## FORUM Screening for HIV-associated neurocognitive disorders (HANDs) in South Africa: A caution against uncritical use of comparative data from other developing countries

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The prevalence of HIV-associated neurocognitive disorders necessitates community-based screening. In recent years, progress has been made in developing more localised comparative data for use in such screening on the African continent. These studies used measurements that are considered fair, easily accessible, and quick to administer. However, the variance in available international data limits their usefulness and poses a risk to the appropriate streaming of individuals. Here, examples are presented of variance in both cross-national and local demographic screening and neuropsychological test scores, with the aim of cautioning practitioners against undue reliance on general African data for classification of individuals. Recommendations are provided for the development of appropriate norms, specific to local communities.

S Afr J HIV Med 2013;14(1):17-19. DOI:10.7196/SAJHIVMED.855

South Africa (SA) is home to the world's largest population of people living with HIV and AIDS (PLWHA), with an estimated HIV prevalence of 16.9% among SA adults (aged 15 - 49 years) in 2008.<sup>[1]</sup> Recent figures suggest that 17 - 25% of HIV patients in SA display cognitive impairment,<sup>[2,3]</sup> the diagnosis of which is largely dependent on the deviation of test scores from standardised norms. HIV-associated neurocognitive disorders (HANDs) are diagnosed using the Frascati model,<sup>[4]</sup> which requires neuropsychological scores to be compared with normative data using standard deviation (SD) as an indicator of impairment.

The classification of neurocognitive impairment requires clinical attention as it influences decisions on treatment initiation, the management of daily living, and so forth. Owing to the large number of people affected and the prevalence of impairment, large-scale screening is imperative and streams identified individuals towards further investigation. This process requires measurements that are fair, easily accessible and quick to administer. In this regard, the International HIV Dementia Scale (IHDS) and Grooved Pegboard (GP) are arguably the most widely used instruments for HAND screening in limited-resource communities,<sup>[5]</sup> and these have been shown to differentiate between the HIV statuses of asymptomatic patients in sub-Saharan Africa.<sup>[67]</sup>

### The problem of variance

Data from the IHDs and GP tests, and from the rest of the World Health Organization (WHO) HIV battery, have been reported from various sites in sub-Saharan Africa. This is positive progress, as the developing world norms differ from those of industrialised countries,<sup>[8]</sup> and practitioners may need to use comparative data from Africa when no local data are available. However, despite these positive developments, the issue of data variability across countries has not been resolved.<sup>[9]</sup> An example of the range of scores for HIV-negative respondents on the IHDS and GP is provided in Table 1. Table 2 provides an example of the range of scores for HIV-negative respondents for some of the tests used across countries in Eastern and Southern Africa.

In terms of screening, there are some difficulties when comparing SA scores with other African data for local use. For example, the IHDS total score range equals an SD of ±1 across some countries (Table 1). Given that the recommended cut-off for streaming towards further investigation for possible neurocognitive impairment is  $\leq 10$ ,<sup>[7]</sup> this could have significant implications for individuals across different countries. Additionally, the range of the IHDS memory recall subtest differs noticeably between different demographic subgroups within one location.<sup>[12]</sup> The GP-non-dominant hand test (GP-NDH) also differs significantly across countries. This is an important HAND screening mechanism, and the variance in published data creates difficulties for interpretation and further streaming.

Similar problems are faced in terms of diagnosis. For example, the range of the Trail Making Test (TMT) scores differs by more than  $\pm 1$  SD between different demographic subgroups within one location.<sup>[12]</sup> The Digit Symbol Modalities Test (DSMT) differs further by an SD of  $\pm 2$  between countries.

Country	Test	N	Mean	SD
Zambia <sup>[10]</sup>	IHDS total	57	10.10	
	IHDS memory recall	57	3.40	
	GP-NDH	57	97.50	
Uganda <sup>[11]</sup>	IHDS	25	11.10	±0.80
Uganda <sup>[7]</sup>	IHDS total	100	11.00	±1.00
	IHDS memory recall	100	3.60	±0.60
	GP-NDH	100	102.70	±25.20
South Africa <sup>[6]</sup>	GP-NDH	24	80.83	±9.20
South Africa <sup>[12]</sup>	IHDS memory recall (female; aged 18 - 29 years)		3.77	±0.47
	IHDS memory recall (male; aged 18 - 29 years)		3.39	±0.55
	IHDS memory recall (female; aged 30 - 50 years)		3.66	±0.48
	IHDS memory recall (male; aged 30 - 50 years)		3.19	±0.96

## Table 1. Scores for IHDS and GP-NDH tests conducted among HIV-negative respondents in East and Southern Africa

SD = standard deviation; IHDS = International HIV Dementia Scale; GP-NDH = Grooved Pegboard-non-dominant hand test.

