Validity and reliability of the Neurodevelopmental Screening Tool (NDST) in screening for neurodevelopmental disorders in children living in rural Kenyan coast [version 1; peer review: 2 approved]

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Abstract

Background: There are no data on the precise burden of neurodevelopmental disorders (NDD) in Africa, despite high incidence of risk factors. Ten Questions Questionnaire (TQQ) has been used extensively in Africa to screen neurological impairments but not autism spectrum disorders (ASD) and attention-deficit hyperactivity disorders (ADHD). The Neurodevelopmental Screening Tool (NDST) has reliably assessed NDD in Asia; its validity in Africa is unknown.

Methods: Using NDST and TQQ, we screened 11,223 children aged 6-9 years in Kilifi, Kenya. We invited all screen-positives and a proportion of screen-negative children for confirmatory diagnosis of NDD using clinical history, neuropsychological assessments and interviews.

Results: In total, 2,245 (20%) children screened positive for NDD. Confirmatory testing was completed for 1,564 (69.7%) screen-positive and 598 (6.7%) screen-negative children. NDST’s sensitivity was 87.8% (95%CI: 88.3-88.5%) for any NDD, 96.5% (95%CI:96.1-96.8%) ASD and 89.2% (95%CI: 88.7-89.8%) for ADHD. Moderate/severe neurological impairments’ sensitivities ranged from 85.7% (95%CI: 85.1-86.3%) for hearing impairments to 100.00% (100.0-100.0%) for motor impairments. NDST had higher sensitivities than TQQ for epilepsy (88.8 vs 86.7), motor impairments (100.0 vs 93.7) and cognitive impairment (88.2 vs 84.3). Sensitivities for visual and hearing impairments were comparable in both tools. NDST specificity was...
82.8% (95%CI: 82.1-83.5%) for any NDD, 94.5% (95%CI: 94.0-94.9%) for ASD and 81.7% (95%CI: 81.0-82.4%) for ADHD. The specificities range for neurological impairments was 80.0% (95%CI: 79.3-80.7%) for visual impairments to 93.8% (95%CI: 93.4-94.3%) for epilepsy. Negative predictive values were generally very high (≤100%), but most positive predictive values (PPV) were low (≤17.8%). Domain specific internal consistency ranged from 0.72 (95%CI: 0.70-0.74) for ADHD to 0.89 (95%CI: 0.87-0.90) for epilepsy.

**Conclusions:** NDST possesses high sensitivity and specificity for detecting different domains of NDD in Kilifi. Low PPV suggest that positive diagnoses should be confirmed when samples are drawn from a population with low disease prevalence.

**Keywords**
Screening, neurodevelopmental disorders, Africa,
Introduction

Neurodevelopmental disorders (NDD) such as autism spectrum disorders (ASD), attention deficit hyperactivity disorders (ADHD) and cognitive impairment are common in low- and middle-income countries (LMIC), but there are few epidemiological studies in Africa\(^1\). Despite the high incidence of risk factors for NDD such as environmental toxins, perinatal complications and intracranial infections, the precise burden of these disorders is unknown in Africa\(^2\). Few available studies are based on single neurological conditions such as cognitive impairments\(^1\), not detecting other important conditions like ASD and ADHD, since the screening was conducted with the Ten Questions Questionnaire (TQQ). The TQQ is a brief and easy to use tool that has been widely used in LMIC to screen for neurological impairment and disability\(^3\). This lack of epidemiological data for NDD in Africa is in part ascribed to lack of awareness about their existence in the community, which is now changing following awareness from epidemiological studies of related neurological disorders\(^4\). The challenge, however, remains on availability and development of reliable tools for screening and diagnosis of NDD in Africa; this is likely to change given the recent development of a cadre of local psychologists and neurodevelopmental researchers\(^5\).

Recently, studies in Asia have developed a tool for screening of developmental disorders in children, specifically the Neurodevelopmental Screening Tool (NDST). This tool was used to screen neurodevelopmental disorders in India, but the estimates differed with region/settings (10–18%)\(^6\), which may suggest: (i) that the high burdens of NDD are unique to those regions, and/or (ii) that the reliability and validity of NDST in detecting neurodevelopmental disorders differs across the regions. Although the reliability (test-retest and inter-rater agreement) of NDST was examined and found to be acceptable\(^7\), the clinical validity (sensitivities, specificities, positive and negative predictive values) were not reported. It is important to evaluate the validity of screening tools since a tool with low sensitivity results to false-negatives, thereby underestimating the burden of NDD, while those with a low specificity allows false-positives and overestimation of NDD.

