Neurocognitive screenings for HIV-associated neurocognitive disorders An update

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DO WE NEED SCREENING FOR HAND?

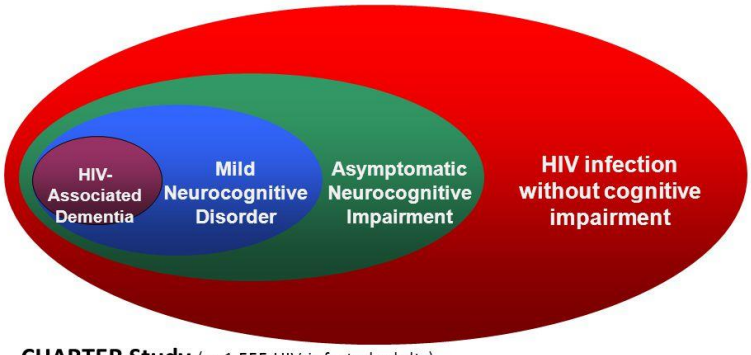
- Screening for HAND has been argued to be an unnecessary burden on the HIV care as the detection of mild HIV-related impairment is challenging in the presence of multiple comorbidities, and treatment options are limited.

Spectrum of HAND

	No alternative cause	Delirium absent	Acquired impairment in ≥ 2 cognitive abilities	Interferes with daily functioning
symptomatic eurocognitive npairment (**ANI**)	✓	✓	✓	No
lild Neurocognitive isorder (**MND**)	✓	✓	✓	Mild
IV-Associated ementia (**HAD**)	✓	✓	Marked	Marked

Antinori A, et al. Neurology 2007;69:1789–99

Neuropsychological impairment in the era of cART



CHARTER Study (n=1,555 HIV-infected adults)
52% had NP impairment: HAD 2%, MND 12%, ANI 33%

Heaton RK, et al. Neurology 2010;75:2087–96

7th IAS Conference on HIV Pathogenesis, Treatment and Prevention 2013

HAND prevalence

Clinical Infectious Diseases
MAJOR ARTICLE
HIV/AIDS

A Screening Strategy for HIV-Associated Neurocognitive Disorders That Accurately Identifies Patients Requiring Neurological Review

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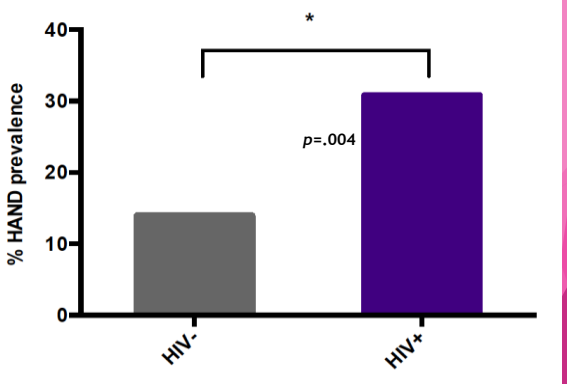
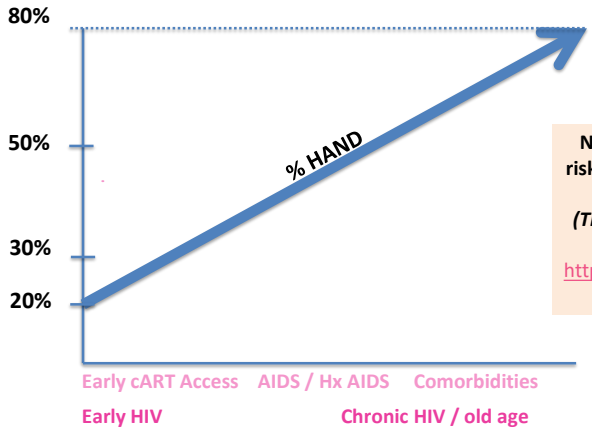
Table 1. Demographic and Clinical Characteristics in the Study Population Stratified by Human Immunodeficiency Virus Status

