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Development and Validation of the Alcohol and Drug Cognitive Enhancement (ACE) Screening Tool

Drug and Alcohol Network

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Background

The prevalence of cognitive impairment in individuals seeking treatment for substance use disorder is between 20% and 80%.[1] Neuropsychological assessment is costly, and most alcohol and other drug (AOD) services do not have any, or timely, access to clinical neuropsychologists to assess clients with suspected cognitive impairment. As such, it has become increasingly important to screen individuals accessing AOD services for cognitive impairment to ensure that treatment is targeted to a client's capacity and that they can be retained in treatment.

To meet service needs, the aim of the current project was to develop a brief and simple screening tool that frontline AOD staff can administer at intake to assess for risk of cognitive impairment. People who screen positive can then be asked to complete a performance-based screen for cognitive impairment.

The full title of the tool is the *Alcohol and Drug Cognitive Enhancement (ACE) Screening Tool*. For simplicity, this document will refer to it as the Screening Tool.

Development of the tool

In consultation with AOD workers, academic staff, and clinical neuropsychology colleagues, and after reviewing the relevant literature, the primary author developed a list of risk factors for cognitive impairment among those with substance use disorder (SUD). Given that substance use was an obvious risk factor, and that AOD services already collect data regarding history of substance use, the risk factors generated in the development of the current tool were not directly related to the person's substance use history.

Traumatic brain injury, overdose, epileptic seizures, other neurological conditions, prenatal substance use and neurodevelopmental learning and behavioural disorders were considered to be the major factors that may contribute to cognitive impairment in individuals with SUD.[2,3,4,5,6,7]

History of head injury

It is well established that substance misuse increases the risk of physical injury. Between 36% and 51% of hospital admissions for traumatic brain injury (TBI) are due to incidents that occurred while intoxicated.[8,9,10] Not surprisingly, it has been suggested that TBI may be a primary cause of cognitive impairment in individuals with SUD. A recent study in a residential SUD treatment facility found that 67% of residents had a history of TBI and half of those residents had cognitive impairment.[2] The literature suggests that, as the number of TBI and episodes of loss of consciousness increases, more chronic cognitive impairments are observed.[11,12,13] Moreover, individuals who have a history of TBI are more likely to experience poor SUD treatment outcomes, which is likely attributable to impaired cognition.[14,15]

History of overdose

Between 48% and 68% of heroin users will experience at least one non-fatal overdose.[16,17] A non-fatal opiate overdose is defined by a loss of consciousness and hypoventilation, which can result in hypoxic brain injury and severe cognitive impairment.[18,19] Considering the prevalence of overdose among opiate users, there is very limited research on the cognitive consequences of these events. The few studies that have investigated the effects of non-fatal overdose report both acute and chronic neuropsychological deficits. For example, Dassanayake et al. (2012) assessed a group of 107 patients who had recently been admitted to hospital for an overdose of central nervous system depressants.[20] The study found significantly poorer performance on neuropsychological tasks assessing visual attention, visuomotor skills, executive functions, working memory, impulsivity and decision-making relative to controls matched for gender, education and IQ. Similarly, Darke et al. (2000) found that the number of heroin overdoses in a group of methadone maintenance patients significantly and independently predicted performance on measures of information processing, attention, problem-solving, short-term memory and long-term memory.[3] Participants who had experienced overdose performed significantly worse than healthy controls on all measures. The methadone maintenance patients had been in the program for a median of five years, suggesting that the observed deficits may represent chronic cognitive impairment.

History of epileptic seizures

The term epilepsy is used to describe the presence of recurrent seizures, and does not denote a particular underlying aetiology.[21] According to emergency department records, 40-50% of admissions for seizures are alcohol-related.[22] Seizures are common following withdrawal from alcohol and typically present 6-48 hours after discontinuation of use, but not all alcohol-related seizures are the result of withdrawal.[23] It has been suggested that with each additional episode of withdrawal in people with chronic alcohol dependence, seizures increase in both frequency and

intensity causing permanent epileptogenic alterations in the brain that can result in recurring seizures long after the cessation of alcohol.[24,25,26] Although there is evidence to suggest that epileptic seizures relate to cognitive impairment, there is limited evidence that alcohol-related seizures are directly associated with cognitive impairment.[27,28,29] Given the association between chronic alcohol use and the increased likelihood of developing epilepsy or unprovoked seizures, a higher frequency of seizures may act as a proxy for determining the extent and severity of substance use and thereby the likelihood of cognitive impairment that is secondary to drug use.[4]

