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Research Paper

# Evaluating construct and criterion validity of NeuroScreen in assessing neurocognition among hospitalized Ugandan first-episode psychosis patients

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ABSTRACT

*Introduction:* Neurocognitive impairment (NCI) is commonly exhibited among patients experiencing their first episode of psychosis. However, there are few resources in many low-income countries, such as Uganda, that allow for the administration of extensive neurocognitive test batteries for the detection of NCI. *NeuroScreen* is a brief tablet-based neurocognitive assessment battery that can be administered by all levels of healthcare staff. We examined the validity of *NeuroScreen* to assess neurocognition and detect NCI in first-episode psychosis (FEP) patients in Uganda.

*Methods:* We enrolled 112 participants FEP patients and matched controls at Butabika Mental Referral Hospital. Each participant completed *NeuroScreen* and a traditionally administered neurocognitive battery: the MATRIC Consensus Cognitive Battery (MCCB). We examined correlations between participant performance on *NeuroScreen* and the MCCB. A ROC curve determined sensitivity and specificity of *NeuroScreen* to detect NCI as determined by MCCB criterion.

*Results:* There was a large, statistically significant correlation between overall performance on *NeuroScreen* and the MCCB [$r(112) = 0.64$, $p < .001$]. Small to large correlations were found between tests in the MCCB and *NeuroScreen* batteries. The ROC curve of *NeuroScreen* performance to detect MCCB-defined NCI had an area under curve of 0.80 and optimal sensitivity and specificity of 83 % and 60 %, respectively.

*Conclusion:* There was a moderate positive correlation between overall performance on both batteries. *NeuroScreen* shows promise as a valid assessment battery to assess neurocognition and detect NCI in FEP patients in Uganda. Further studies of *NeuroScreen* in healthy individuals and in a range of mental disorders are recommended.

## 1. Introduction

Severe neurocognitive deficits, which may be diagnosed as neurocognitive impairment (NCI), are a core symptom domain in psychotic disorders. Among people living with psychotic disorders, NCI is estimated to contribute to a larger portion of disease burden than any

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positive, negative, or behavioral symptoms of psychosis (Emsley et al., 2008; Green et al., 2019; Whiteford et al., 2013). Individuals with psychosis have been found to exhibit impairment in general intellectual functioning, as well as specific neurocognitive domains, such as executive functioning, memory, processing speed, and motor speed (Aas et al., 2014). NCI is also a key predictor of functional outcomes and general quality of life among patients with psychotic disorders (Green et al., 2004; Mwesiga et al., 2020a, 2020b). An existing body of research suggests that long-term neurocognitive outcomes for patients with psychotic disorders may be improved if interventions are introduced during a person's first psychotic episode (Albert and Weibell, 2019; Cuesta et al., 2012; Marshall and Rathbone, 2011). Thus, given the high risk of NCI in this population, the integration of neurocognitive assessment, which is the standard method of detecting NCI into the routine care of individuals experiencing first episode psychosis (FEP), is essential to support optimal functioning and improve clinical outcomes (Faber et al., 2011; Schulz and Murray, 2016). This need is especially pertinent in low- and middle-income countries (LMICs) where there is limited access to psychiatric care and antipsychotic treatments (McCreadie et al., 2002; Mossaheb et al., 2013; Thirthalli et al., 2011).

Comprehensive neurocognitive assessments require administering a battery of tests that can assess performance across multiple domains. Research by the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) initiative recommends the following domains for neuropsychological assessment in patients with psychotic disorders: i) working memory, ii) attention/vigilance, iii) verbal learning and memory, iv) visual learning and memory, v) reasoning and problem solving, vi) information processing speed, and vii) social cognition (Green and Nuechterlein, 2004; Mwesiga et al., 2020a, 2020b; Nuechterlein et al., 2004). Consequently, the MATRICS Consensus Cognitive Battery (MCCB) is recommended as the "gold standard" neuropsychological battery across these seven domains for patients with psychotic disorders (Nuechterlein et al., 2008). The total testing time (excluding rest breaks and time needed to score tests) for the MCCB may be 90 min or more (Mwesiga et al., 2021; Nuechterlein et al., 2008), presenting limitations in its implementation in many resource-limited health settings. Furthermore, administration of the MCCB requires specialized training and supervision by an experienced clinician (Nuechterlein and Green, 2006). This a notable limitation in Uganda, where there are only 0.008 psychiatrists and 0.01 psychologists per 100,000 people (Kigozi et al., 2010).