Characteristic	HIV+ n = 254	HIV− n = 72	*P* Value
Age (median y)	48.5 (15.1)	48.7 (12.0)	0.9
Gender (% male)	99.6	97.2	0.06
Ethnicity			
White (%)	86.6	90.3	0.42
Asian (%)	5.1	8.3	0.32
Education			
Primary (%)	1.1	0.0	1.0
Secondary (%)	29.5	23.6	0.38
Trade school (%)	17.3	13.9	0.45
College (%)	52.0	62.5	0.12
History of HIV-associated brain involvement (%)	12.6	. . .	. . .
Non-HIV central nervous system condition (%)	15.3	. . .	. . .
Depressive symptoms (depression anxiety stress scale > 13; %)	26.0	19.5	0.25
Alcohol use disorder (current 12 mo; %)	9.2	5.6	0.33
Substance use disorder (current 12 mo; %)	19.9	2.8	0.0005
Hepatitis C virus RNA positive (%)[a]	4.1	0.0	0.04
HIV men-who-have-sex-with-men transmission (%)	92.9		
Duration of HIV (mean y)	14.1 ± 8.6	. . .	. . .
Centre for Disease Control category C (%)	15.4	. . .	. . .
Plasma HIV RNA <200 copies/mL (%)	83.4	. . .	. . .
Plasma HIV RNA <50 copies/mL (%)	78.7	. . .	. . .
CD4+ T lymphocyte count (median cells/μL)	592 (355)	. . .	. . .
Currently taking cART (%)	91.7	. . .	. . .
High central nervous system penetrating-effectiveness cART regimen (≥7; %)[b]	87.0	. . .	. . .



https://www.ncbi.nlm.nih.gov/pubmed/27325690

HAND in different population worldwide depends on cART access and timing, rate of Historical AIDS & immune compromise, comorbidities

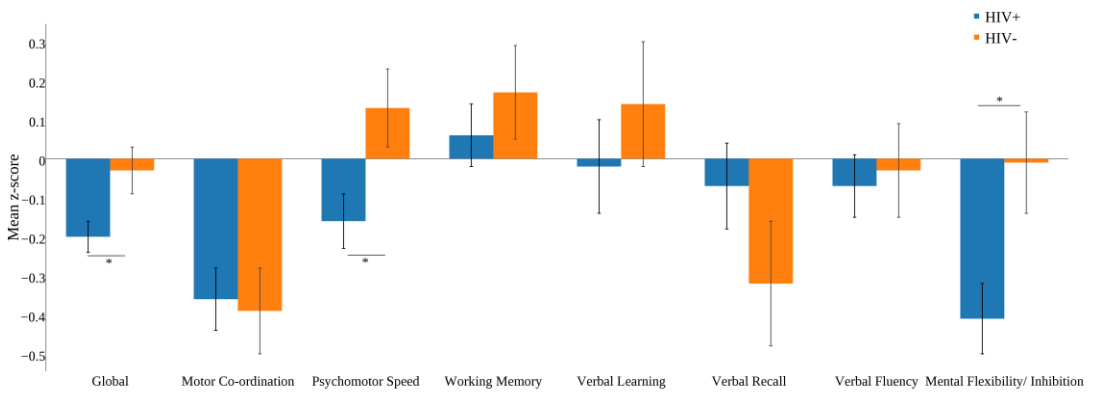


Not all HIV+ people have same risk for HAND: ~50% will probably never have HAND
(This figure does not account for pediatric HIV or old age)
https://www.ncbi.nlm.nih.gov/pubmed/29198283

https://www.ncbi.nlm.nih.gov/pubmed/29198283

Incident cognitive decline in the Australian HIV and Brain Aging Cohort Study

A greater proportion of HIV+ (**14.0%**) participants ***declined*** as compared to HIV- cases (**4.5%**) (non-significant difference: p=.11, Φ=.13