The NDST has not been piloted in Africa, yet it allows screening for a wider range of NDD, which have not been assessed together in sub-Saharan Africa and which are often comorbid\(^8\). Since the validity and reliability of screening tools may depend on cross-cultural interpretation of the disorders\(^6\), it is important to examine the validity of NDST in Africa before its use in the much needed epidemiological studies.

We set up a two-stage large epidemiological study to estimate the burden of neurodevelopmental disorders in a rural area on the Kenyan coast, which allowed us to examine the validity of NDST in detecting NDD in this region. Additionally, we compared the psychometric properties of the NDST to those of the TQQ which has been previously validated for detecting neurological impairments in this setting\(^9\). The validity of the TQQ in detecting neurological impairment has been acceptable across different studies, but few studies have compared it with other screening tools for NDD such as NDST. There is need to compare the validity of TQQ with that of NDST in one study.

Methods

Ethical statement

Prior to commencement of data collection, ethical approval for this study was obtained from the Scientific and Ethics Review Unit, Kenya under protocol number KEMRI/5ERU/CGMR-C/3000. Written informed consent to use and publish de-identified patients’ data was obtained from caregivers of the participants.

Study settings

This study was conducted in a rural area the of the Kenyan coast in a demographic surveillance area referred to as the Kilifi Health and Demographic Surveillance System (KHDSS)\(^10\), which is located in Kilifi County. Vital statistics on births, deaths and migration patterns (in or out) in KHDSS are updated every four months. The main population in KHDSS is the Mijikenda ethnic group, the majority of whom are subsistence farmers and a few fishermen. The literacy levels are low, and Kilifi County is one of the poorest administrative regions in Kenya. The health services for neuropsychiatric and NDD in this area are poorly developed\(^11\).

Sampling

Data were collected between March 2015 and August 2016. The sampling frame for this study comprised children aged 6–9 years living within KHDSS, who form a total population of about 35,000. The age group of 6–9 years was chosen because this is when most NDD become apparent and is when most children in sub-Saharan Africa enrol for school. Each child had an equal probability of being randomly selected to participate in the study so long as they met criteria for age and living within KHDSS. Children would be excluded if they out-migrated or died during the period of study. This validation study was nested in a large epidemiology study which aimed at screening about 15,000 children randomly selected from the 35,000 children. Screening about 15,000 randomly selected children would detect neurodevelopmental disorders with a precision or margin of error of <1%, assuming a conservative prevalence of 6.1% in the community. The RAND () command of MySQL was used to select the eligible children.

Study design and procedures

The study was implemented using a two-stage design; stage I involved screening of NDD in the community and stage II involved further clinical assessment of all those who screened positive in stage I and a proportion of those who screened negative. Screen- negative participants were included in stage II to obtain reference diagnostic categories for validating against NDST screening status. Eligible participants were identified using the MySQL software then trained interviewers fluent in the local dialects visited the households and explained the study to the parents or close caregivers of eligible children. The NDST and TQQ were then administered to parents or caregivers to participate in the study. All children with a positive response in at least one of the NDST items and every 5th child screening negative in all NDST items were
invited to the Neuroscience Unit at the KWTRP in Kilifi County Hospital for comprehensive clinical assessments (stage II).

Neurodevelopmental disorders were defined as the presence of either epilepsy, ADHD, ASD, hearing impairments, visual impairments, motor impairments or cognitive impairment. Epilepsy was defined as a history of two or more unprovoked seizures according to recommendations by International League Against Epilepsy (ILAE). Hearing impairment was defined as a 41–70 dB loss in the best ear and difficulty in hearing even with a hearing aid. Visual impairment was defined as visual acuity of worse than 6/18. Motor impairment was defined as difficulty in holding implements, dressing and sitting upright but able to move around with help; severe impairment as inability to walk and absence of functional use of hands. Cognitive impairment was defined as a z-score of below −2 in the Ravens Matrix test. Z-scores were calculated as a function of the difference between the mean of an individual child and the mean of a representative sample, divided by the standard deviation of the mean of the representative sample. For standardization, z-scores were calculated separately for each age-year.