History of maternal AOD use

Fetal exposure to teratogens (e.g. alcohol or other drugs) has been shown to exert wide ranging effects on behavioural, cognitive and physical development.[6,30] The severity of the effects subsequent to teratogenic exposure depend on dose, stage of fetal development, frequency of exposure during fetal development, polysubstance use, genetics and postnatal factors, such as the quality of the care-giving environment.[6,31,32] Research predominantly investigates the effects of the maternal use of alcohol and cannabis on cognition, growth and behaviour in the child.

The effects of high doses of alcohol on child development are well documented and can be observed in the range of presentations that fall under the umbrella term of fetal alcohol spectrum disorder.[33] The neuropsychological profile underlying fetal alcohol spectrum disorder, which represents the most severe cases of exposure, causes executive dysfunction, visuospatial impairment and memory difficulties.[34,35,36] It is not surprising then that prenatal alcohol exposure has been associated with externalising disorders such as attention deficit hyperactivity disorder (ADHD), SUD and conduct disorder, which have a shared neurocognitive profile of executive function deficits.[30,37,38] Two reviews also found evidence of an association between even moderate doses of prenatal alcohol consumption and cognitive deficits in adolescents.[39,40,36]

Findings regarding the effects of prenatal cannabis use on cognition in children are inconsistent, and few studies have focused on enduring deficits beyond adolescence. Two of three longitudinal studies reported that prenatal cannabis exposure was associated with verbal and memory dysfunction in children aged 3-4 years, and deficits in learning, memory, language, attention and executive functions in children up to 10 years. [41,42,43] However, a larger and more recent longitudinal study failed to replicate those findings.[44]

History of stroke or other neurological conditions

It is well documented that permanent and measurable cognitive deficits frequently result from neurological conditions such as stroke, Parkinson's disease and multiple sclerosis. [45,46,47,5] It has been suggested that patients seeking treatment for neurological conditions may be at a higher risk of developing SUD because of cognitive deficits that can exacerbate SUD behaviours and the potential misuse of the medications used to treat those conditions.[48]

History of neurodevelopmental learning and behavioural disorders

The neuropsychological profile underlying ADHD is that of executive dysfunction.[49,50] More than a quarter of clients seeking treatment for SUD are comorbid for ADHD, but estimates as high as 44% have been reported. [51,52] The heterogeneous disorder presents as three different clinical categories (hyperactive impulsive, inattentive, combined hyperactive inattentive), however the hyperactive impulsive subtype is most often associated with SUD.[53] It has been suggested that the inhibitory control deficit that characterises this subtype serves as the linking mechanism between ADHD and SUD.[7] Studies using neuroimaging techniques support that theory, revealing similar patterns of hypoactivity in key brain regions associated with impulse control in both ADHD adults and individuals with SUD.[52,54] ADHD is considered a key predisposing factor to developing SUD, and is

associated with earlier use of substances and higher psychiatric comorbidities resulting in more complex treatment trajectories than SUD alone. [55,56,57] [58,59]

Asperger's syndrome, which has been absorbed by autism spectrum disorder in the *Diagnostic and Statistical Manual of Mental Disorder* (5th ed.; APA, 2013), is also characterised by deficits in aspects of executive function.[60,61] The disorder is frequently comorbid with ADHD, but individuals generally exhibit the combined hyperactive inattentive subtype or the inattentive subtype as opposed to the impulsive subtype often found in SUD populations.[62] This might explain why the disorder has been found to have a relatively low SUD risk.[63] However, given the high comorbidity with ADHD and associated deficits in executive function, the presence of the disorder in SUD may further complicate treatment progress.