Within the neurocognitive assessment field, there is increasing interest in the development and use of computerized testing batteries (Baker et al., 1985; Gur et al., 2010; Kane and Kay, 1992; Schatz and Browndyke, 2002). Additionally, there is growing evidence of the effectiveness of using mobile health tools as a part of standard treatment/care in patients with psychotic disorders (Chivilgina et al., 2020). *NeuroScreen* is a tablet-based application initially designed to assess neurocognition among people living with HIV (PLWH) (Robbins et al., 2014). *Neuroscreen* has demonstrated clinical utility in United States, South Africa, and Thailand (Robbins et al., 2022, 2021, 2018; Robbins, 2020) and in 2022 was reccomended by the Joint United Nations Programme on HIV/AIDS for use in screening for HIV-related NCI (UNAIDS and World Health Organization, 2022). *NeuroScreen* consists of tests that are automatically timed and scored, thus eliminating the need for examiner time keeping, hand scoring, and calculations and score conversion. Additionally, audio-visual instructions are provided, improving its utility among low-literacy populations. The application is administered on an Android operating system tablet that can be used in a variety of remote locations. Furthermore, it does not require internet connection at the time of administration, as testing data are saved locally and uploaded only once a secure internet connection is established. Unlike the MCCB, *NeuroScreen*, has been translated into and adapted for Luganda and Luo, two major indigenous languages in Uganda (Robbins, 2020). Optimal neuropsychological test performance relies on tests being available in languages easily understood by patients (Brickman et al., 2006). For example, a study of native and non-native English speakers in the U.S. demonstrated that non-native speakers performed worse on language-mediated neuropsychological tests (Kisser et al., 2012).

Although *NeuroScreen* has been validated for use among PLWH in South Africa and HIV-affected youth in the United States and Thailand (Robbins et al., 2022, 2021, 2018), it has yet to be evaluated for use among patients with psychosis. The purpose of this study was to evaluate construct and criterion validity of *NeuroScreen* in assessing neurocognition in FEP patients in Uganda.

## 2. Methods

### 2.1. Study design, setting, and participants

This cross-sectional study was conducted at Butabika National Psychiatric Mental Referral Hospital in Kampala, Uganda. The hospital has a 600-bed facility that serves inpatients and outpatients, with approximately three acute psychiatric inpatient units. As a national referral hospital, there are also outpatient clinics for prenatal care, HIV care, and dental treatment. Butabika sets the national policy agenda for mental health along with the Ministry of Health and is responsible for various levels of mental health training, making it an ideal site for conducting the current study (Mwesiga et al., 2020a, 2020b; Petersen et al., 2017).

Inclusion criteria were: 1) a confirmed diagnosis of psychosis using the Mini International Neuropsychiatric Interview (MINI; Sheehan et al., 2010), 2) 18–60 years old, 2) negative HIV blood test, 3) negative syphilis blood test, and 4) no substance use disorder. A maximum age of 60 was set to exclude participants who may exhibit neurocognitive decline associated with normal aging and dementia; this was based on the United Nations definition of "older adult" (UN Population Division, 2017). Patients with a current or historical diagnosis of substance use disorder were excluded from the study, considering these conditions could have confounding effects on neurocognitive functioning (Nakasujja et al., 2012; Nakimuli-Mpungu et al., 2006; Sacktor et al., 2005). Prior to completing neurocognitive assessments, we ensured that patients had positive symptom resolution. On the day of testing, medication dosages were re-scheduled to avoid sedation effects during performance of study evaluations. A full description of our testing procedure for FEP patients has been previously described (Mwesiga et al., 2022).

Study controls matched by age, sex, and education were recruited from the dental unit at Butabika Hospital and assessed on the day of recruitment. Inclusion criteria for control participants were: 1) no evidence of psychosis or substance use and 2) no evidence of HIV/AIDS or syphilis.