Clinical evaluation comprised neuropsychological assessments using structured diagnostic questionnaires as detailed below. A diagnosis of epilepsy was confirmed through clinical history that included presence of seizures as defined by ILAE recommendations. Cognition was measured using the Ravens Coloured Progressive Matrix Test and Kilifi Naming test. The Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) measured ADHD. Autism spectrum disorders diagnosis was done by clinical review using the American Psychiatric Association (APA) Diagnostic and Statistical Manual of Mental Disorders (DSM-V) criteria that followed the Autism Diagnostic Observation Schedule (ADOS) structure. Vision was assessed with Sonksen-Silver Acuity system and hearing assessed with Kamprex screening audiometer model number SM-950.

The questionnaires were administered by trained neuropsychological assessors. All the tools including NDST were translated into the lingua franca, Kiswahili, through a standardised forward and back translation process as in previous studies in the area. All the tools were piloted to test their comprehensibility and revised accordingly before use in the epidemiological survey. Participants of the pilot tests were randomly selected from community members who attended the Kilifi County Hospital as caregivers of patient. Administration of the tools was supervised by a developmental psychologist, child and adolescent psychiatrist and child neurologist. Final versions of tools used are available as extended data.

Statistical analysis
Data were entered using MySQL, and analysed using STATA software (version 13.1, Stata Corp LP, College Station, TX, USA) and R-statistical software (version 3.4.0 (2017-04-21)). Sensitivities, specificities, and positive and negative predictive values of detection of NDD by NDST were computed by comparing screening outcomes in stage I against diagnoses in stage II using the “diagtest” syntax in STATA. Discrete variables were compared using Pearson’s Chi-squared, or Fisher’s exact test where observations in a cell were sparse (less than 5). Internal consistency of the NDST items was assessed by computing the Cronbach’s alpha.

Results
General description
In total, 15,000 children were eligible to participate in the study of whom 11,223 (74.8%) children were available for visitation, consenting and to screening. The excluded children could not be traced within the KHDSS. Of those who were screened, 49% were female. Of the 11,223 children, 2,245 (20%) screened positive for at least one neurodevelopmental disorder in stage I. In total, 2,162 children were assessed in stage II: 1,564 (69%) of the screen-positive and 598 (6.7%) randomly selected screen negatives. The 681 screen-positive participants from stage I who did not participate in stage II either refused to participate, were lost to follow up or died as summarised in Figure 1. There was no difference in the sexes of those who were assessed in stage II.

Internal consistency of NDST questions
The total internal consistency of the 39 NDST questions as measured by Cronbach’s alpha was 0.84 (95%CI: 0.82-0.85). The internal consistency of the specific domains ranged from 0.72 (95%CI: 0.70-0.74) for ADHD to 0.89 (95%CI: 0.87-0.90) for epilepsy (Table 1).

Validity of NDST in detecting all NDD
The false negatives of NDST was 10.1%, with false positive proportion of 17.1%. This translated to a sensitivity of 87.8% (95%CI: 88.3-88.5%) and a specificity of 83.3% (95%CI: 82.7-84.0%). The positive predictive value was low, but the negative predictive value was very high (95%CI: 88.3-88.5%) and a specificity of 83.3% (95%CI: 82.7-84.0%). The sensitivity for having ASD or ADHD (89.5% vs. 88.8%) was higher than for neurological conditions, as was the specificity (82.1% vs. 80.0%) (Table 2).

Validity of NDST in detecting presence of ASD or ADHD
ASD was diagnosed in 80 children, of whom 2 (2.5%) were classified as false negatives by NDST in stage I. Of those without ASD in stage II, 2,167/11,143 (19.4%) were classified as false positives by NDST in stage I. Therefore, the sensitivity for NDST in detecting ASD was 96.5% (95%CI: 96.1-96.8%), while the specificity was 80.6% (95%CI: 79.9-81.3%). Screening with ASD specific questions improved the specificity of NDST by about 15% (Table 3). Positive predictive values of NDST were low but the negative predictive values were high (Table 2).