Specific learning disorders may be comorbid with SUD, although this has been inconsistently reported in the literature. In one study, the prevalence of dyslexia in a small sample of SUD treatment clients was found to be almost 10-fold that in the general population.[64] However, another study found a lower prevalence of substance use among university students with dyslexia.[65]

In the absence of a formal diagnosis for ADHD, specific learning disorder or other developmental conditions, indicators of poor academic engagement, such as repeating grades, learning disabilities and school suspension or expulsion, may help to identify the presence of neurodevelopmental conditions.[66,67,68,69]

Subjective cognitive difficulties

Using a sample of 126 polysubstance misusers and 32 healthy controls, Hagen et al. (2016) found a self-report inventory to more accurately predict SUD status compared with objective measures of decision-making, inhibition, attention and task switching.[70] Results from the self-report inventory were also significantly associated with social factors such as unstable income, conflict with caregiver, and unstable housing. As such, subjective appraisal of cognitive impairment may be an additional valid indicator of underlying cognitive impairment.

Questionnaire development

Questions about the identified risk factors of head injury, seizures, maternal AOD use, overdose, neurological conditions and neurodevelopmental learning and/or behavioural disorders, as well as subjective cognitive impairment, were generated. They were worded simply to maximise comprehension in a population characterised by mild cognitive impairment and relatively low levels of education. As well as simplifying questions, some redundancy was factored in. For example, an affirmative response to the question, 'Did you repeat any grades at school?' may indicate learning and/or behavioural difficulties for an individual respondent. Given that the consultation team considered head injury and overdose severity to be potentially significant determinants of the risk of cognitive impairment, follow-up questions about whether each of these phenomena (if present) required hospitalisation were added to the questionnaire.

For the sake of brevity and simplicity, only 'yes' or 'no' responses were required, although 'unsure' was also provided as an option for the question about maternal AOD use. Additionally, optional follow-up questions were included if more detail was considered necessary. Total score was calculated by summing 'yes' responses for the 12 items.

The result of this process was the following 12 questions.

Head injury

- Have you ever lost consciousness following a blow to the head?
- If yes, how many times?
- Did you ever have to go to hospital following a head injury?
- If yes, how many times?

Seizures

- Have you ever had an epileptic seizure?
- If yes, how many times or how often?

Overdose

- Have you ever had a drug or medication overdose?
- If yes, how many times?
- Did you ever have to go to hospital following an overdose?
- If yes, how many times?

Maternal AOD use

- Did your mother use alcohol or other drugs when she was pregnant with you?

Other neurological conditions

- Have you ever had a stroke or any other neurological conditions that might affect your thinking skills?
- If yes, what was it and when did it occur?

Neurodevelopmental learning/behavioural disorder

- Did you ever have learning difficulties or have to attend special education classes at school?
- Have you ever been diagnosed with or suspected of having a developmental condition such as ADHD, Asperger's or a learning disability?

- Did you repeat any grades at school?
- Were you ever suspended or expelled from school?

Subjective cognitive difficulties

  - Do you experience memory or other thinking difficulties?
- If yes, since when?

Readability

Readability was assessed via Readability Formulas.[71] Results indicated a reading age of 8-9 years (i.e. Year 3 or 4 level).

Validation of the ACE Screening Tool

Validation of the tool involved establishing:

- test-retest reliability
- construct validity
- criterion validity.

Validation sample

The Screening Tool was administered to a group of SUD (n=650) and normal control (n=209) participants. The SUD participants were enrolled in NSW-based residential AOD treatment services and were therefore not currently using substances, with the exception of those in opiate substitution programs. See Table 1 for sample characteristics.

Table 1. Sample characteristics

Characteristic	Substance use disorder (n=650)		Normal control (n=209)	
Gender (%Male)	62%		39%	
	Mean	Standard deviation	Mean	Standard deviation
Age	36.3	10.6	29.7	13.4
Education	10.8	2.0	13.3	2.1
Test of Premorbid Functioning	92.5	12.5	103.8	14.1
Primary substance of use	Number	%		
Alcohol	241	37		
Methamphetamine	265	41		
Other stimulants	20	3		
Heroin	51	8		
Other opiates or opioids	14	2		
Sedatives, hypnotics or tranquilisers	8	1		
Cannabis	51	8		

Test-retest reliability

Test and retest data were available for n=36 SUD and n=40 normal control individuals. The median test-retest interval was 39 days for the SUD group, 76 days for the normal control group and 47 days for the entire sample. See Table 2 for the sample characteristics.