### 2.2. Instruments

#### 2.2.1. MATRICS Consensus Cognitive Battery (MCCB)

The MCCB is considered the "gold standard" for assessing neurocognition among patients with psychosis (Nuechterlein et al., 2008). The MCCB assesses for impairment in seven neurocognitive domains: (i) working memory, (ii) attention and vigilance, (iii) verbal learning and memory, (iv) visual learning and memory, (v) reasoning and problem-solving, (vi) information processing speed, and (vii) social cognition (Green et al., 2004; Nuechterlein et al., 2008). The battery comprises 10 different neuropsychological tests: (a) the Trail Making Test (TMT): Part A; (b) Brief Assessment of Cognition in Schizophrenia (BACS): Symbol Coding; (c) Hopkins Verbal Learning Test-Revised (HVLT-R); (d) Wechsler Memory Scale-Third Edition (WMS-III): Spatial Span; (e) Letter-Number Span (LNS); (f) Brief Visuospatial Memory Test-Revised; (g) Category Fluency: Animal Naming; (h) Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT): Managing Emotions (D & H); and (i) Continuous Performance Test-Identical Pairs (CPT-IP), MATRICS International Version 2. The complete battery takes approximately 90

min to complete. The MCCB administration procedure has been as previously described in Nuechterlein et al. (2008).

#### 2.2.2. NeuroScreen

A full description of the neurocognitive tests in *NeuroScreen* can be found in Robbins et al. (2022). Briefly, this battery consists of 12 tests measuring neurocognitive domains of executive functioning and processing speed (Trail Making 1, Trail Making 2, Trail Making 3, Visual Discrimination 1, Visual Discrimination 2), learning and memory (Verbal List Learning and Verbal List Learning Delayed Recall), and working memory (Number Span Forward, Number Span Backward). In addition, there is a number input task (Number Speed) and motor functioning task (Finger Tapping-Dominant Hand, Finger Tapping Non-dominant Hand). Tests are embedded in a graphical user interface, allowing the administrator to enter patient data, generate instant raw results, and save raw scores to a secure, password-protected website and an internal storage card. The test-taker completes these tests under the supervision of an administrator. Some tests require the test-taker to complete tasks directly on the touchscreen interface of the tablet; for tests of verbal learning and working memory, the administrator takes control of tablet to administer the test and record the test-taker's responses.

### 2.3. Research procedures

Informed consent was obtained from all study participants. Both participants with psychosis and controls completed the MCCB and *NeuroScreen* on the same day. Half of the sample completed *NeuroScreen* after completing the MCCB and receiving a break of 30–60 min. The other half completed *NeuroScreen* before completing the MCCB. All batteries were administered by two experienced clinical psychologists.

English is the official language of Uganda and widely taught in the school system; in addition, Luganda is an indigenous language widely spoken in Kampala (Sawe, 2017). As our sample spoke both languages, participants had the option of completing the Luganda-language version of *NeuroScreen* (developed in consultation with a professional translator). The MCCB, however, has not been translated to any Ugandan local language; thus, the MCCB was administered only in English.

### 2.4. Data analysis

Descriptive analyses were conducted to examine participants' demographic characteristics (i.e., age, sex, education). For comparative analyses of performances on test batteries, raw scores from both the MCCB and *NeuroScreen* tests were converted to T scores based on the performance of the healthy controls. Using the full sample of patients and controls, we calculated Pearson correlation coefficients between all the individual tests contained in *NeuroScreen* and MCCB. To compare general performance between the two batteries, we took the mean of all T scores available for each battery of tests to create a "global T score" for *NeuroScreen* and MCCB for each participant.

Using the MCCB criterion for general NCI (Revell et al., 2015), participants were diagnosed with NCI if they performed: a) two or more standard deviations below the sample mean in one domain of the MCCB; or b) one standard deviation below the sample mean in two MCCB domains. To examine sensitivity and specificity of *NeuroScreen* as it relates to these criteria, a receiver operating characteristic (ROC) curve was generated, using the *NeuroScreen* global T score as the classifier variable for NCI.