ADHD was diagnosed in 280 children, of whom 30 (210.7%) were classified as false negatives by NDST in stage I. Of those without ADHD in stage II, 2,167/11,143 (18.2%) were classified as false positives by NDST in stage I. Therefore, the sensitivity for NDST in detecting ADHD was 89.2%
Validity of NDST in detecting neurological impairments

False negative classification proportion for epilepsy by NDST was 11/98 (11.2%) while false positives classification was 2,158/11,125 (19.4%). The sensitivity for detecting epilepsy by NDST was 88.8% (95%CI: 88.2-89.3%), with specificity was 80.6% (95%CI: 79.8-81.3%). Use of the question on seizure disorders improved the specificity by 13%. Positive predictive values were low while negative values were high (Table 2).

False negative classification for cognitive impairment by NDST was 6/51 (11.7%), while false positive classification was 2,200/11,172 (19.6%). The sensitivity for detecting cognitive impairment by NDST was 88.2% (95%CI: 87.6-88.5%), with specificity being 80.3% (95%CI: 79.5-81.0%). Positive predictive and negative values are shown in Table 2.

False negative classification for motor impairments by NDST was 0/16 (0%), while false positive classification was

### Table 1. Internal consistency for the Neurodevelopmental Screening Tool (NDST) questions for each domain measured with Cronbach's alpha. CI=confidence interval.

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Number of questions</th>
<th>Cronbach's alpha (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autism spectrum disorders (ASD)</td>
<td>11</td>
<td>0.82 (0.78-0.86)</td>
</tr>
<tr>
<td>Attention deficit hyperactivity disorder (ADHD)</td>
<td>4</td>
<td>0.72 (0.70-0.74)</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>2</td>
<td>0.89 (0.87-0.90)</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>13</td>
<td>0.85 (0.83-0.87)</td>
</tr>
<tr>
<td>Motor impairments</td>
<td>4</td>
<td>0.75 (0.69-0.81)</td>
</tr>
<tr>
<td>Visual impairments</td>
<td>7</td>
<td>0.74 (0.71-0.77)</td>
</tr>
<tr>
<td>Hearing impairments</td>
<td>3</td>
<td>0.76 (0.73-0.79)</td>
</tr>
</tbody>
</table>
The sensitivity for detecting moderate/severe motor impairments by NDST was 100.0% (95%CI: 100.0-100.0%), while the specificity was 80.1% (95%CI: 79.3-80.8%). Positive predictive and negative values are shown in Table 2.

False negative classification proportion for visual impairments by NDST was 0/8 (0%), while false positive classification was 2237/11,215 (19.9%). The sensitivity for visual impairments was 100.0% (95%CI: 100.0-100.0%), with specificity being 80.0% (95%CI: 79.3-80.7%). Positive predictive and negative values are shown in Table 2.

Comparison of NDST with TQQ in detecting neurological disorders

The NDST had higher sensitivities than TQQ for epilepsy, motor impairments and cognitive impairment, but sensitivities for visual and hearing impairments were comparable in both

Table 2. Validity of all Neurodevelopmental Screening Tool (NDST) questions in detecting neurodevelopmental disorders in 11,223 children screened in stage I and 2,162 assessed in stage II.

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Sensitivity (%) (95% CI)</th>
<th>Specificity (%) (95% CI)</th>
<th>Positive predictive value (%) (95% CI)</th>
<th>Negative predictive value (%) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASD</td>
<td>96.5 (96.1-96.8)</td>
<td>80.6 (79.9-81.3)</td>
<td>3.7 (3.3-4.0)</td>
<td>99.9 (99.9-100)</td>
</tr>
<tr>
<td>ADHD</td>
<td>89.2 (88.7-89.8)</td>
<td>81.7 (81.0-82.4)</td>
<td>11.1 (10.5-11.7)</td>
<td>99.6 (99.5-99.7)</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>88.8 (88.2-89.3)</td>
<td>80.6 (79.8-81.3)</td>
<td>3.8 (3.5-4.2)</td>
<td>99.9 (99.8-99.9)</td>
</tr>
<tr>
<td>Cognitive impairment</td>
<td>88.2 (87.6-88.5)</td>
<td>80.3 (79.5-81.0)</td>
<td>2.00 (1.7-2.3)</td>
<td>99.9 (99.8-99.9)</td>
</tr>
<tr>
<td>Motor impairments</td>
<td>100.0 (100.0-100.0)</td>
<td>80.1 (79.3-80.8)</td>
<td>0.7 (0.6-0.9)</td>
<td>100.0 (100.0-100.0)</td>
</tr>
<tr>
<td>Visual impairments</td>
<td>100.0 (100.0-100.0)</td>
<td>80.0 (79.3-80.7)</td>
<td>0.4 (0.3-0.5)</td>
<td>100.0 (100.0-100.0)</td>
</tr>
<tr>
<td>Hearing impairments</td>
<td>85.7 (85.1-86.3)</td>
<td>80.0 (79.3-80.7)</td>
<td>0.3 (0.2-0.4)</td>
<td>99.9 (99.9-100)</td>
</tr>
<tr>
<td>Any neurological impairment*</td>
<td>88.8 (88.3-89.4)</td>
<td>80.0 (79.3-80.7)</td>
<td>0.3 (0.2-0.4)</td>
<td>97.6 (96.9-98.2)</td>
</tr>
<tr>
<td>Having ASD or ADHD‡</td>
<td>89.5 (88.9-90.0)</td>
<td>82.2 (81.5-82.9)</td>
<td>13.6 (13.0-14.3)</td>
<td>99.6 (99.5-99.7)</td>
</tr>
<tr>
<td>All neurodevelopmental disorders</td>
<td>87.8 (88.3-88.5)</td>
<td>83.3 (82.7-84.0)</td>
<td>20.4 (19.6-21.1)</td>
<td>99.3 (99.1-99.5)</td>
</tr>
</tbody>
</table>

