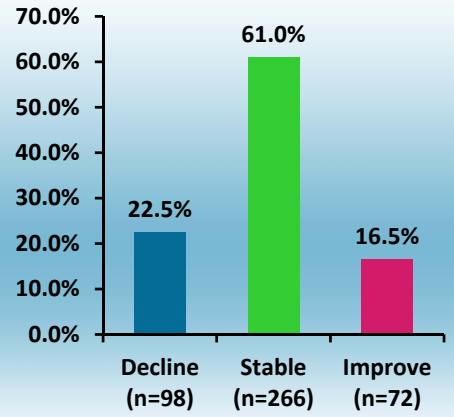
Method

- 436 longitudinal CHARTER participants with at least 4 visits (ending at visit 7); Mean (SD) follow-up: 35.0 (10.0) months
  - 2,680 total visits
- Study visits approximately 6 months apart included comprehensive laboratory, neuromedical and neuropsychological (NP) assessments
- Regression-based norms for NP change used to assess cognitive decline*
- Time dependent survival analysis was used to examine predictors of NP decline
  - Also included multivariable cox regression modeling with time-dependent predictors

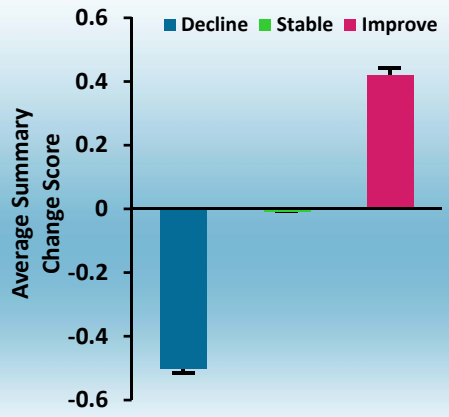
*Cysique et al., 2011

Results

NP Change Status in CHARTER Sample with >4 Visits



Mean (SE) Change Scores Across Longitudinal Visits



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Results cont.

- In a multivariable model, improvement in mean scaled score was predicted by its baseline value (*P*=0.002) and its interaction with group (*P*=0.02)
- **Treated participants with the lowest baseline mean scaled** scores demonstrated the most improvement (figure 1)
- For both groups, improvement was greater over longer durations when global mean scaled score is low but remains essentially stable for higher baseline mean scaled scores *(P*<0.01)
- Whether the participants in the Treated group started treatment prior to baseline was not a significant predictor

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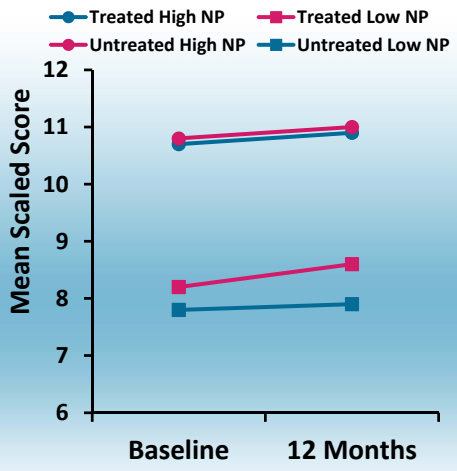
Mean Scaled Scores in Treated and Untreated Groups, Stratified by High and Low Baseline Mean Scaled Score

Predictor	F	*P*
Group	0.4	ns
ART duration prior to BL	0.01	ns
Time from BL	8.6	0.0045
BL Global Mean SS	10.01	0.0022
BL Global Mean SS x Group	5.6	0.0210
BL Global Mean SS x Time between visits	7.3	0.0087

Figure 1



ns=not significant ($P \geq 0.05$); BL =baseline; SS =scaled score

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