## 3. Results

The final dataset contained 65 participants with psychosis and 47 controls participants ($N = 112$) who completed both *NeuroScreen* (with an average complete time of approximately 27 min) and MCCB (with an average time of 130 min to complete and score results). The average age of participants was 29.12 years ($SD = 9.37$, range = 18–56 years). The average years of education was 11.22 years ($SD = 2.99$, range = 0–15 years), which corresponds to attaining some secondary or high school education. Most participants (66 %) were female. There were no significant differences between participants with psychosis and controls in terms of age, sex, or education. Details regarding other characteristics are presented in Table 1.

For the full sample of 112 participants, a correlation matrix between tests in *NeuroScreen* and the MCCB is presented in Table 2. Within the processing speed domain of the MCCB, the highest correlation was between TMT: Part A and Visual Discrimination 2 [$r(112) = 0.56$, $p < .05$]. Within the verbal learning domain of the MCCB, the highest correlation was between HVLT-R Trial 2 and Verbal List Learning [$r(112) = 0.22$ p $< .05$]. Within the working memory domain of the MCCB, the highest correlation was found between Letter Number Sequencing and Number Span Forward [$r(112) = 0.29$, $p < .01$]. A significant, positive association was found between MCCB and *NeuroScreen* global T scores [$r(112) = 0.64$, $p < .001$] (Table 3).

From the full sample of 112 participants, 58 % of them met the MCCB criteria for NCI. Results from ROC analysis of all participants indicated an area under curve (AUC) of 0.80 ($p < .001$) for *NeuroScreen* to detect MCCB defined NCI (Table 4). Using a cut-off *NeuroScreen* global T score of 50 yielded optimal sensitivity and specificity of 83 % and 60 %, respectively.

## 4. Discussion

Our study extends the *NeuroScreen* literature to patients with psychosis, a population susceptible to NCI. Our aim was to establish validity measures of *NeuroScreen* in reference to the MCCB, which is considered the standard neurocognitive assessment battery for psychosis patients (Green et al., 2004; Nuechterlein et al., 2004) and has specific criterion to define NCI (Revell et al., 2015). There were significant positive associations between performance on tests of *NeuroScreen* and MCCB, with the performance on MCCB tests of processing speed domain having large correlations with performance on certain *NeuroScreen* tests. Of note, there are tests between the two batteries that are of similar design: for example, both *NeuroScreen* and MCCB contain a processing speed test of "trail making" in which the participant is presented numbered circles and asked to draw a line connecting the circles in numerical order as fast as possible. However, considering that *NeuroScreen* and the MCCB are administered on different interfaces, it is understandable that even conceptually similar tests measuring the same neurocognitive domain would not yield entirely comparable performances. The fact that overall performance between the two batteries had a moderate correlation suggests the batteries have similar psychometric properties despite different modalities of administration.

With sensitivity analysis, the demographically adjusted performance scores of *NeuroScreen* yielded an area under curve value close to 0.80 which is generally considered "excellent" diagnostic accuracy (Hosmer

**Table 1**
Background characteristics of the sample of participants.

| | Total ($N = 112$) Mean ($SD$) | Cases ($N = 65$) Mean ($SD$) | Controls ($N = 47$) Mean ($SD$) | $t$-Test statistic, df | P-value |
|---|---|---|---|---|---|
| Age | 29.12 (9.37) | 27.88 (9.73) | 30.83 (9.18) | −1.67, 111 | 0.099 |
| Years of education | 11.22 (2.99) | 11.41 (2.78) | 10.96 (3.26) | 0.78, 111 | 0.438 |

| | Total frequency | Case frequency | Control frequency | $X^2$, df | P-value |
|---|---|---|---|---|---|
| Sex | 34 % male<br>66 % female | 32 % male<br>68 % female | 36 % male<br>64 % female | 0.050, 1 | 0.823 |