ASD=autism spectrum disorders; ADHD=attention deficit hyperactivity disorder; CI=confidence interval.

Table 3. Comparison of validity of all Neurodevelopmental Screening Tool (NDST) questions vs domain specific questions in detecting neurodevelopmental disorders in 11,223 children screened in stage I and 2,162 assessed in stage II.

<table>
<thead>
<tr>
<th>Impairment</th>
<th>Sensitivity (%) (95% CI)</th>
<th>Specificity (%) (95% CI)</th>
<th>Positive predictive value (%) (95% CI)</th>
<th>Negative predictive value (%) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Disorder specific questions</td>
<td>All questions</td>
<td>Disorder specific questions</td>
<td>All questions</td>
</tr>
<tr>
<td>ASD</td>
<td>94.2 (93.9-96.6)</td>
<td>96.5 (96.1-96.8)</td>
<td>94.5 (94.0-94.9)</td>
<td>80.6 (79.9-81.3)</td>
</tr>
<tr>
<td>ADHD</td>
<td>43.2 (42.3-44.1)</td>
<td>89.2 (88.7-89.8)</td>
<td>94.8 (94.4-99.3)</td>
<td>81.7 (81.0-82.4)</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>61.2 (60.3-62.1)</td>
<td>88.8 (88.2-89.3)</td>
<td>93.8 (93.4-94.3)</td>
<td>80.6 (79.8-81.3)</td>
</tr>
</tbody>
</table>

ASD=autism spectrum disorders; ADHD=attention deficit hyperactivity disorder; CI=confidence interval.

2229/11207 (19.8%). The sensitivity for detecting moderate/severe motor impairments by NDST was 100.0% (95%CI: 100.0-100.0%), while the specificity was 80.1% (95%CI: 79.3-80.8%). Positive predictive and negative values are shown in Table 2.

False negative classification proportion for visual impairments by NDST was 0/8 (0%), while false positive classification was 2237/11,215 (19.9%). The sensitivity for visual impairments was 100.0% (95%CI: 100.0-100.0%), with specificity being 80.0% (95%CI: 79.3-80.7%). Positive predictive and negative values are shown in Table 2.

False negative classification proportion for hearing impairments by NDST was 1/7 (14.2%), while false positive classification was 2,239/11,216 (19.9%). The sensitivity for detecting hearing impairments by NDST was 85.7% (95%CI: 85.1-86.3%), with specificity being 80.0% (95%CI: 79.3-80.7%). Positive predictive and negative values are shown in Table 2.

Comparison of NDST with TQQ in detecting neurological disorders

The NDST had higher sensitivities than TQQ for epilepsy, motor impairments and cognitive impairment, but sensitivities for visual and hearing impairments were comparable in both
tools. However, TQQ had slightly higher specificities than NDST (Table 4).

