

Cognitive Function in Low-Income and Low-Literacy Settings:

Validation of the Tablet-Based Oxford Cognitive Screen in the Health and Aging in Africa: A
Longitudinal Study of an INDEPTH Community in South Africa (HAALSI)

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Abstract

Objectives: 1. Assess validity of the Oxford Cognitive Screen (OCS-Plus), a domain-specific cognitive assessment designed for low-literacy settings, especially in low- and middle-income countries (LMIC); 2. Advance theoretical contributions in cognitive neuroscience in domain-specific cognitive function and cognitive reserve, especially related to dementia.

Method: In a cross-sectional study of a sample of 1,402 men and women aged 40-79 in the Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI), we administered OCS-Plus along with health and sociodemographic assessments. HAALSI is a representative sample of older adults in Agincourt, South Africa contributing to normative understanding of cognition in LMIC. We report measure distributions, construct and external validity of the OCS-Plus.

Results: OCS-Plus has excellent construct and external validity. Intra-class correlations between similar basic measures of orientation in OCS-Plus and in HAALSI assessments was 0.79, and groups of people performing well on the OCS-Plus verbal memory also showed superior performance on HAALSI verbal memory. The OCS-Plus scores showed consistent associations with age and education and domain-specific associations with alcohol and depression. Younger respondents and the more educated did better on all assessments.

Discussion: The OCS-Plus represents a major methodological advance in dementia studies in LMICs, and enhances understanding of cognitive aging.

Keywords: cognition, cognitive screens in LMIC, HAALSI, OCS-Plus, INDEPTH, Agincourt, South Africa

Introduction

The greatest burden of dementia will rest in developing countries, yet optimal screening tools suited for low- and middle-income countries (LMICs) are limited (Kalaria et al., 2008). By 2040, an estimated 70% of the 80 million people with dementia will reside in LMICs, where many older adults have little formal education and low levels of literacy (Ferri et al., 2006). Educational attainment is a consistent predictor of cognitive function across countries, including LMICs (McArdle, Smith, & Willis, 2009; Strauss et al., 2010). Furthermore, cognitive abilities decline sharply with age (Barrett et al., 2011; Strauss et al., 2010), a particular challenge for LMICs such as South Africa, where life expectancy is expected to rise dramatically (Bor, Herbst, Newell, & Bärnighausen, 2013). Currently, 2-4% of the sub-Saharan African population over 60 are estimated to have dementia or some form of cognitive decline (WHO, 2012). The HIV/AIDS epidemic may significantly alter patterns of cognition and dementia in late adulthood (Mateen & Mills, 2012). It seems clear that there may be improved approaches to assessing cognition more tailored to social conditions of older adults in sub-Saharan Africa (Hendrie et al., 2006).

Pioneering work on dementias in LMIC has emerged over the last decades (Ogunniyi et al., 2000; Prince, Acosta, Chiu, Scazufca, & Varghese, 2003; Rodriguez et al., 2008). However, studies assessing cognitive disorders in sub-Saharan Africa involve (with some notable exceptions) small samples, and are clinic-based (Mateen & Mills, 2012). Population-based studies incorporating neuropsychometric testing are particularly rare for this region, as are contextually validated assessments of cognitive function and dementia (Mayeux et al., 2011; Seshadri et al., 2011; D. R. Weir et al., 2011). Developing cognitive assessments for population-based studies that emphasize validity will elucidate the growing international burden of cognitive decline and dementia. Reliable cross-country epidemiological estimates are compromised by

limitations in available cognitive screening tools. There is also increased awareness that early detection of dementia—to which available screening tools are less sensitive (McLane et al., 2014; Swainson et al., 2001)—is critically important for prevention and diagnosis.

A key challenge in detecting cognitive dysfunction within and across countries is that education is not only a likely causal factor contributing to true differences in cognitive function, but also a biasing factor in measurement, to the extent that some cognitive tests are sensitive to education levels even conditioning on true variation in cognition (Berkman, 1986; Glymour, Kawachi, Jencks, & Berkman, 2008; Glymour, Tzourio, & Dufouil, 2012).