**Table 2**
Correlation Matrix: NeuroScreen and MCCB test performance. MCCB tests are grouped by neurocognitive domains.

| | | NeuroScreen T scores | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | MCCB T scores | Trail making test 1 | Trail making test 2 | Trail making test 3 | Visual discrimination 1 | Visual discrimination 2 | Finger tapping dominant hand. | Finger tapping: non-dominant hand | Number speed total | Number span total | Number span total: backward trial | Verbal list learning total trials | Verbal list learning: total recall |
| Processing Speed | Symbol-coding | 0.35** | 0.09 | 0.25* | 0.44** | 0.56** | 0.22 | 0.28* | 0.55** | 0.14 | 0.26* | 0.13 | 0.13 |
| | Category fluency: Animal naming | 0.14 | 0.14 | 0.20* | 0.23* | 0.28* | 0 | 0.08 | 0.23* | 0.16 | 0.26* | 0.1 | 0.02 |
| | Trail making test: Part A | 0.29* | 0.06 | 0.09 | 0.27* | 0.56** | 0.33** | 0.37 | 0.49** | 0.13 | 0.28* | 0.09 | 0.14 |
| Attention | Continuous performance test: Identical pairs (mean of trials) | 0.32** | 0.15 | 0.19 | 0.42** | 0.62** | 0.27* | 0.32** | 0.52** | 0.06 | 0.30** | 0.08 | 0.16 |
| Working memory | Wechsler Memory Scale®: Spatial Span | 0.18 | 0.09 | 0.16 | 0.37** | 0.40** | 0 | 0.04 | 0.36** | −0.01 | 0.25* | −0.04 | 0.04 |
| | Letter number span | 0.36** | 0.23* | 0.27* | 0.38** | 0.41** | 0.20* | 0.26* | 0.50** | 0.29* | 0.25* | 0.22* | 0.16 |
| Verbal memory | Hopkins verbal learning test (total trials) | 0.16 | 0.31** | 0.17 | 0.34** | 0.33** | 0.14 | 0.15 | 0.26* | 0.20* | 0.35** | 0.18 | 0.12 |
| Visual memory | Brief visual spatial memory test (total trials) | 0.28* | 0.19 | 0.21* | 0.36** | 0.50** | 0.09 | 0.16 | 0.48** | 0.22* | 0.28* | 0.16 | 0.27* |
| Reasoning problem solving | Neuropsychological Assessment Battery®: Mazes | 0.32* | 0.18 | 0.34** | 0.36** | 0.52** | 0.17 | 0.27* | 0.47** | 0.20* | 0.24* | 0.11 | 0.14 |

*Note.* Pearson correlation coefficients are presented in the correlation matrix.
* $p < .05$.
** $p < .001$.

**Table 3**
Pearson correlation coefficients between NeuroScreen and MCCB T scores.

| | NeuroScreen global T scores |
|---|---|
| MCCB global T scores | 0.64** |

** $p < .001$.

and Lemeshow, 2000). A *NeuroScreen* global T score of 50 was the optimal "cut-off" value for NCI diagnosis, based on the Youden' Index for our ROC. However, in adjusting the cut-off score to increase the sensitivity of capturing a sample of participants with NCI: from a review of the full distribution of global T scores on the ROC curve, a value of 57 yielded the strongest sensitivity to detect NCI at 98 %, at the expense reducing specificity down to 18 %. Although specificity would be reduced, adjustments to increase sensitivity may be something to consider in a setting where clinicians wish to use *NeuroScreen* to identify as many patients with psychosis as possible with suspected NCI. Follow up testing with traditional batteries could then be done to establish the severity of impairment.

### 4.1. Study limitations

This study had several limitations. Our demographic-adjusted standard scores were based on a relatively small control sample; future studies are needed that include larger samples of controls to provide more robust normative data across *NeuroScreen* tests. The MCCB was not translated into the indigenous language of the region (Luganda) hence cross-cultural language bias may have compromised its ability to serve as the fair NCI detection for this population (Fernández and Abe, 2018). It is noteworthy that while all the participants completed the MCCB in English, 43 % opted to complete the Luganda language version of *NeuroScreen* that was offered, suggesting that there is a need to tailor neurocognitive assessments to language preferences.

