A MOBILE APP TO SCREEN FOR NEUROCOGNITIVE IMPAIRMENT IN HIV

Improving and Scaling-up Neurocognitive Assessment

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Disclosures

- None

Background

- Neurocognitive impairment (NCI) is very common among people living with HIV (PLWH), even those virally suppressed
  - About 50% of PLWH have NCI – most have mild NCI[1]
  - NCI in HIV is associated with increased risk for[2-7]:
    - Mortality
    - Developing more severe NCI
    - Poor antiretroviral therapy (ART) adherence
    - Employment difficulties
    - Impaired activities of daily living (ADLs)
    - Poor decision making (e.g., condomless sex)

Background

- NCI in HIV thought to be mostly ‘subcortical’ in nature with some ‘cortical’ features[8]
  - Basal ganglia
  - Neocortex
  - White matter tracts connecting those regions
- Neurocognitively speaking this equates to
  - Speed of information processing/processing speed
  - Attention/working memory
  - Motor skills

Background

- In research, the Frascati criteria are often used to describe HIV-related NCI[9]
  - Nomenclature: HIV-associated Neurocognitive Disorder (HAND)
    - Asymptomatic Neurocognitive Impairment (ANI)
    - Mild Neurocognitive Disorder (MND)
    - HIV-Associated Dementia (HAD)
- Requires neuropsychological evaluation
  - Examine neurocognitive performance across numerous neuropsychological domains

Background

- Globally, there are approximately 37 million PLWH[10]
  - 18.5 million likely have NCI
    - Poor adherence + condomless sex = high HIV transmission risk
- Detecting NCI[11-13]
  - Enable providers to track and monitor neurocognition, detect early signs
  - Educate patients about its impact and how to manage it
  - Provide additional supports and referrals; minimize impact on ART
  - Help allocate resources better and refer to treatments (when available)
  - Adjust ART regimens

Background

- Routine screening recommended as good clinical practice[11-13]
  - However, not routinely done
- Screening for NCI faces numerous challenges
  - No clear policies or guidelines exist
  - HIV-provider knowledge of it varies greatly – may not be on clinicians 'radar'

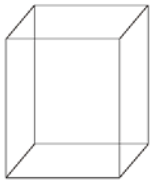
Background

- Assessment of neurocognitive functions
  - Gold-standard = full neuropsychological assessment, requires:
    - Neuropsychologist
    - 2 – 4 hours to administer, more time to score and interpret
    - Specialized forms and equipment
    - Not feasible for routine care
    - Not scalable for the 37 million PLWH

HIV DEMENTIA SCALE

DEPARTMENT OF NE

Maximum Score	Score	
		MEMORY - REGISTRATION Give four words to recall (dog, hat, green, p Then ask the patient all 4 after you have sa
4	( )	**ATTENTION** Anti-saccadic eye movements: 20 commar _____errors of 20 trials ≤3 errors = 4; 4 errors = 3; 5 errors = 2; 6 e
6	( )	**PSYCHOMOTOR SPEED** Ask patient to write the alphabet in upper across the page and record time. _____ in seconds. <21 sec = 6; 21.1 to 24 sec = 5; 24.1 to 27 s 30.1 to 33 sec = 2; 33.1 to 36 sec = 1; >36 s
4	( )	**MEMORY/RECALL** Ask for 4 words from Registration above. (For words not recalled, prompt with a "sen animal (dog); piece of clothing (hat), color Give 1/2 point for each correct word after
2	( )	**CONSTRUCTION** Copy the cube below; record time: _____ <25 sec = 2; 25 to 35 sec = 1; >35 sec = 0



TOTAL SCORE: _____ /16

International HIV Dementia Scale (IHDS)

Memory-Registration – Give four words to recall (dog say each. Then ask the patient all four words after yo if the patient does not recall them all immediately. Te recall of the words again a bit later.

1. Motor Speed: Have the patient tap the first two fin as widely and as quickly as possible.
   - 4 = 15 in 5 seconds
   - 3 = 11-14 in 5 seconds
   - 2 = 7-10 in 5 seconds
   - 1 = 3-6 in 5 seconds
   - 0 = 0-2 in 5 seconds

   ____

2. Psychomotor Speed: Have the patient perform the non-dominant hand as quickly as possible: 1) Clench Put hand flat on surface with palm down. 3) Put hand the side of the 5th digit. Demonstrate and have patient
   - 4 = 4 sequences in 10 seconds
   - 3 = 3 sequences in 10 seconds
   - 2 = 2 sequences in 10 seconds
   - 1 = 1 sequence in 10 seconds
   - 0 = unable to perform

   ____

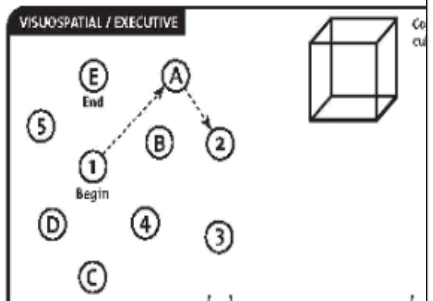
3. Memory-Recall: Ask the patient to recall the four w prompt with a semantic clue as follows: animal (dog); vegetable (bean); color (red).
   - Give 1 point for each word spontaneously reca
   - Give 0.5 points for each correct answer after p
   - Maximum – 4 points.