Cognitive neuropsychology theory emphasizes the independence and dissociation of specific cognitive domains. This independence is apparent in focal brain injury studies (e.g., in stroke (Demeyere, Riddoch, Slavkova, Bickerton, & Humphreys, 2015), and in many subtypes of neurodegeneration. Aside from Alzheimer's disease (AD), which is characterized by precipitous memory decline, other dementias have specific domain profiles: fronto-temporal dementia, semantic dementia, cortico-basal degeneration, posterior cortical atrophy. These are characterized by domain-specific impairments and often cannot be diagnosed with current dementia screens (Cullen, O'Neill, Evans, Coen, & Lawlor, 2007).

Traditional screens for dementia such as the Mini Mental State Examination (MMSE) (Folstein, Folstein, & McHugh, 1975) take a binary view of cognition, relying on a summary score from subtasks with a single cut-off value for impairment. Due to the nature of subtasks, this single value is heavily weighted on verbal memory performance. In addition, the MMSE is typically subject to ceiling performance and low sensitivity (Hoops et al., 2009; O'Bryant et al., 2008). Other dementia screens, such as the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) and Addenbrooke's Cognitive Examination, contain measures of

domains other than memory, but they lack domain-specific normative data and are almost exclusively language-based. These screens, therefore, are inappropriate for populations with language deficits (Demeyere et al., 2015) or low literacy.

Here we report validation of the Oxford Cognitive Screen for Dementia (OCS-Plus), an innovative domain-specific and domain-general tablet-based approach to cognition assessment. OCS-Plus was developed as a novel screening tool, based on cognitive neuropsychology theory, and provides continuous performance measures, both (i) domain-specific: language; memory; visuo-spatial abilities and (ii) domain-general: selective and sustained attention; executive functioning. Importantly, OCS-Plus is administered via tablets, with respondents themselves completing tasks, their performance and timing automatically recorded and scored—an important improvement over measures derived from examiner-scored responses to interview questions.

OCS-Plus offers a series of important advantages, including: improved design emphasizing visual-oriented assessments minimizing language effects; time-efficient tests targeting distinct cognitive domains; mobile technology implementing automatic scoring, increasing test sensitivity, standardizing administration, and facilitating deployment in large population studies.

The OCS-Plus approach provides a critical stepchange in population cognitive screening by building comprehensive and refined cognitive profiles incorporating both domain-specific and domain-general measures. These profiles facilitate early identification of decline in more than the traditional memory domain, enabling detection of other types of dementia and early stages of AD. Furthermore, OCS-Plus tests avoid ceiling effects and increase performance range in

healthy populations by including more challenging non-verbal tasks and automatically deriving timing measures.

In this paper, OCS-Plus is validated in a population of older adults in rural South Africa against standard questionnaires (construct validity) and in relation to associations with a number of variables including physical and mental health, age, education, and alcohol consumption (external validity). This work contributes to provision of age and education related norms for these measures in population based studies in low and middle income countries (LMIC).

Methods

We draw on data from the Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI), a cohort study in Agincourt, South Africa, designed as one of the international sister studies of Health and Retirement Study (HRS) (Arokiasamy, Bloom, Lee, Feeney, & Ozolins, 2012; Borsch-Supan et al., 2013; Sonnega et al., 2014; Steptoe, Breeze, Banks, & Nazroo, 2013; Zhao, Hu, Smith, Strauss, & Yang, 2014). HAALSI investigates drivers and consequences of non-communicable diseases and HIV among older adults. The study setting, Agincourt sub-district of rural northeast South Africa, is an area of poverty, low education, high unemployment, and consequent labor migration. The population of 110,000 has been followed since 1992 under the Agincourt Health and Socio-Demographic Surveillance System (Kahn et al., 2012). A total of 5,059 women and men aged 40 and over were enrolled in HAALSI between November 2014 and December 2015; recruitment procedures and eligibility criteria are described elsewhere (Gómez-Olivé et al., 2016). The survey response rate was 85.9%. Respondents completed a household questionnaire capturing demographics, education, employment history, cognitive and physical functioning, self-reported health history, and social, HIV, and cardiometabolic risk factors. A random subsample of the household