Discussion

This study demonstrates that NDST can be reliably used to screen for NDD in rural areas of Kenya. The sensitivities were high for all domains, suggesting that most of the NDD can be identified in the community. The specificities were also high, and therefore little diagnostic resources would be used in confirming a diagnosis of NDD screened with NDST, which is further supported by very high negative predictive values. The study reported low positive predictive values (PPV) which may have been the result of low population prevalence of NDD among randomly sampled children from this community. This low PPV therefore supports the need for setting up a two or three stage study design to confirm diagnosis among screen-positive children. The internal consistency was excellent, underpinning the general relatedness or correlation of all the 39 neurodevelopmental questions.

These results are comparable to those of a study from India23, albeit with some differences. For instance, in the Indian study that tested the tool on 4000 families, NDST achieved optimal sensitivity and specificity using only 11 of the 39 questions23. The differences are not surprising since these studies are from dissimilar settings with unique cultural perspectives that can influence the perception of NDD. Additionally, the present study’s research team had prior experience in conducting neuropsychiatric studies24, which may have improved the ratings of NDST for conditions related to those in previous studies. Lastly, questionnaire adaptation process is crucial and can influence validity and reliability of the tool; focus group discussions and in-depth interviews with community members were applied in Kilifi to understand the local idioms for NDD in this area22.

Not only were sensitivities and specificities of the NDST high in each domain of NDD but were also high in all domains combined, which suggests that the NDST questions can be used to detect the range of NDD. These findings are important in that screening positive in one domain may increase the likelihood of being positive for another domain, as documented in a recent study of epilepsy25, which a few of those who screened negative for seizures in stage I, were found to be positive for epilepsy in stage II. Thus, NDST can be used to reliably measure all NDD in one epidemiological study.

Although sensitivities were high for NDD, it is important to adjust estimates from stage II for sensitivity to avoid underestimating the true burden of the conditions. It is likely that participants not detected by NDST (where sensitivity is not 100%) had mild rather than moderate or severe impairments. Sensitivity is not only determined by the quality of a tool, but also by expertise and training level of staff tasked with identifying NDD in stage II. The good specificities for NDST, especially with use of disorder-specific questions, suggests NDST may be particularly useful in identifying children requiring care in poor regions without the training capacity and diagnostic expertise of NDD. The low positive values advocate for confirmation of the positive status from NDST, which is not a major limitation since most epidemiological studies in Africa often use a two or three stage design to confirm diagnosis26,27. Given that negative predictive values were very high, only few children screening negative on NDST would need to be evaluated further in stage II, which saves resources particularly for epidemiological studies in low- and middle-income countries.

The slightly higher sensitivities for ADHD and ASD compared to neurological conditions, underlines NDST as the tool of choice for screening ASD and ADHD, for which there are few epidemiological studies in Africa28. The very high sensitivity measures for motor impairments and visual impairments (100%) indicates the ease with which these problems can be detected in the community. For example, moderate to severe motor impairment are easily visible, while moderate to severe visual impairments are detrimental, making them conspicuous and easier to report. Compared to other disorders, hearing impairments had relatively lower sensitivity (85%), which may

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<table>
<thead>
<tr>
<th>Impairment</th>
<th>Sensitivity (%) (95% CI)</th>
<th>Specificity (%) (95% CI)</th>
<th>Positive predictive value (%) (95% CI)</th>
<th>Positive predictive value (%) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cognitive impairment</td>
<td>84.3 (83.6-84.9)</td>
<td>84.4 (83.7-85.0)</td>
<td>2.4 (2.1-2.69)</td>
<td>99.9 (99.8-99.9)</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>86.7 (86.1-87.3)</td>
<td>84.7 (79.3-85.3)</td>
<td>4.7 (4.3-5.1)</td>
<td>99.8 (99.7-99.3)</td>
</tr>
<tr>
<td>Motor impairments</td>
<td>93.7 (93.3-94.2)</td>
<td>84.2 (83.5-84.8)</td>
<td>0.8 (0.6-1.0)</td>
<td>99.9 (99.9-100.0)</td>
</tr>
<tr>
<td>Visual impairments</td>
<td>100.0 (100.0-100.0)</td>
<td>84.1 (83.4-84.8)</td>
<td>0.4 (0.3-0.6)</td>
<td>100.0 (100.0-100.0)</td>
</tr>
<tr>
<td>Hearing impairments</td>
<td>85.7 (85.0-86.3)</td>
<td>84.1 (83.4-84.8)</td>
<td>0.3 (0.2-0.4)</td>
<td>99.9 (99.9-100.0)</td>
</tr>
<tr>
<td>Any neurological impairment*</td>
<td>86.4 (85.7-87.0)</td>
<td>85.1 (84.4-85.8)</td>
<td>7.8 (7.3-8.3)</td>
<td>99.7 (96.9-99.8)</td>
</tr>
</tbody>
</table>
mean that low concentration/inattention or ear illnesses such as otitis media can be confused for hearing problems in this rural area. Further work on community perception of domains of NDD is justified.