   ____

Total International HIV Dementia Scale Score: This is items 1-3. The maximum possible score is 12 points should be evaluated further for possible dementia.

MONTREAL COGNITIVE ASSESSMENT (MOCA)

VISUOSPATIAL / EXECUTIVE



NAMING

MEMORY — Read list of words, subject must repeat them. Do a trials. Do a recall after 5 minutes. FACE; 1st trial; 2nd trial

ATTENTION — Read list of digits (1 digit/ sec.). Subject has to repeat them. Subject has to repeat them. Read list of letters. The subject must tap with his hand at each letter A. [ ] F B A C M N A. Serial 7 subtraction starting at 100 [ ] 93 [ ] 86 [ ] 4 or 5 correct subtractions: 3 p

LANGUAGE — Repeat : I only know that John is the one to help today. [ ] The cat always hid under the couch when dogs were. Fluency / Name maximum number of words in one minute that begin with the

ABSTRACTION — Similarity between e.g. Banana - orange = fruit [ ] train -

DELAYED RECALL — Has to recall words WITH NO CUE: FACE [ ] VELVET [ ] CHURC [ ]

Optional — Category cue; Multiple choice cue

ORIENTATION — [ ] Date [ ] Month [ ] Year [

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Administered by:

The mini mental state examination

Orientation
- Year, month, day, date. season _____/5
- Country, county, town, hospital, ward (clinic) _____/5

Registration
- Examiner names three objects (for example, apple, pen, and table)
- Patient asked to repeat objects, one point for each. _____/3

Attention
- Subtract 7 from 100 then repeat from result, stop after five subtractions. (Answers: 93, 86, 79, 72, 65)
- Alternatively if patient errs on subtraction get them to spell world backwards: D L R O W
- Score best performance on either task. _____/5

Recall
- Ask for the names of the objects learned earlier. _____/3

Language
- Name a pencil and a watch. _____/2
- Repeat: 'No ifs, and or buts.' _____/1
- Give a three stage command. Score one for each stage (for example, 'Take this piece of paper in your right hand, fold it in half and place it on the table.' _____/3
- Ask patient to read and obey a written command on a piece of paper stating: 'Close your eyes.' _____/1
- Ask patient to write a sentence. Score correct if it has a subject and a verb. _____/1

Copying
- Ask patient to copy intersecting pentagons.
- Score as correct if they overlap and each has five sides. _____/1