respondents aged 40-79 were then invited to either a follow-up visit at Agincourt research laboratory or home, where they completed OCS-Plus assessments between May-December 2015. We present data from 1,402 respondents (508 men, 894 women) who completed OCS-Plus language and memory tasks and HAALSI Computer-Assisted Personal Interview (CAPI) cognition tests. Compliance and test conditions for OCS-Plus executive and attention tasks are provided in Supplemental Table 1. Two-thirds of the HAALSI cohort were sampled for a follow up visit. Approximately 75% of those sampled for follow up consented to a second visit during which time venous blood, clinical exams and the OCS-Plus were administered. Among those who consented to the follow up visit, no one refused to participate in the cognitive assessment.

Measures

OCS-Plus Assessment

OCS-Plus comprises nine short tests of domain-specific and domain-general cognitive performance: language, memory (intentional and incidental), executive functioning (task switching and rule finding), attention (auditory) and praxis. OCS-Plus runs as a stand-alone application on Windows Surface Pro tablets and was developed using Matlab (MathWorks, 2012) and Psychophysics Toolbox (Brainard, 1997; Kleiner et al., 2007; Pelli, 1997).

Administration takes 20-30 minutes. OCS-Plus's graphical user interface guides interviewers through a fixed task list, provides full scripts for each task, ensuring standardized administration and intuitive framework for immediate response scoring. Interviewer and respondent interaction with tablets occurs via dedicated stylus; touch input is disabled to avoid accidental input.

For each task, the interviewer documents the administration condition by selecting from a pre-defined "condition of test" list. Timing is automatically recorded; for most tasks, accuracy of response is also automatically scored. Exceptions include tasks involving interpretation of

respondent's speech or drawing. Here we describe and report accuracy scores for eight of the nine tasks. Screen images available upon request. The praxis task requires manual offline scoring and data have not yet been analyzed.

Stimuli were adapted to linguistic and cultural context and validated on a gender- and age-matched population subsample. Visual stimuli were black and white original line drawings presented on a white background. Auditory stimuli were voice recordings of a female native speaker of the local language, Shangaan.

A summary provided in Supplemental Table 2 details the OCS-Plus tasks in the order they were administered, together with illustrations of respondent visual displays and description of derived scores.

Language Tasks

Picture Naming. Respondents were asked to name a series of four objects with low frequency names. The line drawings of each object were presented one at a time, shown in the middle of the screen. Answers were audio-recorded and their accuracy immediately scored by interviewers. Respondents scored 1 for a correct answer, maximum total score of 4.

Semantics. Respondents were presented with four sets of known objects. In the first and second sets, the interviewer asked the respondent to identify a specific object (i.e. ostrich, pineapple). In the third and fourth sets, the interviewer asked the respondent to identify the object that fit a semantic category (i.e. vegetable, bird). Respondents scored 1 for a correct answer, maximum total score of 4.

One picture-naming stimulus and two non-target (distractor) semantics stimuli formed part of the incidental memory task later in the assessment.

Memory Tasks

Orientation. Respondents were asked open-ended questions about the year, month, date, and current president. Answers were audio-recorded and response accuracy for each item scored by interviewers immediately after response was given. Respondents scored 1 for each correct answer, with a maximum of 4 total.

Word Encoding. Respondents were shown and read out loud five words, asked to remember them, then immediately asked to recall the words (first immediate recall). Responses were audio-recorded and interviewers marked recalled words. Respondents scored 1 for each recalled word, maximum total score of 5. Respondents were then informed that recall of these words would be tested later; words were again shown, read out loud, and their recall tested in a similar fashion (second immediate recall).

Word-Delayed Recall and Recognition. After performing the trails non-verbal executive task that took 4 to 5 minutes, respondents were asked to recall the words (delayed recall). Responses were audio-recorded and scored 1 for each correct word. For each word not recalled, respondents were presented with a list of 4 words on the screen, of which one was the learned word and the rest were semantically related words. Respondents were asked to indicate the word they recognized as the one learned (delayed recognition). Respondents scored 1 for each recalled word, maximum score of 5. Respondents also scored 1 for each recognized word, maximum combined score of 5.