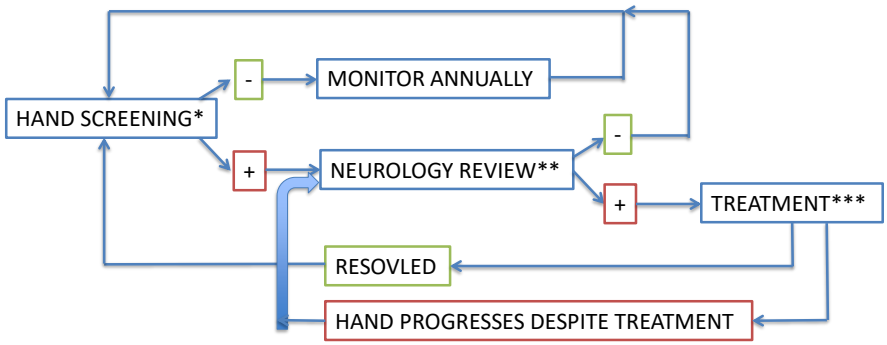
Screening using a geriatric framework?

- A greater number of comorbidities plus neurocognitive impairment in HIV+ persons will likely have worse neurological prognosis, so screening is warranted.
- Without screening, some patients go undiagnosed, while a HAND diagnosis is associated with less adherence, unemployment, and mortality.
- Furthermore with an aging HIV epidemic, controlled HIV, and HAND may be risk factors for dementia.

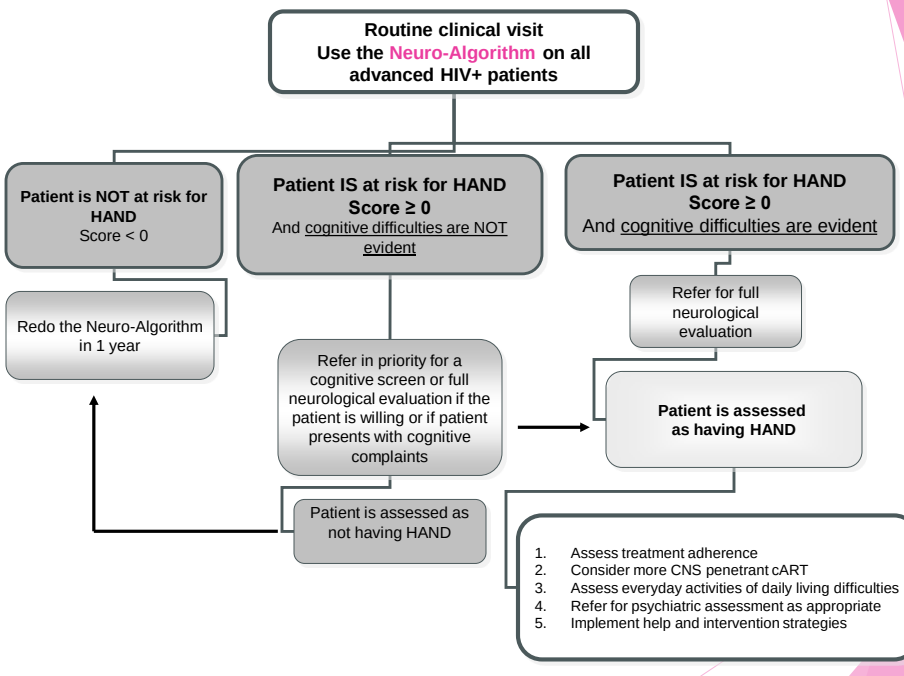
A proposed screening algorithm

- **To address this challenges, our group has proposed an algorithm that streamlines screening:**
  - 1. A 20-minute gold standard-validated screening of neurocognition, mood and everyday functions is targeted towards patients at risk for mild HAND based on recognized factors including age 50+.
  - 2. A positive screen triggers a full neurology review.
  - 3. A negative screen triggers annual monitoring.
  - 4. The neurology care triggers tailored evidence-based psychosocial interventions.
  - 5. Management of modifiable age-related comorbidities is implemented as a dementia risk reduction strategy.
  - 6. ART adjustment for CSF viral load escape are considered.
  - 7. Detection of any forms of dementia triggers other relevant care.