Total score: _____/30

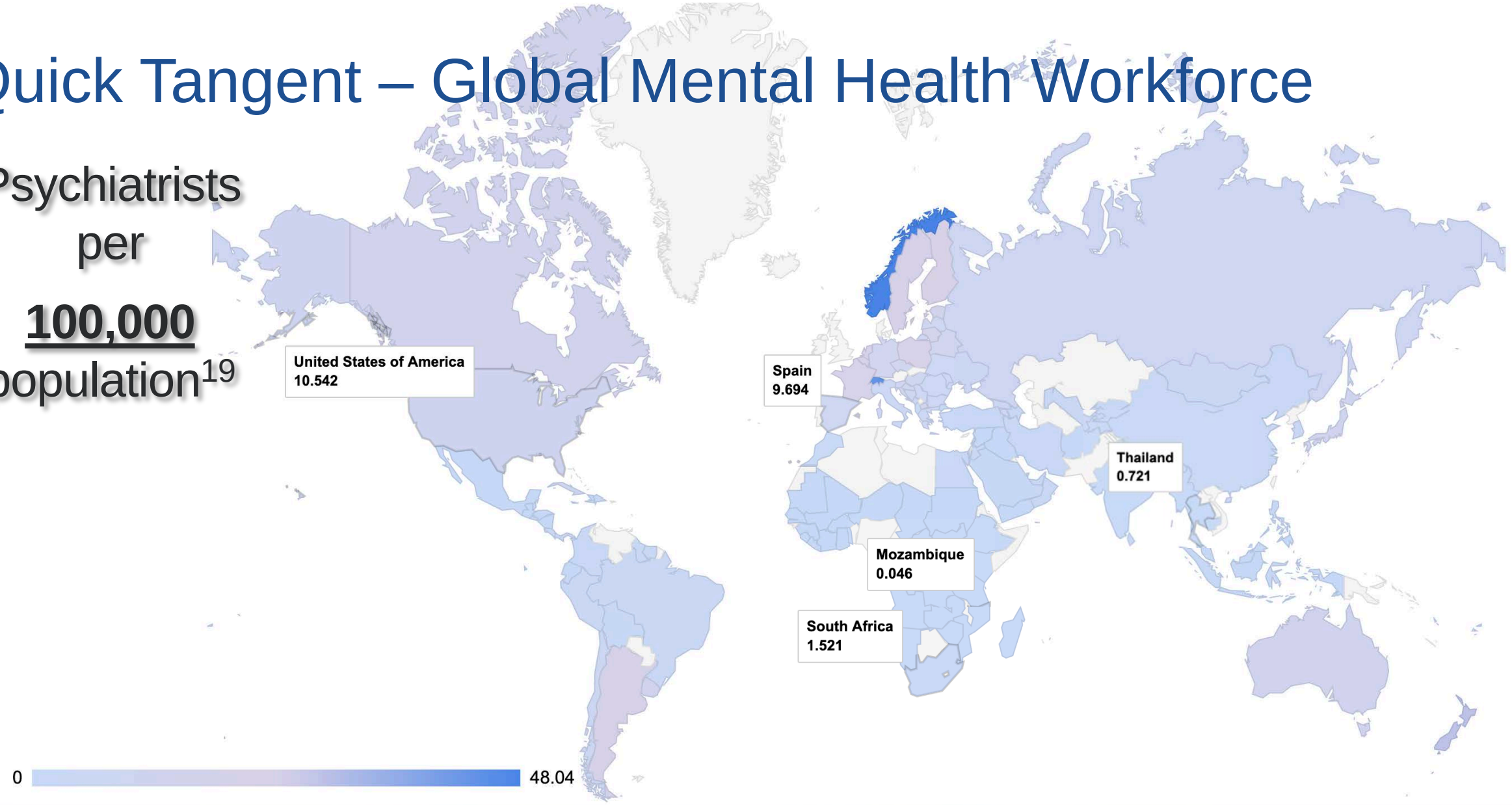
Background

- Many shortcomings of currently available screening tests
  - Poor sensitivity and specificity to detect milder forms of NCI[14,15]
  - Some not appropriate for certain populations[16]
    - MoCA in South Africa
      - Black, isiXhosa-speaking adults could not draw 3D cube
      - Scores more similar to MoCA Alzheimer norms
  - Some not appropriate for use by full range of healthcare workforce[17-18]
    - IHDS when used by community health workers in South Africa can grossly over- or under-estimate impairment

Quick Tangent – Global Mental Health Workforce

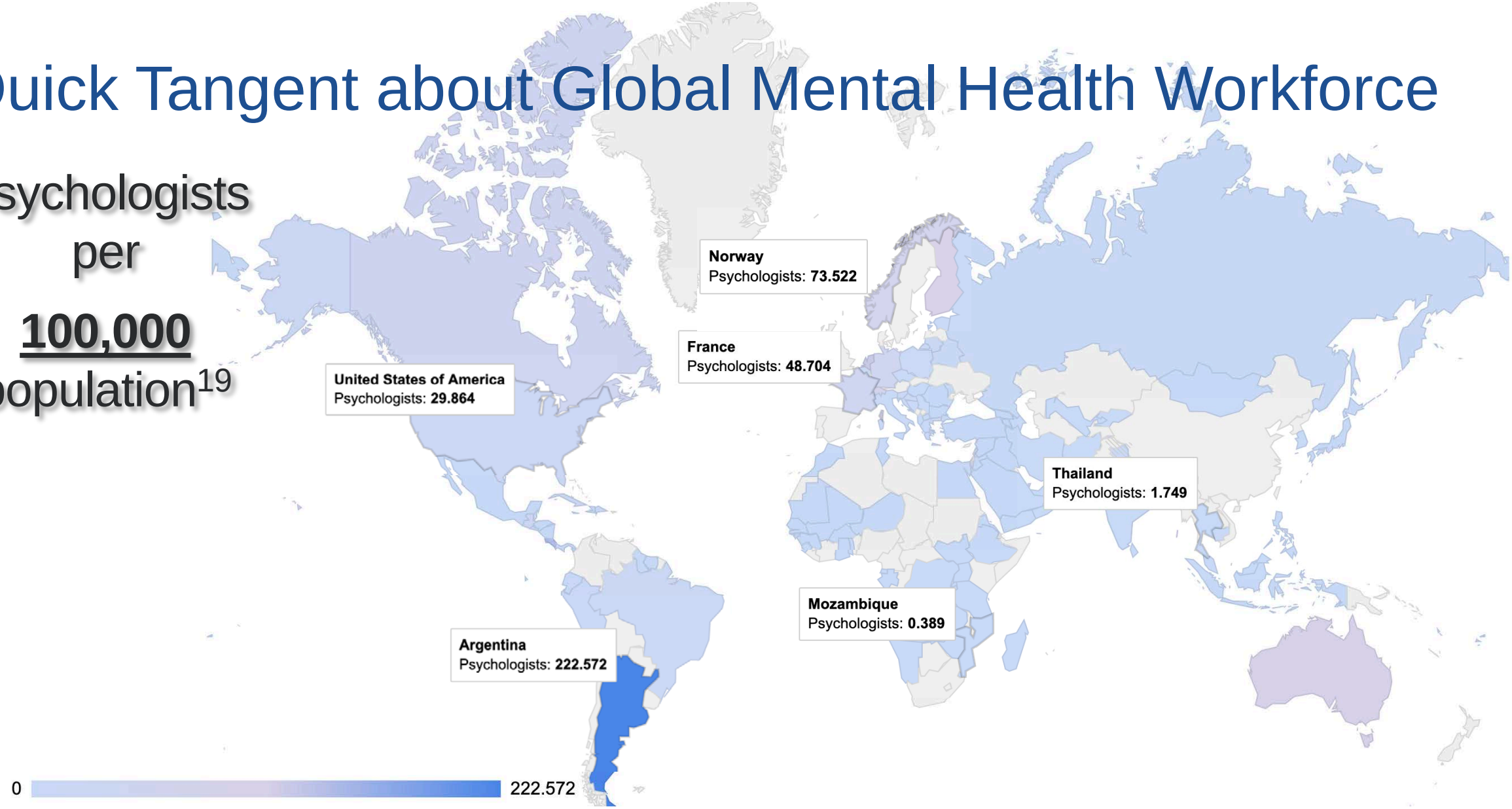
Psychiatrists per

100,000 population[19]