Table 2. Retest sample characteristics

Characteristic	Substance use disorder (n=36)		Normal control (n=40)	
Gender (%Male)	81%		45%	
	Mean	Standard deviation	Mean	Standard deviation
Age	38.6	6.9	28.2	12.6
Education	10.9	1.3	13.5	1.9
Test of Premorbid Functioning	98.2	13.4	109.6	11.7
Primary substance of use	Number	%		
Alcohol	10	28%		
Methamphetamine	8	22%		
Heroin	14	39%		
Other opiates or opioids	4	11%		

Test-retest reliability was established using the intraclass correlation coefficient, which was 0.968, 95% CI [0.950, 0.980] (n=76), calculated based on an absolute agreement, two-way mixed effects model, representing excellent test-retest reliability.[72]

Construct validity

Construct validity is concerned with whether a test is related to other measures of the same construct. In the case of the Screening Tool, the presence of cognitive impairment risk factors is expected to predict impairment on tests of cognitive functioning. Thus, to examine the construct validity of the Screening Tool, its correlations with tests of cognitive functioning were examined. Specifically, the Montreal Cognitive Assessment (MoCA) total score, Behaviour Rating Inventory of Executive Functioning – Adult version, Global Executive Composite (BRIEF-A GEC), Test of Premorbid Functioning standard score, Alpha Score, Stroop Interference trial score and Five Point Test Unique Designs score were used.[73,74,75,76,77,78] Standardised versions of these measures were used to correct for age and education where appropriate. Specifically, the MoCA score was education corrected as per Nasreddine et al. (2005), the BRIEF-A GEC score was age corrected as per the manual, the Test of Premorbid Functioning score was age corrected as per the manual, Alpha Score was corrected for age as per Craik et al. (2017) and Five Point Test Unique Designs was corrected for age and education as per Goebel et al. (2009).[71-75]

Table 3 shows the Pearson correlations between the Screening Tool and measures of cognitive functioning for the total and SUD samples. Missing data were excluded pairwise. The Screening Tool was significantly correlated with all measures in the total sample, and with the BRIEF-A, Test of Premorbid Functioning, Alpha Score and Stroop in the SUD sample. Apart from the BRIEF-A, the correlations were of a small magnitude.

Overall, the results reveal that the Screening Tool is significantly correlated with measures of cognitive impairment, and therefore construct validity is established.

Table 3. Pearson correlations between the Screening Tool and measures of cognitive functioning for the total and SUD samples

Test	Total sample Pearson r (n)	SUD sample Pearson r (n)
MoCA	-0.287** (338)	-0.029 (129)
BRIEF-A GEC	0.480** (816)	0.369** (607)
Test of Premorbid Functioning standard score	-0.258** (839)	-0.097* (632)
Alpha Score	-0.277** (591)	-0.175** (510)
Stroop Golden Version Interference Trial	-0.240** (791)	-0.103* (582)
Five Point Test Unique Designs	-0.160* (841)	-0.028 (633)

*p≤0.05, **p≤0.001

Criterion validity

Criterion validity is concerned with a test's ability to discriminate between populations or conditions of interest. The purpose of screening for cognitive impairment in an SUD population is to identify individuals who may benefit from specific cognitive strategies or interventions to support their engagement in, and completion of, AOD treatment programs.

The American Academy of Clinical Neuropsychology consensus conference has outlined that: 'Neuropsychological impairment is abnormal neurocognitive or neurobehavioral capacity. Impairment may result from loss of previously acquired skill or result from atypical development, may be transient or fixed across time, and can have variable impact on functional capacity and disability. Test scores, per se, do not define impairment. A combination of factors, including test scores that deviate from expectations, and other findings related to functional capacity, identify neuropsychological impairment.'[79]

In view of this definition that defines cognitive impairment as a broader concept than just poor performance on a cognitive test, we have sought to establish a criterion for impairment based on two factors: poor performance on a cognitive test; and abnormal results on a self-report inventory.

The distinction between impairment on performance-based tests and self-report inventories within the SUD population has been made.[70] That is, it is possible for a person to perform poorly on a performance-based test yet experience no functional cognitive impairment. Conversely, an individual may perform within normal limits on a performance-based cognitive test yet experience significant functional cognitive difficulties in everyday activities.