PROPOSED HAND MANAGEMENT ALGORITHM THAT INCORPORATES TREATMENT



*Screening procedures have been published and validated in primary care. Bloch et al., 2016. The screening streamline HIV+ patients in need of an extensive neurological care versus those who simply need a monitoring (Cysique et al., 2010)
** Neurological exam, MRI, comprehensive neuropsychological testing, CSF and blood exam
*** Treatment is PERSONALIZED depending on HIV duration, medical and ARV history, severity and mechanistic causes of HAND AND FURTHER ADAPTED is 1st treatment options is failing based on full neurology re-review.



Which cognitive screens?

Screen Versus Gold Standard NP Impairment Rates and Standard Criterion Validity Indexes for Studies where Sensitivity and Specificity is 70% or Higher (%)

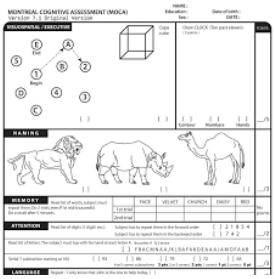
Study	Screen	Cut-off	Sample	Sensitivity	Specificity	Accuracy
Morgan	HDS	*T*<40	**HAD only**	93	73	-
Moore	4 NP tests	4 tests *T* < 40, *or* 2 tests *T* < 40 + 1 test *T* < 35, *or* 2 tests *T* < 35, *or* 1 test *T* < 40 + 1 test *T*< 30, *or* 1 test *T* < 25	Entire sample	87	87	-
Moore	3 NP tests	3 tests *T* < 40 *or* 1 test *T* < 40 + 1 test *T* < 35, *or* 1 test *T* < 30	Entire sample	87	76	-
Cysique	CogState	-	Entire sample	81	70	-
Carey	NP tests (HVLT-R & ndGP)	*T*<40 on 1 test *or* T<35 on 2 tests	Entire sample	78	85	83
Morgan	HDS	*T*<40	**MND only**	77	73	-
Carey	NP tests (HVLT-R & Cod)	*T*<40 on 1 test *or* T<35 on 2 tests	Entire sample	75	92	87
Moore	2 NP tests	2 tests *T* < 40 *or* 1 test *T* ≤ 35	Entire sample	73	83	-
Sacktor (American)	IHDS	≤10.5	Entire sample	71	79	-
Becker	CAMCI	-	Entire sample[c]	72	98	-

Notes. **Consideration of the sample in question is needed for the proper selection of the screen.**

More recent screens examples/studies

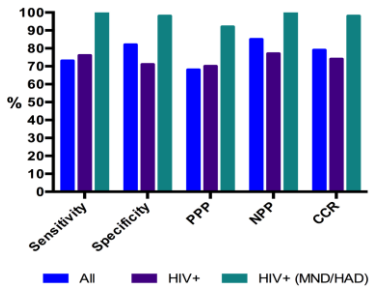
All these tools needs norms!

MoCA MONTREAL COGNITIVE ASSESSMENT



https://www.ncbi.nlm.nih.gov/pubmed/29508103

COGSTATE ASSESS • MONITOR • IMPROVE



https://www.ncbi.nlm.nih.gov/pubmed/27325690

+IADL
+Mood

This screening procedure can be designed to be adaptable to other languages and cultures.

iPad version being tested in CALD HIV+ Australian

Which screen for monitoring?

- Screens' pros and cons for cognitive health monitoring in frontline HIV care and research setting

	Validated for repeated testing	Clinical tool	Requires neuropsychologist administration	Requires neuropsychologist scoring	Fully computerised with automated report	Requires neuropsychologist interpretation	Costs [1]
Combined neuropsychological tests	Yes	Yes	Yes	Yes	No [2]	Yes	Indirect / Direct
CogState Battery	Yes	No	No [3]	No	Yes	Yes	Direct
HDS	No	Yes[4]	No	No	No	No [4]	Free

Computerised platforms other complexities!