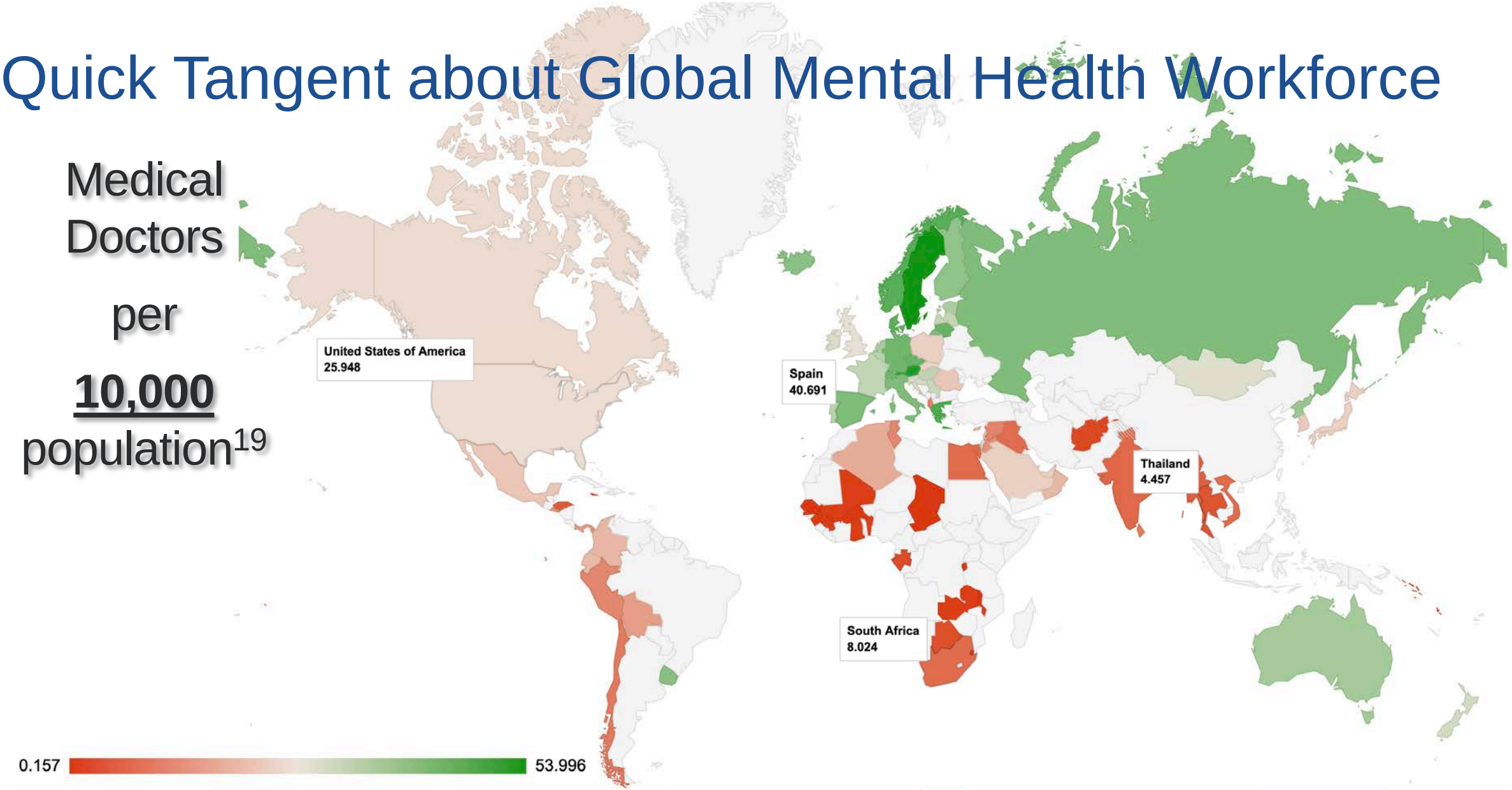
Quick Tangent about Global Mental Health Workforce

Psychologists per **100,000** population[19]



Quick Tangent about Global Mental Health Workforce

Medical Doctors per **10,000** population[19]