Incidental Memory. Respondents were presented with a set of four line drawings and asked to identify the item previously seen during the assessment. Three sets were presented in fixed order. Each set contained 3 previously unseen items, and 1 item presented earlier: 1 target item from picture-naming task, 2 distractor items from the semantics task. A fourth similar set

was presented including written words, with 1 target verbal memory word and 3 distractors. Respondents scored 1 for each recognized item, maximum total score of 4.

Executive Function Tasks

Trails. Respondents were presented with an arrangement of dark grey circles and light grey squares of different sizes and asked to draw lines on the screen with stylus to connect them in certain orders. Arrangements were pseudo-random, ensuring that correct connections would not intersect with other shapes or correct connections. To hold the respondent's engagement, when the line intersected a shape, visual and auditory feedback was given. Performance was timed and automatically scored.

There were two baseline conditions and one set-switching condition. Each condition was preceded by interviewer demonstration and two practice runs; assessment only followed successful completion. During test runs, respondents were given no prompts or feedback regarding accuracy or completeness of the trail, and each task finished when respondent indicated the trail was complete.

Test runs for first baseline condition consisted of an arrangement of 8 circles and 8 squares. Respondents were asked to connect circles from small to large. Respondents scored 1 for each correct connection (maximum score: 7). Test runs for second baseline condition consisted of a similar arrangement, with respondents asked to connect squares from large to small. Scoring remained the same. In the switch condition test, respondents were asked to alternate connections between squares and circles, alternating in size, starting with the largest square followed by the smallest circle, and continuing until all shapes were connected. Scoring was similar, this time with a maximum score of 14. For respondents who scored at least 2 in baseline condition, executive score was the switch condition score as a percentage of highest

baseline score. An additional binary score was derived to record whether respondents failed to learn the task.

Rule Finding. Respondents were presented with a set of 12 squares and 12 triangles randomly arranged in an 8-by-3 grid. All shapes were light grey, with the exception of one item per row that was dark grey. During the task, a red dot moved across the shapes following certain rules. Current and previous positions of the dot were always marked. At each move, respondents were asked to use the stylus to tap the position they predicted the dot would assume next. After one practice rule, respondents received no feedback, but accuracy could be inferred from the subsequent position.

There were five rules in total, and transitions from one rule to next were not signaled. Four rules were positional (shape colors were irrelevant), but for the final rule both position and shade were relevant. Respondent scored 1 for each correctly predicted move. The first move in every rule—where only guessing was possible—was not scored. Two consecutive correctly predicted moves within a rule were scored as rule found, with a maximum score of 5. An additional binary score recorded whether respondents failed to learn tasks, resulting in 0 rule score.

Auditory Attention

OCS-Plus includes an auditory attention task assessing selective and sustained attention to words presented repeatedly in an audio recording.

The task included 3 target words (goodbye, down, no), 3 semantically related distractors (hello, up, yes), and 3 unrelated distractors (and, eat, day). Each word was presented 9 times, split across 3 blocks, each containing 3 presentations of each word. The order of words within

each block was pseudo-randomized. Interstimulus interval was assigned randomly from a selection of 1s, 2.5s, and 3s.

Respondents used the stylus to tap a blue button in the middle of the screen as soon as they heard any target word, and to tap a yellow button beneath the blue one upon hearing any other word. Respondents were not told about the identity of distractor words prior to testing.

The test run was preceded by a maximum of 3 practice runs, in which respondents were presented a short audio recording comprising 1 presentation of each target and semantically related words. Following each practice run, respondents were presented with target and distractor words, 1 per row, and asked to identify target words. Assessments only proceeded to test run if respondents either responded correctly to practice or correctly identified target words. An additional binary score was derived to record whether respondents passed the practice.