New promising tablet-based screenings can be easily integrated to this proposed algorithm

NeuroScreen

- Android tablet app for healthcare workers to administer
- Automates many aspects of cognitive testing
- Standardized instructions – always the same – most with audio-visual based instructions for low-literacy populations – available in English, Xhosa, Luganda, Swahilli, Shona, Spanish, and Thai (in progress)
- 10 brief tests (plus error scores, and reaction times) across multiple domains approximately 25-minutes to administer:
  - **Learning**: 5 item word list, words played via audio recording – always same volume and at same rate;
  - **Memory**: 5-minute delayed recall of 5 words, app automatically timed;
  - **Processing speed**: Basic Trail Making, shape detection, shape discrimination, number input, all automatically timed;
  - **Motor**: Finger Tapping (dominant and non-dominant hands);
  - **Executive**: Trail Making – alternate between colors and numbers
  - **Working** Memory: Number Span (Numbers played via audio recording – always same volume and at same rate)


JMTM
ORIGINAL ARTICLE
A SMARTPHONE APP TO SCREEN FOR HIV-RELATED NEUROCOGNITIVE IMPAIRMENT

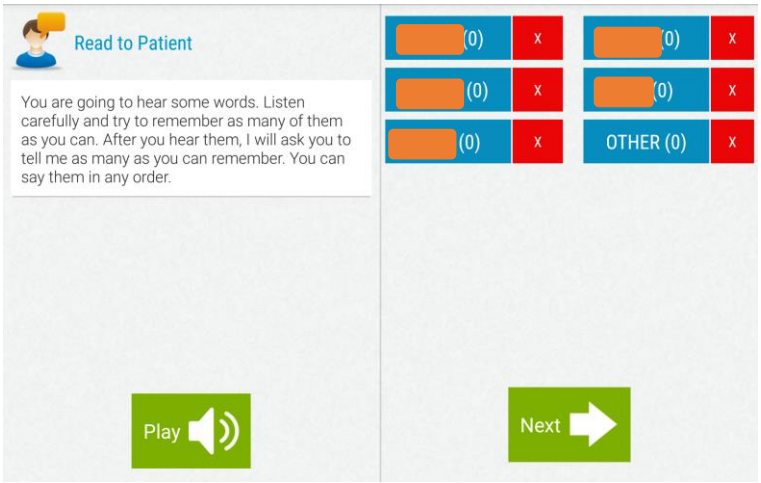
JMIR MHEALTH AND UHEALTH
Original Paper
A Mobile App to Screen for Neurocognitive Impairment: Preliminary Validation of NeuroScreen Among HIV-Infected South African Adults