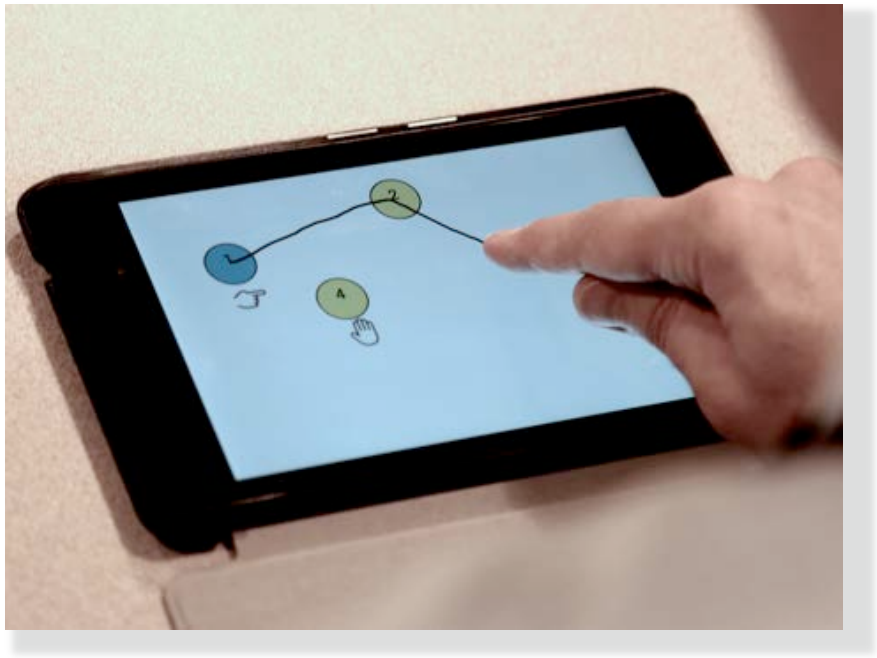


Background

- How and who can screen for NCI?
- What about an app?
  - Consulted with software engineers from South Africa
  - Worked with engineers and neuropsychologists, psychiatrists, and psychologists to develop smartphone prototype
    - Android OS – has larger market share in low- and middle-income countries (devices less expensive than Apple)
    - Developed neurocognitive tests that could be implemented on a touchscreen device and that would be sensitive to the NCI observed in HIV (processing speed, attention, and motor)

Background

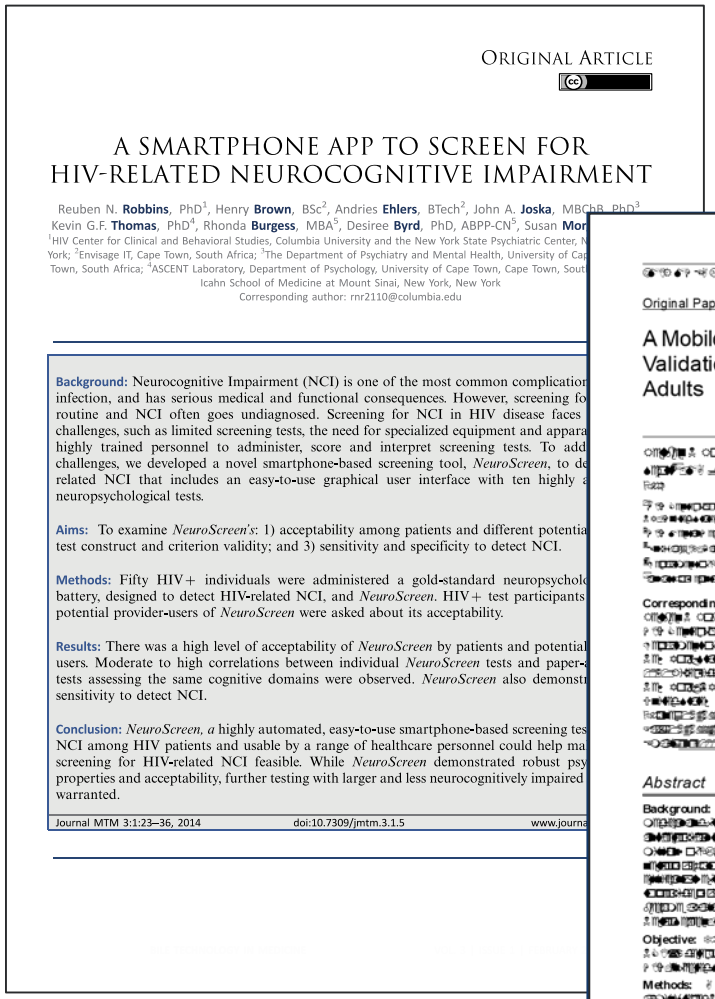
NeuroScreen



There’s an app for that!

Background

- NeuroScreen Android OS tablet app[20-22]
  - Highly automates neurocognitive test administration
  - Designed to be used by all levels of clinical staff
  - Assesses neurocognitive domains of:
    - Processing speed (3 tests)
    - Attention/Working memory (2 tests)
    - Motor (2 tests)
    - Learning and Memory (1 test)
    - Executive functioning (1 test)
  - Results synced with server and available electronically



ORIGINAL ARTICLE

A SMARTPHONE APP TO SCREEN FOR HIV-RELATED NEUROCOGNITIVE IMPAIRMENT

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Background: Neurocognitive Impairment (NCI) is one of the most common complicatior infection, and has serious medical and functional consequences. However, screening fo routine and NCI often goes undiagnosed. Screening for NCI in HIV disease faces challenges, such as limited screening tests, the need for specialized equipment and appara highly trained personnel to administer, score and interpret screening tests. To add challenges, we developed a novel smartphone-based screening tool, *NeuroScreen*, to de related NCI that includes an easy-to-use graphical user interface with ten highly a neuropsychological tests.

Aims: To examine *NeuroScreen's*: 1) acceptability among patients and different potentia test construct and criterion validity; and 3) sensitivity and specificity to detect NCI.