HAALSI Household Measures and Assessments

In the HAALSI survey, respondents were interviewed in Shangaan during home visits by trained fieldworkers using CAPI. Respondents were asked background questions on household members and household socioeconomic and social characteristics, age, educational attainment, employment status, and health. In these analyses, we include questions regarding age, taken from administrative records of date of birth; education, defined by years of schooling and categorized as no education, some primary education, or completion of primary education or more; depression, measured with an 8-item Center for Epidemiological Studies Depression Scale (CES-D) (Radloff, 1977), with yes/no scoring of symptoms reported in the last week; consumption of any alcohol in the previous 30 days (a measure of general consumption not alcoholism), scored yes/no; and activities of daily living (ADLs) (walking across room, bathing, eating, getting in or out of bed, toileting), scored yes if positive to any (Katz, Ford, Moskowitz, Jackson, & Jaffe,

1963; Sonnega et al., 2014). Literacy was assessed separately from education; respondents were asked whether they could read or write. Household wealth is the quintile ranking of scores derived from principal components analysis of ownership of household items, livestock, and vehicles (Filmer & Pritchett, 2001).

The HAALSI cognitive function assessment consisted of standard questions drawn from HRS to assess cognitive competencies (Sonnega et al., 2014). The series spans three cognitive domains: memory, orientation, and executive functioning. The questions include self-rated past and present memory, working memory, orientation, and a mini-mental state exam. Here we describe results on memory and orientation.

Memory

Immediate Word Recall. Respondents remember as many words as possible, in any order, from a list of 10 words read by the interviewer. Word retention was immediately tested and words recalled were documented. If no words were recalled, interviewers read out the same list again up to three additional times. Regardless of recall success, interviewers told respondents that their recall would be assessed later. Four unique lists were stored in CAPI, and one list was randomly chosen for each respondent to reduce any potential bias.

Delayed Word Recall. After an average of one minute, respondents were asked to recall any of the 10 words. Words recalled were documented. The one minute delay was shorter than commonly used in similar surveys and resulted from a faster interview pace than anticipated based on our pilot studies. The short delay may limit the sensitivity of this measure.

Orientation. Respondents name the current month, date, year, and president. Accuracy of response (correct/incorrect/not known/refusal) was recorded for each question. Note that these questions are identical to those in OCS-Plus orientation task.

Statistical Approach

We use several methods to test validity of the OCS-Plus. We first document overall distributions of OCS-Plus scores, as well as variation in scores by age and education. We assess convergent validity by testing intra-class correlations and report the extent to which comparable HAALSI CAPI and OCS-Plus scores are associated. We examine OCS-Plus relationships between delayed word recall performance and ability to learn executive tasks. Finally, we complete multiple regression analyses for each of the OCS-Plus scores, including conditions we hypothesized would illustrate convergent and divergent external validity. We test for interactions between age and education to assess the impact of education on age-related differences.

Results

Table 1 describes the HAALSI cohort sociodemographic and health characteristics and distributions for the OCS-Plus validity sample of 1,402. Results indicate that, while there are more women in the OCS-Plus sample than in the overall HAALSI cohort, on most other dimensions the differences are small. An important feature of this cohort of rural South Africans is the overall low level of education. Over 45% of the cohort had no formal education and roughly 30% had only some primary education. Employment was 19% in men and 12.9% in women. It should be noted that most South Africans aged 60 or older receive the state old-age pension and do not commonly work in the formal work sector so these percentages are low.

TABLE 1 HERE

Supplemental Figure 1 presents distributions of OCS-Plus task scores pooled by age and education. A tendency to perform to ceiling was noted on the Orientation task, a standard measure in all dementia screens. The Rule Finding distribution of scores, however, exhibited a tendency to floor, with the majority of respondents not scoring higher than 20% (finding only 2

rules), though the full range was present with 15% of the sample finding more than 2 rules. Other tests, particularly incidental memory, demonstrated a very good range of variability across all scores. However, we note that these distributions were collapsed across age, sex, and education and therefore reflect these sample characteristic distributions as well as test score distributions (discussed below).

Figure 1 presents distributions for OCS-Plus task scores by age decade and education level. Since only 10.5% of the sample had 12 or more years of education, this group was combined with those with 8-11 years. The association between education and task performance was clearly apparent in all OCS-Plus tasks, with higher scores associated with higher levels of education. Although weaker, associations between age and performance were also evident, particularly for the oldest age group. We discuss in detail these associations in multivariate analyses with formal tests of significance, controlling potential confounders.

FIGURE 1 HERE

The next set of analyses assessed construct validity by comparing OCS-Plus scores and HAALSI CAPI scores on the two tasks that were similar, namely orientation and delayed word recall. Overlapping corresponding score distributions are shown in Figure 2.