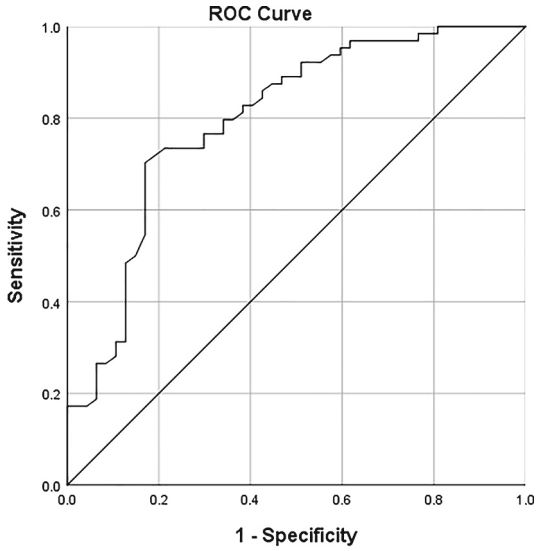
### 4.2. Clinical implications

Our findings provide evidence for construct and criterion validity of the *NeuroScreen* battery of tests to assess neurocognition and detect NCI in psychosis patients in Uganda. The association of *NeuroScreen* tests with those in a battery with similar neurocognitive domains provides evidence for its construct validity in assessing neurocognition among patients with psychosis. This builds on previous findings that demonstrate the ability of this application to perform similarly or better than traditional neuropsychological batteries (Robbins et al., 2018; Zipursky et al., 2013). The ability of *NeuroScreen* to detect MCCB-defined NCI impairment based on cut-off performance scores provides criterion validity for its use to detect NCI in this population. We believe these validity measures provide a strong argument that *NeuroScreen* holds promise to address the need for neurocognitive assessment integration in routine care for FEP patients in low-resource settings like Uganda. This is reinforced by *NeuroScreen* being a largely self-contained tool to be used by any clinical staff with minimal training, and its benefits over traditional test batteries (short completion time, mobility, availability in indigenous Ugandan languages).

## 5. Conclusion

This study has shown the *NeuroScreen* to be a valid instrument for the detection of NCI among patients with psychosis. Early intervention in FEP is critical for improved prognosis among patients with psychosis (Albert and Weibell, 2019; Coentre et al., 2011; Moe et al., 2018). Computerized neurocognitive testing has already been transformative in clinical neuropsychological testing. The increased availability of automated, lay-health worker administered, and culturally appropriate mobile instruments has great potential to provide clinically necessary assessments to improve health outcomes in vulnerable populations in

**Table 4**
ROC analysis of NS global T score as classifying variable for MCCB-defined NCI.




| Area Under Curve | S.E. | P value | 95% CI, Upper Bound | 95% CI, Lower Bound |
|---|---|---|---|---|
| .80 | .044 | .000 | .712 | .884 |

low-resource settings. Future research directions in Uganda include collecting *NeuroScreen* data from healthy individuals and those with a range of mental disorders, which will generate normative data for the population. While doing this, we can also gather feedback from examiners and examinees to ensure we are integrating culturally appropriate testing into routine care.

## Ethical approval

The study obtained approval from: Human Research Ethics Committee (HREC) of the Faculty of Health Sciences, University of Cape Town (UCT) (#574/2017), the Ugandan National Council of Science and Technology (UNCST) (#HS142ES) and the School of Medicine Research and Ethics committee (SOMREC) (#REC REF 2017-153) of the College of Health Sciences, Makerere University. Institutional permission to carry out study was obtained from the administration of Butabika Hospital.

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## CRediT authorship contribution statement

**Nana Asiedu:** Conceptualization, Methodology, Validation, Formal analysis, Writing – original draft, Visualization. **Emmanuel Kiiza Mwesiga:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Data curation, Writing – original draft, Visualization, Supervision, Project administration. **Dickens Akena:** Conceptualization, Writing – original draft, Supervision. **Corey Morrison:** Writing – original draft, Visualization. **Joy Louise Gumikiriza-Onoria:** Investigation, Data curation. **Angel Nanteza:** Investigation, Data curation, Project administration. **Juliet Nakku:** Investigation, Writing – original draft, Project administration. **Nastassja Koen:** Conceptualization, Writing – original draft, Supervision. **Noeline Nakasujja:** Conceptualization, Writing – original draft, Writing – review & editing, Supervision, Project administration. **Wilber Ssembajjwe:** Formal analysis. **Christopher M. Ferraris:** Writing – review & editing. **Anthony F. Santoro:** Writing – review & editing. **Dan J. Stein:** Conceptualization, Writing – original draft, Writing – review & editing, Supervision. **Reuben N. Robbins:** Methodology, Validation, Formal analysis, Writing – original draft, Writing – review & editing.

## Declaration of competing interest

The authors declare no conflict of interest.

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