To move beyond the mere use of performance-based measures to indicate cognitive impairment, and to mitigate the risk of false positives from self-report, particularly when there are high levels of psychological distress, a ternary variable was calculated to be used as a standard with which to conduct analyses to establish criterion validity.[80]

Establishing the criterion

A subset of the entire sample for whom both BRIEF-A and MoCA results were available were used to examine criterion validity. Sample characteristics are presented in Table 4.

Table 4. Criterion validation sample characteristics

Characteristic	Substance use disorder (n=127)		Normal control (n=209)	
Gender (%Male)	63%		39%	
	Mean	Standard deviation	Mean	Standard deviation
Age	35.7	9.2	29.7	13.4
Education	11.0	1.8	13.3	2.1
Test of Premorbid Functioning	93.0	13.5	[a]103.8	14.1
Primary substance of use	Number	%		
Alcohol	41	32.3%		
Methamphetamine	34	26.8%		
Other stimulants	29	22.8%		
Heroin	9	7.1%		
Other opiates or opioids	7	5.5%		
Sedatives, hypnotics or tranquilisers	4	3.1%		
Cannabis	3	2.4%		

[a] based on n=207

Individuals were classified as impaired on the MoCA using the cutoff score of <26, which has already been established in the literature.[1] They were also classified as impaired on the BRIEF-A GEC if they had a t-score ≥65, which has also been established as a cut score in the existing literature.[72] A ternary severity variable was then constructed with the following values: 0 = neither impaired on the MoCA or BRIEF-A (Intact), 1 = impaired on *either* the MoCA or the BRIEF-A (some impairment), and 2 = Impaired on *both* the MoCA and BRIEF-A (impaired).

To validate this severity criterion variable, it was predicted that both MoCA and BRIEF-A GEC scores would vary across each of its levels. To test this, one-way analyses of variance with MoCA total and BRIEF-A GEC scores as the dependent variables, respectively, and severity as the independent variable were conducted.

It was predicted that the MoCA score would be lower for the impaired group than the some impairment group and that it would be lower for the some impairment group than the Intact group. There was a significant difference between severity level and MoCA total score, $F(2,333) = 139.199$, $p<0.001$. Post-hoc Bonferroni tests revealed a significant difference between each of the severity groups, as seen in Figure 1.