Methods: Fifty HIV+ individuals were administered a gold-standard neuropsycholo battery, designed to detect HIV-related NCI, and *NeuroScreen*. HIV+ test participants potential provider-users of *NeuroScreen* were asked about its acceptability.

Results: There was a high level of acceptability of *NeuroScreen* by patients and potential users. Moderate to high correlations between individual *NeuroScreen* tests and paper- tests assessing the same cognitive domains were observed. *NeuroScreen* also demonstr sensitivity to detect NCI.

Conclusion: *NeuroScreen, a* highly automated, easy-to-use smartphone-based screening tes NCI among HIV patients and usable by a range of healthcare personnel could help ma screening for HIV-related NCI feasible. While *NeuroScreen* demonstrated robust psy properties and acceptability, further testing with larger and less neurocognitively impaired warranted.

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Original Paper

A Mobile App to Screen for Neurocognitive Impairment: Preliminary Validation of NeuroScreen Among HIV-Infected South African Adults

Corresponding Author:

Abstract

Background:

Objective:

Methods:

Results:

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(page number not for citation purposes)

American Psychological Association

Neuropsychology

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A Culturally Fair Test of Processing Speed: Construct Validity, Preliminary Normative Data, and Effects of HIV Infection on Performance in South African Adults

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Objectives: Impaired processing speed (PS) is a feature of cognitive profiles associated with neurological disorders particularly prevalent in low- or middle-income countries (LMICs). However, commonly used PS tests are not validated for use in LMICs. We assessed, using a sample of healthy South African adults, the construct validity of PS tests contained within NeuroScreen (a tablet-based application and test battery designed to be culturally fair), and established preliminary normative data for those tests (Study 1). Moreover, because South Africa has the highest population prevalence of people living with HIV and PS deficits are a core feature of HIV-associated cognitive impairment, we assessed whether NeuroScreen could detect PS impairment in a sample of HIV-infected South African adults (Study 2). ***Methods:*** In Study 1 (N = 112 healthy adults) and Study 2 (the Study 1 sample, plus n = 102 HIV-infected adults), we administered Neuroscreen and a standardized paper-and-pencil neuropsychological test battery. ***Results:*** In Study 1, factor analyses indicated that NeuroScreen PS scores loaded onto one factor and converged with scores on paper-and-pencil PS tests. Regression modeling indicated that age significantly predicted NeuroScreen PS performance (i.e., younger participants performed better). In Study 2, HIV-infected participants performed significantly more poorly on NeuroScreen PS tests than their HIV-uninfected counterparts. Moreover, a significantly larger proportion of HIV-infected participants displayed impaired PS when judged against the regression-based norms. ***Conclusions:*** These results suggest that NeuroScreen has cross-cultural utility in assessing adult PS performance, and that it might be useful in tracking trajectories of PS decline within HIV infection.

General Scientific Summary
This is the first study to show that NeuroScreen (a tablet-based application and test battery designed to be culturally fair) allows adequate assessment of adult processing speed (PS) performance in a resource-challenged low- or middle-income country. Using a South African sample, the study confirms NeuroScreen has the potential to detect the kinds of PS deficits commonly observed in HIV-infected individuals, and to track disease-related PS decline over time.

Keywords: construct validity, cross-cultural, HIV, normative data, processing speed, South Africa

speed (PS), defined as the swiftness with which one
mplete mental tasks, is a complex cognitive function
compromised in neurological disorders, including
ted with HIV infection (Dobryakova, Costa, Wylie,

DeLuca, & Genova, 2016; Kore et al., 2015; Lu, Chan, & Lam, 2017). The faster one's PS, the more quickly information is made available to higher-level cognitive operations (e.g., working memory [WM] and executive functioning [EF]), and the more likely it

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Study Aims

- NeuroScreen tablet app
  - Adapt NeuroScreen for South Africa (i.e., Xhosa-language version)
  - Evaluate NeuroScreen acceptability and ease of use among community health workers (i.e., lay counselors)
  - Evaluate NeuroScreen's ability (i.e., sensitivity and specificity) to detect gold-standard defined NCI ***when administered by community health workers***

Method

- 11 HIV lay counselors recruited from local clinics for acceptability and usability focus group
- One hundred two adults living with HIV recruited from another study (RCT of a multimedia based ART adherence intervention)
  - From two public health clinics in the Western Cape, South Africa
  - Underwent neuromedical evaluation
  - Administered NeuroScreen by lay counselor
  - Complete 2 – 3 hour gold-standard neuropsychological asse

Method

- Global Deficit Score (GDS) calculated from the neuropsychological test battery (higher scores = more impairment)[23]
  - GDS ≥ 0.5 = NCI
    - GDS of 0.5 – mild impairment
      - GDS Algorithm (All Tests): Successive FT Dom, Successive Finger ND, Pegs Dom, Pegs Ndom, HVLT Total, HVLT Delay, BVMT Total, BVMT Delay, Digit Symbol, Symbol Search, Spatial Span Total, TMT A, CTT 1, CTT 2, Digit Span Total, WCST Persev Error, WCST Trials to 1st, WCST FMS, Animal Fluency, Fruit & Veg Fluency