FIGURE 2 HERE

The two measures of orientation were virtually identical in the two sets of assessments and the intra-class correlation was highly significant, $p < 0.0001$, Cronbach alpha 0.8.

Comparisons of two measures of delayed word recall were less straightforward, since the two procedures employed were very different. The HAALSI CAPI instrument asked respondents to learn and later recall 10 words. Between the first presentation of words and delayed recall, words were presented again up to three times without recording number of rehearsals or intermediate recalls. Time delay between presentation of words and delayed recall was very short, averaging 1 minute, during which two short numerical tasks were performed. By contrast, the OCS-Plus word memory task (intentional memory) involved only two presentations of a shorter word list comprising only 5 words, followed by a much longer executive non-verbal task. It is not surprising, then, that the intra-class correlation between the two scores was low, Cronbach alpha 0.3. However, further analysis was performed splitting respondents into two groups: high intentional memory performance (> 3 words in the delayed recall OCS-Plus task) versus low performance (≤ 3). We found those with good OCS-Plus intentional memory performance also had superior performance on the HAALSI CAPI task ($t(1400)=6.8$, $p<0.001$).

We then examined relationships between intentional memory performance and ability to learn executive tasks with a Pearson Chi square between an operational score for high intentional verbal memory performance and binary score derived for ability to learn the executive task. We predicted that intentional verbal memory would not be associated with non-verbal executive tasks, but would be associated with the auditory attention task that included an important verbal memory component. Indeed, analyses revealed that intentional verbal memory performance was independent of ability to learn the rule finding task (Cramer's $V=0.027$, $p=0.32$) and of ability to learn the trails task (Cramer's $V=0.41$, $p=0.15$); it was associated with ability to learn the auditory attention task (Cramer's $V=0.091$, $p=0.001$). This dissociation between intentional verbal memory and executive function performance is a critical finding highlighting the

importance of non-verbal executive tests in informing detection of deficits outside the memory domain.

In our final set of analyses, we conducted multiple regressions for each OCS-Plus score, with gender, age, education, employment status, household wealth, depressive symptoms, and current alcohol included as independent variables. We conducted these analysis to establish external validity—or convergent validity. We hypothesized that OCS-Plus scores would be positively associated with education, employment, and wealth, and negatively associated with age, depressive symptoms, and alcohol use. Results are shown in Table 2.

TABLE 2 HERE

The most consistent finding was the association of education with OCS-Plus scores across all cognitive domains. Furthermore, as expected, age was associated with all but two (semantics and attention tasks) of the eight OCS-Plus measures. We note that significant differences in performance were found only in the older age group.

Household wealth quintile ranking—an important indicator of socioeconomic conditions in this population—was associated with picture naming and semantics, orientation, rule finding, and attention scores. Alcohol consumption was also significantly related to OCS-Plus measures of semantics, orientation and rule finding. This category of the measures included a broad range of respondents who reported consuming any alcohol in the past 30 days. Depressive symptoms were negatively associated with orientation and picture naming but not with any other scores. Employment was unrelated to cognition except for two significant associations with orientation and picture naming, although few respondents in our study were employed and many were receiving old-age pensions. Convergent validity was established with consistent associations of OCS-Plus scores with age, education, and wealth. Validity was further demonstrated with the

association of alcohol consumption with lower cognitive function. Depressive symptoms were less consistently associated with cognitive outcomes.

To assess divergent validity, or the independence of measures, we examined associations between OCS-Plus and ADL disability, which captures major physical impairment (see Table 2 results). We anticipated no relationship with cognitive function except among the most severely impaired AD respondents. Our analyses found that no OCS-Plus measures were associated with the ADL measure, suggesting divergent validity, since our validity sample excluded respondents likely to have severe dementia. We will be able to confirm this further with longitudinal analyses over the next years with additional waves of data and continued more detailed examination of those most likely to have Alzheimer's Disease or related dementias (ADRD).