HIV Neurobehavioral Research Program at San Diego US new screens

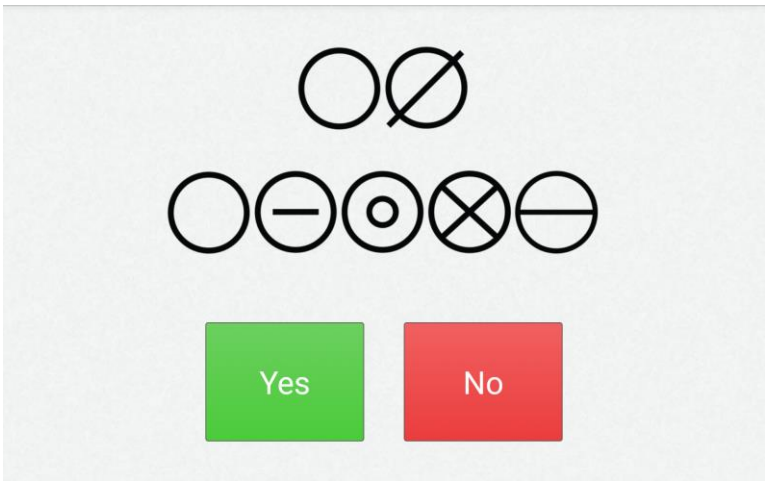
NIH Toolbox cognition. Motor, emotion

Phone screen in development at John Hopkins

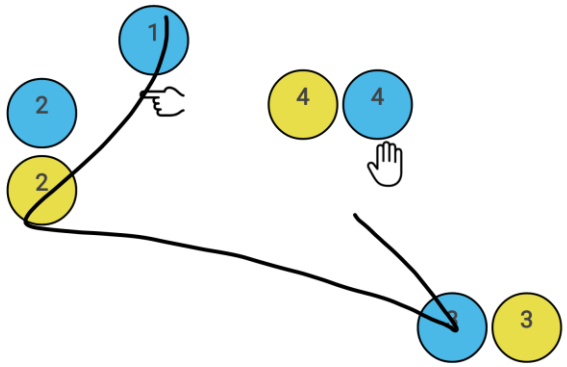
NeuroScreen



NeuroScreen

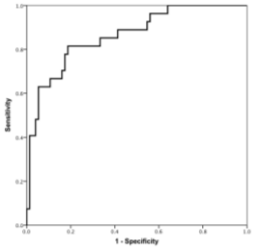


NeuroScreen

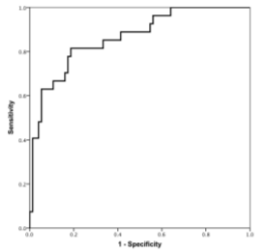


South Africa

- NIH/NICHD Funded Study (R21 HD084197; PI: Robbins)
- 102 HIV+ Adults in Western Cape region [81% female, mean age 33.31 years (range: 19-56)]
- **Community health worker/lay counselor** administered NeuroScreen
- Then administered 'gold standard' neuropsychological test battery by highly trained psychometrist



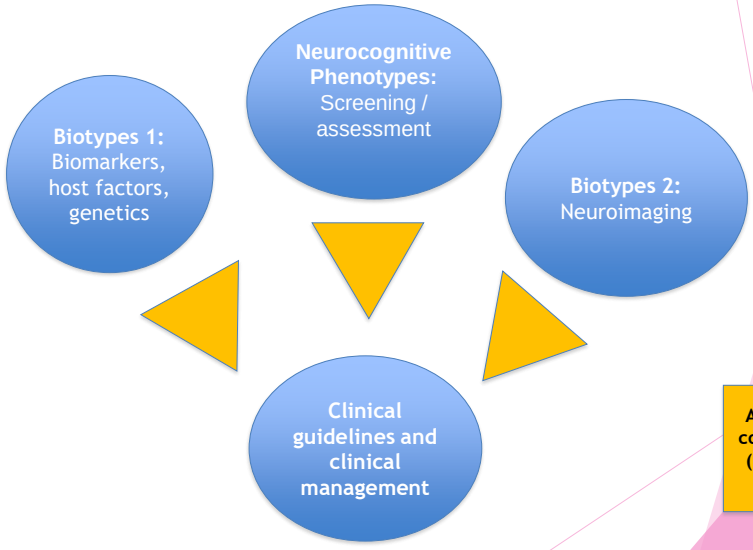
NeuroScreen Score 2 (average completion time 25 minutes) maximized sensitivity at ***81%*** and specificity at ***81%***. AUC = 0.86; 95% CI: 0.78, 0.94.



NeuroScreen Score 3 (average completion time 12 minutes) maximized sensitivity and specificity at ***93%*** and ***71%***. AUC = 0.87; 95% CI: 0.80, 0.94.

International taskforce to revise the HAND diagnostic criteria with the aim of providing clear clinical translation

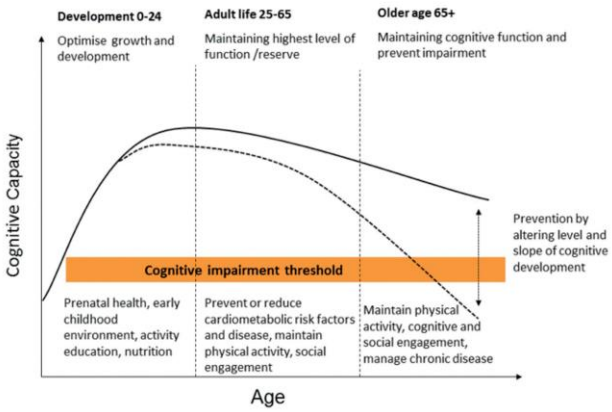
4 Working Groups



All working groups to consider comorbidities (psychiatric, alcohol, drug use) and aging

Thanks to our participants across the world!

Screening for cognitive health is an optimal health strategy for any chronic condition.



Lifecourse Ageing Research Centre (LARC)

Neuroscience Research Australia