Method

- All NeuroScreen scores converted to Z-scores based on the full sample
  - Three composite Z-scores were calculated:
    - Sum of all individual test scores; sum of all individual test scores and total errors from the number speed test; sum of four tests (visual discrimination 1 and 2, trail making 1, and number span total)
  - Logistic regression with NeuroScreen score + age + education + gender predicting gold-standard defined NCI
  - Use predicted probabilities to compute ROC curves to evaluate sensitivity and specificity

Results

- Community health worker focus group:
  - 83% female
  - Mean age 43.17 yrs
  - Four (4) reported ever having used a tablet before, and none currently owned one
  - Five (5) reported currently owning a smartphone
  - Nine (9) reported that the NeuroScreen tablet was “Somewhat easy” to “Very easy” to use; two reported it as “Somewhat difficult” to use
  - Overall acceptability was high. Lay health workers reported that they would feel comfortable and confident using the app in their clinics, and that it could be helpful

Results

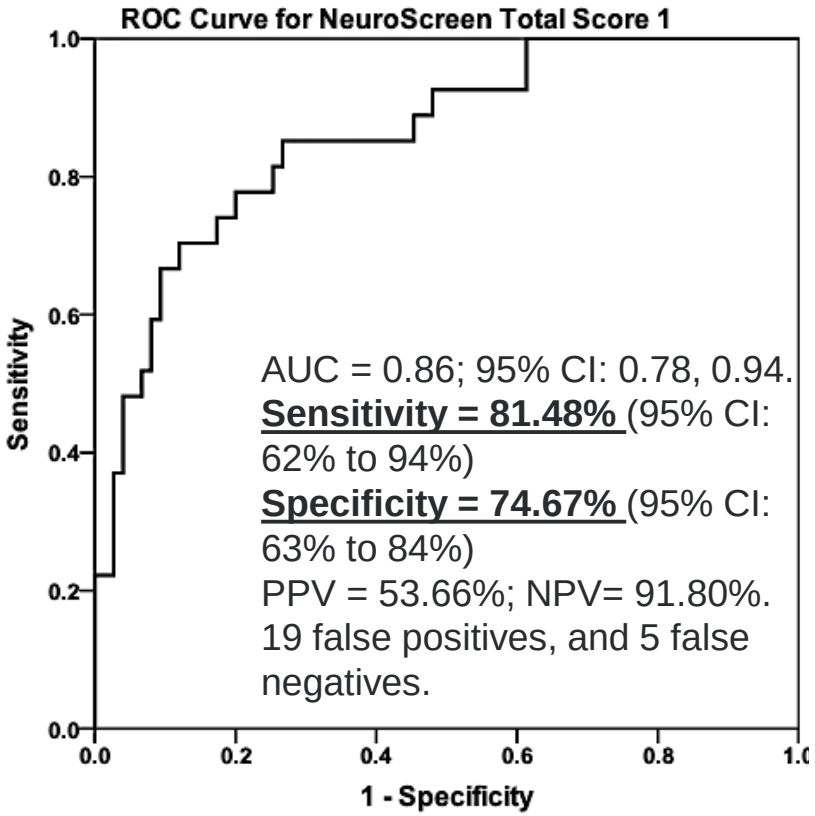
- Psychometric evaluation

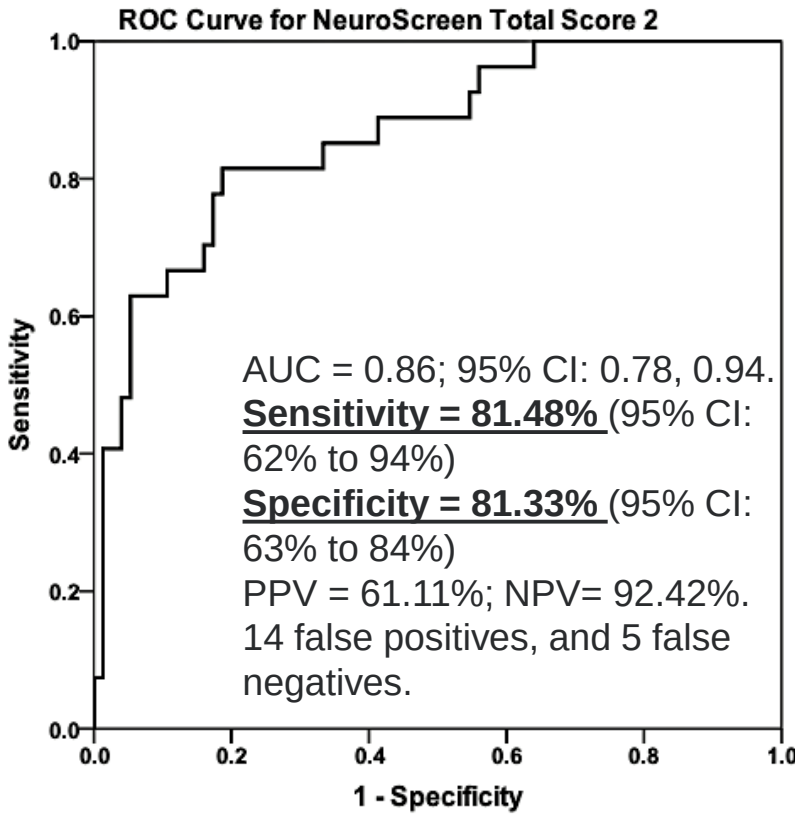
Table 1. Sample Characteristics (N = 102)				
	Mean or %	SD or N	Min	Max
Age	33.31	7.46	19	56
Gender (% Female)	81%	n=83	--	--
Education (years completed)	11.25	1.99	3	14
TBI with LOC>15 minutes	4%	n=4	--	--
Likely learning difficulty	9%	n=9	--	--
Most Recent CD4 Cell Count	501.31	287.41	47	1654
% Most Recent Viral Load Undetectable	91%	n=81	--	--
Note: CD4 Cell Count available for 88 participants; Viral Load data for 81 participants				