This is the largest epidemiological study to validate the utility of NDST in identifying NDD in low- and middle-income countries. It is robust in that focus was given to many domains of NDD. One limitation is the lack of detailed assessment of cognitive impairment that may result in lower sensitivities and specificities of NDST. Neuropsychological assessments can be particularly intensive when administered in over 2,000 participants as in this study, and so NDST could be further evaluated in smaller case-control studies in which more tests of cognitive impairment are feasible.

The NDST appeared superior compared to the TQQ. Firstly, NDST can screen for ASD and ADHD in addition to neurological conditions, while TQQ focuses mostly on the latter. Although TQQ’s sensitivity for visual and hearing impairments compared well with that of NDST, the lower sensitivities for epilepsy, motor impairment and cognitive impairment may result in the underestimation of these conditions and NDD in general. Slightly higher specificities for TQQ over NDST would not add much value, since the relative strength of screening tools should be their ability to detect all conditions during screening, which is determined by high sensitivities rather than specificities. These two conclusions taken together with the fact that TQQ does not ask specific questions for ASD and ADHD places NDST as the screening tool of choice for all NDD.

In conclusion, this study shows that NDST can be used reliably to screen different types of NDD in a rural region of Africa, with high sensitivity and specificity. The tool could reduce the cost of identifying children requiring management for NDD in similar settings in Africa or elsewhere. Low positive predictive values suggest that the prevalence of NDD may be low in this community therefore a multi-stage epidemiological study design is recommended, so that diagnosis can be confirmed at later stages of studies by trained staff, clinicians or experts.

Data availability
Underlying data

This project contains the following underlying data:
- NDST KILIFI DATASET 23MARCH2021-1.tab (data used in calculating the validity of the NDST in assessing neurodevelopmental disorders in a community sample of 6–9-year-old children from Kilifi, Kenya)
- Some NDST paper codes21March2021.do (STATA v15.1 analysis script)

Extended data

This project contains the following extended data:
- MBitta_NDST_Kilifi_Codebook.pdf (Variable codebook containing description, value labels and format - English Version)
- MBitta_NDST_Kilifi_Readme.txt (Readme file containing information on the related research study, terms of access, citation requirements as well as methods of processing)
- NDD 2015 - NDST-English.doc (The English version of the Neurodevelopmental Screen Questionnaire that was used to screen participants at stage I of the study)
- NDD 2015 - NDST-Kigiriana.doc (The Giriama version of the Neurodevelopmental Screen Questionnaire that was used to screen participants at stage I of the study)
- NDD 2015 - NDST-Kiswahili.doc (The Kiswahili version of the Neurodevelopmental Screen Questionnaire that was used to screen participants at stage I of the study)
- NDD 2015 – NeuroExamination (The English version of the clinical evaluation form used to collect data on confirmed diagnoses at stage II)
- NDD 2015 - TQQ.doc (The English version of the Ten Questions Questionnaire that was used to screen participants at stage I of the study)
- Socio demo.docx ((The English version of the Sociodemographic Questionnaire)
- Interview ICF_NDD study.doc (The English version of the Informed Consent form)

Data are available under the terms of the Creative Commons Attribution 4.0 International license (CC-BY 4.0).