# Table 2. Scores for TGT, DSMT, TMT and DS conducted among HIV-negative respondents in East and Southern Africa

Country	Test	N	Mean	SD
Zambia <sup>[10]</sup>	TGT	57	12.3	
Uganda <sup>[7]</sup>	DSMT	100	31.10	±11.30
	TGT	100	6.95	±0.82
	DSF	100	5.30	±0.90
	DSB	100	3.50	±0.90
South Africa <sup>[6]</sup>	TMT-A	24	43.74	±12.40
	DSMT	24	50.54	±11.10
South Africa <sup>[12]</sup>	TMT-A (female; aged 18 - 29 years)		40.73	±17.40
	TMT-A (male; aged 18 - 29 years)		35.89	±8.94
All aged 18 - 29 years ( <i>N</i> =68)	TMT-A (female; aged 30 - 50 years)		48.54	±18.70
All aged 30 - 50 years ( <i>N</i> =42)	TMT-A (male; aged 30 - 50 years)		50.00	±13.60
	TMT-B (female; aged 18 - 29 years)		72.57	±26.00
	TMT-B (male; aged 18 - 29 years)		87.78	±26.50
	TMT-B (female; aged 30 - 50 years)		89.26	±28.40
	TMT-B (male; aged 30 - 50 years)		114.25	±43.10
	DSF (female; aged 18 - 29 years)		6.50	±1.38
	DSF (male; aged 18 - 29 years)		6.33	±1.12
	DSF (female; aged 30 - 50 years)		6.14	$\pm 1.40$
	DSF (male; aged 30 - 50 years)		6.00	±1.07
	DSB (female; aged 18 - 29 years)		3.63	±0.97
	DSB (male; aged 18 - 29 years)		4.56	±0.73
	DSB (female; aged 30 - 50 years)		3.29	±0.83
	DSB (male; aged 30 - 50 years)		3.88	±0.99

TGT = Timed Gait Test; DSMT = Digit Symbol Modalities Test; TMT-A = Trail Making Test A; TMT-B = Trail Making Test B; DS = Digit Span; DSF = Digit Span Forward; DSB = Digit Span Backward.

Digit Span (DS) Forward and Backward scores also display ranges equalling an SD of  $\pm 1$  between some countries (most notably Uganda and South Africa) and even within countries, based on demographics. The Timed Gait Test (TGT) score range equals an SD of  $\pm 6$  between samples in Zambia and Uganda.<sup>[7,10]</sup> This is despite indications in the reported studies suggesting that the samples had broadly similar socio-economic and educational backgrounds.

While it is tempting to believe that the variance is simply due to inter-country differences, there may be a number of reasons why it may not reflect true cross-national or cross-cultural differences. Firstly, it is not always clear whether psychologists, primary healthcare nursing personnel or highly qualified researchers performed the assessments. Some tests (e.g. IHDS) were developed to be administered by primary healthcare workers, while others were (at least historically) firmly placed in the neuropsychological domain (e.g. GP, TMT). Secondly, there is a lack of demographic reporting. The effects of gender, age, education, and so forth, are well documented,<sup>[5,12]</sup> but not equally well-reported across studies, consequently limiting comparison. Thirdly, the samples are often small (*N*<50 in the case of the SA samples), which may not reflect the larger population.<sup>[13]</sup> Fourthly, viral subtypes may further limit comparison between HIV-1 clades.<sup>[8,14]</sup>

Using general scores from African samples may, therefore, not be appropriate when placing people in categories of impairment using SD from normative scores. The intention of this article is to caution researchers and practitioners against an over-reliance on cross-national 'African' data to create 'local' norms, which may result in inappropriate diagnostic classification.

### Looking forward

Given the incidence of HANDs in SA, there is a critical requirement for valid norms to guide screening and eventual diagnosis. The problematic nature of comparing across national (and presumably cultural) borders emphasises the need for assessment that is fair to patients. This includes: firstly, the development of localised norms – in terms of specific communities – that, at the very least, are reported in terms of age, gender and education (socio-economic status, ethnicity and testing language may also be valuable); and secondly, the use of larger samples that have reasonable validity.<sup>[13]</sup> There are further concerns about the responsibility of test administration, in light of the possible effects of the tester on outcome variance.<sup>[15]</sup> Here, a balance must be struck between

making assessment accessible to the community and maintaining the integrity of the neuropsychological nature of the tests. A tiered approach – i.e. screening with the IHDS by primary healthcare workers, referral to community-based psychologists for an expanded battery (e.g. WHO HIV battery), and further referral to specialist clinics for extended neuropsychological assessment – is recommended.

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