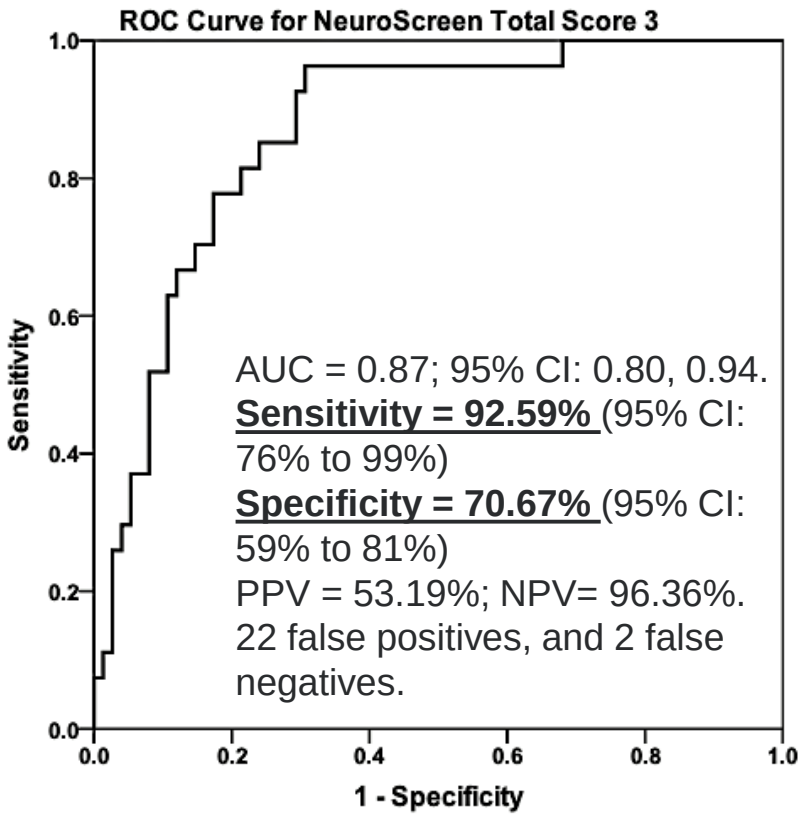
Results

Table 2. Gold-Standard Neuropsychological Test Battery Performance (T-scores)				
Test	Mean	SD	Min	Max
Global T	48.01	4.79	34.00	57.63
Successive Finger Tapping Dominant Hand	46.51	11.29	-1.31	64.05
Successive Finger Non-Dominant Hand	44.98	13.45	-43.87	61.66
Grooved Pegboard Dominant Hand	47.41	7.96	12.67	60.05
Grooved Pegboard Non-Dominant Hand	49.26	3.09	34.09	53.27
HVLT Total Trials 1 - 3	45.97	8.33	24.34	62.67
HVLT Delay Recall Total	44.74	9.86	22.64	67.13
BVMT Total Trials 1 -3	48.40	9.80	28.09	73.75
BVMT Delay Total Recall	49.58	11.48	29.03	72.20
WAIS-III Digit Symbol Coding Total	46.73	10.08	25.45	77.15
WAIS-III Symbol Search Total	47.24	8.95	27.19	64.76
WMS-III Spatial Span Total	50.47	9.65	30.06	73.85
Trail Making Test, Part A	43.82	11.99	-7.48	72.04
Color Trails Test 1	46.72	9.98	12.22	64.02
Color Trails Test 2	48.32	9.73	14.83	66.80
WAIS-III Digit Span Total	49.33	1.21	46.70	52.09
WCST Perseverative Errors	50.74	12.89	3.52	63.76
WCST Trials to 1st Sort	48.10	11.32	29.66	57.98
WCST Failures to Maintain Set	50.59	4.79	31.88	53.94
Animal Fluency Total	49.41	8.70	27.72	70.48
Fruit & Vegetable Fluency Total	51.83	8.75	33.26	72.21

Results







Mean completion time: 23.88 minutes (SD = 6.21)

Completion time: ~12 minutes

Discussion

- NeuroScreen shows promise as an NCI screening tool:
  - For adults living with HIV in South Africa
  - When administered by community health workers/lay counselors
  - Limitations: small sample size, convenience sampling, regionality

Future Directions

- Currently being evaluated to assess NCI among adolescents with perinatal HIV infection in Cape Town, South Africa (R01 HD095256; PI: Robbins)
- Currently adapting app for Thai and will be pilot tested among Thai youth with perinatal HIV (R21 HD098035; PI: Robbins)
- Currently being adapted for Zulu-speaking adolescents and adults as general assessment of NCI
- To date, NeuroScreen has been adapted for use with Shona (Zimbabwe), Luganda (Uganda), Swahili (Kenya), and Thai (Thailand) languages

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