We assessed the interaction between age and education in regression models with the same covariates. Weak positive interactions ($p < 0.05$) were observed for orientation and picture naming, suggesting that education might protect against cognitive decline at older ages (data not shown). It is important to note that we had both age and cohort effects in the cross-sectional sample and were not able to examine the protective effects against decline in cognition as one could with longitudinal data. Future longitudinal data will enable us to distinguish true age-related declines from cohort effects.

Discussion

The innovative tablet-based OCS-Plus approach bypasses limitations of paper-and-pencil assessments and builds on the increasing familiarity with electronic devices now common even in many low-income countries. Indeed, we found high task compliance and good validity of the OCS-Plus in our large, low-education, low-income sample from the rural South African community of Agincourt. We highlight some critical advantages offered by the OCS-Plus

platform in: standardization of administration through scripted instructions; use of visually oriented and simple language tasks that minimize cultural and literacy confounds; and automatic scoring of performance with minimal interviewer input or bias, allowing for significant gains in speed and process of data collection and management. This suggests that OCS-Plus is highly suitable as a cognitive screen within large epidemiological studies, in a variety of cultural and socioeconomic settings. Although the tablet for this study was in a prototype stage it is now being adapted for tablet-based assessments that are more easily and economically implemented. These will be field tested in the coming year avoiding one of the disadvantages of the current OCS-Plus. Its use may increase our ability to understand whether cross-country comparisons reflect genuine differences in risks, giving us important etiologic clues as to the causes and prevention of ADRD and domain specific cognitive declines. To date, our findings underscore the similar age and education patterns seen in other low, middle and high income countries. Although longitudinal data will be more informative regarding age-related declines in cognition, our findings suggest that some of these patterns may be virtually universal even as we enrich our understanding of cognition in low literacy settings (Huang & Zhou, 2013; Kalaria et al., 2008; D. Weir, Lay, & Langa, 2014).

The range of cognitive scores reported in this study demonstrates that OCS-Plus avoids floor and ceiling effects present in other short cognitive screens based primarily on language and memory domain measures. For both domain-specific and domain-general measures, there is a strong effect of education level. Our findings also show that age-related associations with such cognitive domains as language and orientation may be stronger among those with lower levels of education. One possible mechanism by which education may protect against age-related decline is through the construct of cognitive reserve (Stern, 2012), which proposes an experience-

dependent neuroprotective mechanism. This includes factors such as professional attainment, intelligence, and mental stimulation. Strong effects of education in all age ranges suggest that indeed education increases capacity to deal with complex cognitive tasks and preserves function by either enhancing cognitive reserves earlier in life (at time of education) or preserving function through the maintenance of cognitive abilities through behavioral interactions that occur over a lifetime, which has been suggested to repeatedly activate the noradrenergic system (Robertson, 2013). Since the finding in the Dementia Study Project (Del Ser, Hachinski, Merskey, & Munoz, 1999), the neuroprotective effects of education on cognitive decline have been reported numerous times in epidemiological studies.

We must nonetheless interpret these findings very cautiously because they may also still reflect selection processes—especially for older cohorts of respondents whose cognitive abilities may have increased their chances of acquiring higher levels of education even during the period of apartheid and in this setting with limited access to education. Associations with education may also reflect increase familiarity with computers which can alter reliability (Browndyke et al., 2002; Schatz & Browndyke, 2002). Our longitudinal analyses over the next years will enable us to sort this out by observing true age effects and genuine decline in cognition from cohort effects. With further waves of follow up, we will understand better the degree to which education is likely to lead to declines in cognition or interact with age to “protect” against age related declines. This will help us to infer the causal effect of education, though it is not definitive since we do not have an experimental approach to test this association. It will help us to avoid reverse causation but not to rule out the impact of other unobserved conditions. Furthermore, we demonstrate independence of verbal recall and domain-general measures, a critical finding that suggests suitability of our assessment for distinguishing between various types of neurodegeneration, for

detection beyond memory decline typical of Alzheimer's dementia. Another limitation relates to the administration of our assessments. Some measures were not optimally harmonized. In particular the delayed word recall was not standardized in the time between initial delivery and delayed recall or in number of items between the OCS-Plus and the CAPI version limiting our analytic ability. In future studies we will harmonize these aspects of the assessment and for longitudinal assessments we will consider prior testing experience since this may be critical in assessing changes over time (T. A. Salthouse, 2016).