Acknowledgements
We thank the fieldworkers for administering the screening tool in stage I, clinicians for helping with clinical examination and assessors for performing neuropsychological tests. We are also grateful to the late Fredrick Ibinda for setting up and implementing the initial stages of data collection for this study. We thank Professor Philip Bejon for his contribution to the paper. This paper is published with permission from director of KEMRI.
References


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In the paper “Validity and reliability of the Neurodevelopmental Screening Tool (NDST) in screening for neurodevelopmental disorders in children living in rural Kenyan coast” Bitta et al present a comparative prospective cohort epidemiological study comparing the efficacy of the Neurodevelopmental Screening Tool (NDST) to the Ten Question Questionnaire (TQQ) in assessing neurodevelopmental disabilities (NDD). This study was conducted in Kifili County in Kenya. The test population was randomly sampled from 30,000 children ages 6 to 9 years old. A total of 15,000 children were tested, of those approximately 11,200 qualified for the study. All of the patients who screened positive for at least one item on the NDST and 20% of the screen negative patients were further evaluated with formal neuropsychological testing. In the end the authors find that approximately 20% of the patients screened positive for neurodevelopmental disabilities by either the NDST or the TQQ. Of those, 69% were available for further neuropsychological testing. The NDST test was found to have a specificity of 83% and a sensitivity of 88%. Remarkably the negative predictive values of the tests in detecting NDD and other neurological impairments (ADHD, ASD, etc.) approached 100% in all cases. The positive predictive value ranged from less than 1% to 20%. The NDST and the TQQ were very comparable in their sensitivity and specificity for all the variables measured. The benefit of the NDST being that it allows screening for ADHD and ASD.

Strength: This is a well conducted study on a large sample of patients. The authors were careful in ensuring that randomness was maintained in as much as possible, minimizing the risk of sampling error. The extent to which they went to confirm the diagnoses of ADHD, autism, and other neurodevelopmental disorders is quite remarkable, including among other tests the Kiddie Schedule for Affective Disorders and Schizophrenia and the Autism Diagnostic Observation Schedule.

Conclusion: This is an important epidemiological study on the incidence of neurodevelopmental disorders conducted in a sub-Saharan population. The study is important for several reasons:

1. It validates the NDST tool as a measure of NDD, including ADHD and autism in a sub-
Saharan context.

2. It is a proof of concept that such epidemiological studies can and should be conducted in sub-Saharan Africa.

3. It sets up the stage for further studies targeted to children with NDDs, allowing targeting to subgroups, including ADHD and autism. This is a monumental effort in a sub-Saharan country proving that excellent epidemiological research can be done in low- and middle-income countries and preparing the terrain for further studies in low and middle income countries for children with disabilities that have been largely neglected until now.

Questions:
1. How was the patient population selected? The authors state that the patients were randomly selected from 30,000 eligible children. But it is not clear if this represents the entire population of eligible children in the Kilifi Health and Demographic Surveillance System (Kilifi County has a population of about 1.5 million, I am not sure I understand how much of this population is served by the Kilifi Health and Demographic Surveillance System).

2. It is my understanding that the Mijikenda ethnic group the patients were sampled from speak a variety of dialects related to Swahili. The tests were translated in Kiswahili. Is Kishwahili the common language for all the Mijikenda people, or were some populations excluded if they could not understand Kiswahili?

3. One of the cognitive tests used to evaluated intellectual disability was Raven's Progressive Matrices. Yet, it is not clear that this test has been established as a valid measure of IQ in Sub-Saharan Africa. In fact, at least one study suggests otherwise (Wicherts, Jelte M., et al. "Raven's test performance of sub-Saharan Africans: Average performance, psychometric properties, and the Flynn Effect." Learning and Individual Differences 20.3 (2010): 135-151.). It would be helpful to have the authors comment on this issue.

Suggestions:
- It would be useful to have the results for the NDST and TQQ shown in the same table or in the form of a bar graph. This would make direct comparison of the tests visually much easier.

Minor points:
- The abbreviation KWTRP is never defined.

References

Is the work clearly and accurately presented and does it cite the current literature?
Yes

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Child Neurology and epilepsy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 27 September 2021

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Manoja Kumar Das
The INCLEN Trust International, New Delhi, Delhi, India

1. Methodology: Whether NDST and TQQ interviews were blinded (i.e. same person interviewed both NDST and TQQ or different persons? If the same person conducted both interviews, what was the interval between two interviews?).

2. Typo error on page five (second line): Screening with ADHD-specific question, instead of ASD question.

3. I think the NDST tool used in this study was developed by the INCLEN team. The source of the NDST tool should be mentioned in the text. The authors should acknowledge INCLEN in the acknowledgment section.

4. In the discussion, the study on NDD from India should be mentioned (Arora et al., 2018).
References

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Yes

*Competing Interests:* No competing interests were disclosed.

*Reviewer Expertise:* Child health, child development

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.