We also note that OCS-Plus collects a variety of performance and timing information not reported here, although it should be acknowledged that the predictive utility of these data for distinguishing normative cognitive decline from more severe levels of impairment will be explored in future papers. These measures include, but are not limited to, reaction times, commission errors, reversals—all potentially very important in the context of age-related cognitive decline (Sylvain-Roy, Lungu, & Belleville, 2015; Vasquez, Binns, & Anderson, 2016). For example, decline and increased variability in speed and efficiency of information processing may be an important marker of cognitive decline (Der & Deary, 2006; T. Salthouse, 2000, 2009). These can also help predict incident cognitive impairment independent of age (Bielak, Hultsch, Strauss, MacDonald, & Hunter, 2010; Kochan et al., 2013), which has led to the intriguing suggestion that measures of reaction time may represent an index of general neurological integrity at the biological level (Nilsson, Thomas, O'Brien, & Gallagher, 2014).

Conclusion

The tablet-based OCS-Plus assessment provides domain-specific (language and memory) and domain-general (executive and attention) measures of cognition with minimal language content, improving sensitivity and rigor of epidemiological studies by minimizing language and

cultural confound effects and examiner bias, while providing a comprehensive cognitive profile as a tool for early detection of multi-domain decline. OCS-Plus may therefore prove to be critical in understanding the global epidemiology of dementias, but can also translate more broadly to a better understanding of cognition and cognitive decline in populations, across a wide range of education levels. Our work moves the field forward to create the next generation of standardized, sensitive, and validated methods of cognitive assessment likely suitable for large-scale population study settings.

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Table 1. Characteristics of the HAALSI main study sample and the cognition sub-sample.

		Cognition			
		Full sample		sub-sample	
		<i>N</i> = 5,059		<i>N</i> = 1,402	
		n	%	n	%
Sex	Male	2,345	46.4	508	36.2
	Female	2,714	53.7	894	63.8
Age	40-49	918	18.2	291	20.8
	50-59	1,410	27.9	481	34.3
	60-69	1,304	25.8	362	25.8
	70-79	878	17.4	268	19.1
	80+	549	10.9	0	0.0
Education Level	No formal education	2,306	45.7	542	38.7
	Some primary (1-7 years)	1,614	32.0	543	38.8
	Some secondary (8-11 years)	537	10.7	167	11.9
	Secondary or more (12+ years)	585	11.6	147	10.5
Marital Status	Never married	290	5.7	74	5.3
	Separated / divorced	650	12.9	206	14.7
	Widowed	1,540	30.5	376	26.8
	Currently married / cohabitating	2,575	50.9	746	53.2
Household size	Living alone	534	10.6	129	9.2
	Living with 1 other person	538	10.6	129	9.2

	Living in 3-6 person household	2,438	48.2	692	49.4
	Living in 7+ person household	1,549	30.6	452	32.2
Employment	Employed (part or full time)	805	16.0	180	12.9
	Not working	3,719	73.7	1,047	74.7
	Homemaker	521	10.3	174	12.4
Wealth index	Quintile 1 (lowest)	950	18.8	250	17.8
	Quintile 2	979	19.3	273	19.5
	Quintile 3	1,158	22.9	337	24.0
	Quintile 4	977	19.3	274	19.5
	Quintile 5 (highest)	995	19.7	268	19.2
Alcohol use	Currently drinks (in last 30 days)	1,171	23.2	265	18.9
ADLs	Has any ADL disability	456	9.0	76	5.4
Depression	CESD score 0	511	10.4	142	10.1
	CESD score 1	2,362	47.9	649	46.3
	CESD score 2	1,128	22.9	357	25.5
	CESD score 3 or higher	928	18.8	254	18.1

Notes. Not shown: 17 missing education level, 4 missing marital status, 14 missing employment status, 3 missing alcohol use, 130 missing depression score in full sample; and 3 missing education level, 1 missing employment status, in sub-sample. In the full sample, 231 missing wealth index were assigned village mean wealth, 56 missing wealth index were assigned village mean wealth in sub-sample.