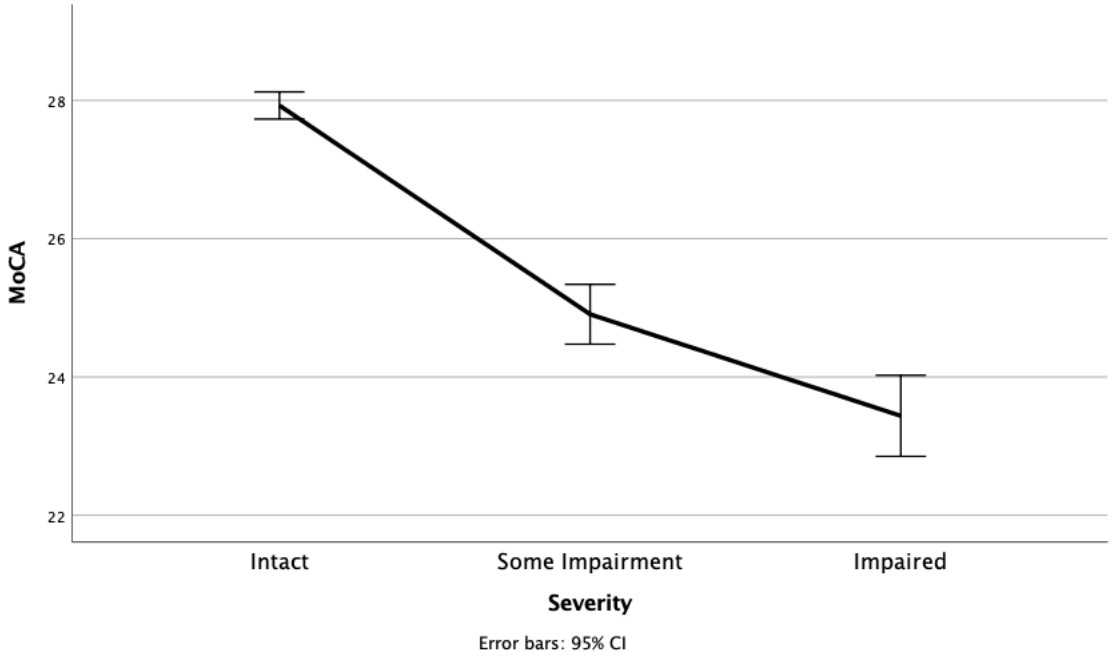

Figure 1. MoCA score by severity

It was predicted that the BRIEF-A GEC score would be higher for the impaired than the some impairment group and that it would be higher for the some impairment than the intact group. There was a significant difference between severity level and BRIEF-A GEC, $F(2,333) = 103.152$, $p<0.001$. Post-hoc Bonferroni tests revealed a significant difference between each of the severity groups, as seen in Figure 2.

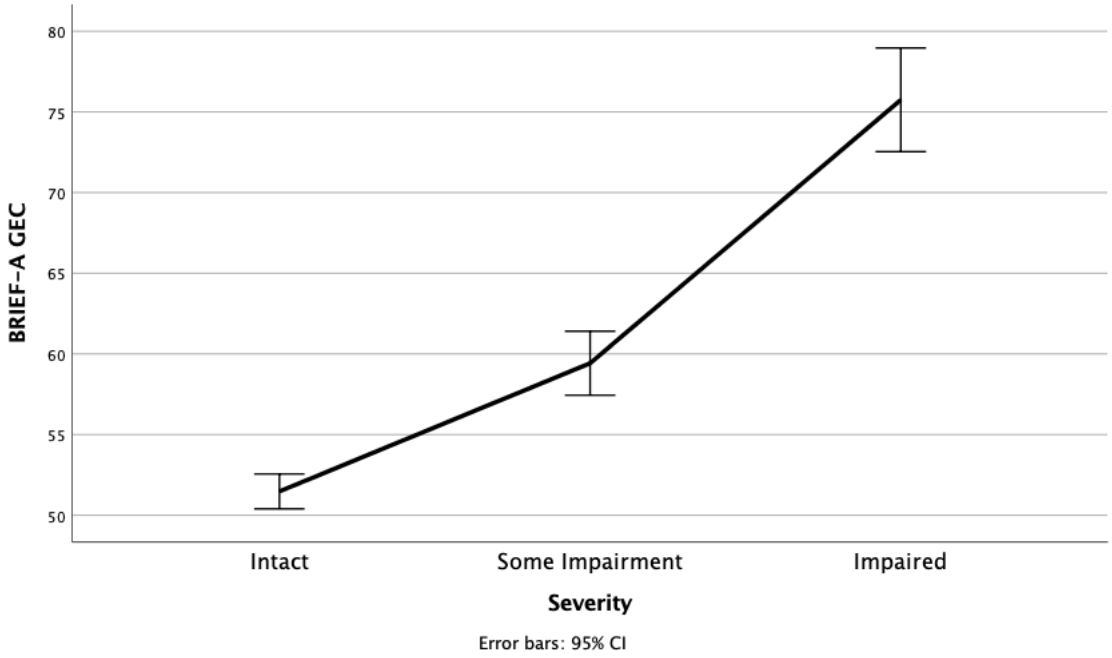

Figure 2. BRIEF-A GEC by severity

Having established the validity of the severity criterion variable, criterion validity would be demonstrated if the Screening Tool discriminated between individuals scoring at each level of the ternary severity variable. It was predicted that the Screening Tool score would be higher for those with impaired than some impairment and that it would be higher for those with some impairment than the intact group. There was a main effect for age, $F(2,333) = 6.399$, $p=0.002$, and education, $F(2,333) =13.343$, $p<0.001$, for severity. Therefore, age and education were entered as covariates in an analysis of covariance with ACE Screening Tool as the dependent variable and severity as the independent variable. There was a significant difference in ACE Screening Tool score across severity levels, $F(2,333) = 46.482$, $p<0.001$. Post-hoc Bonferroni tests revealed significant differences between each of the severity levels, as seen in Figure 3. These results established criterion validity for the ACE Screening Tool.

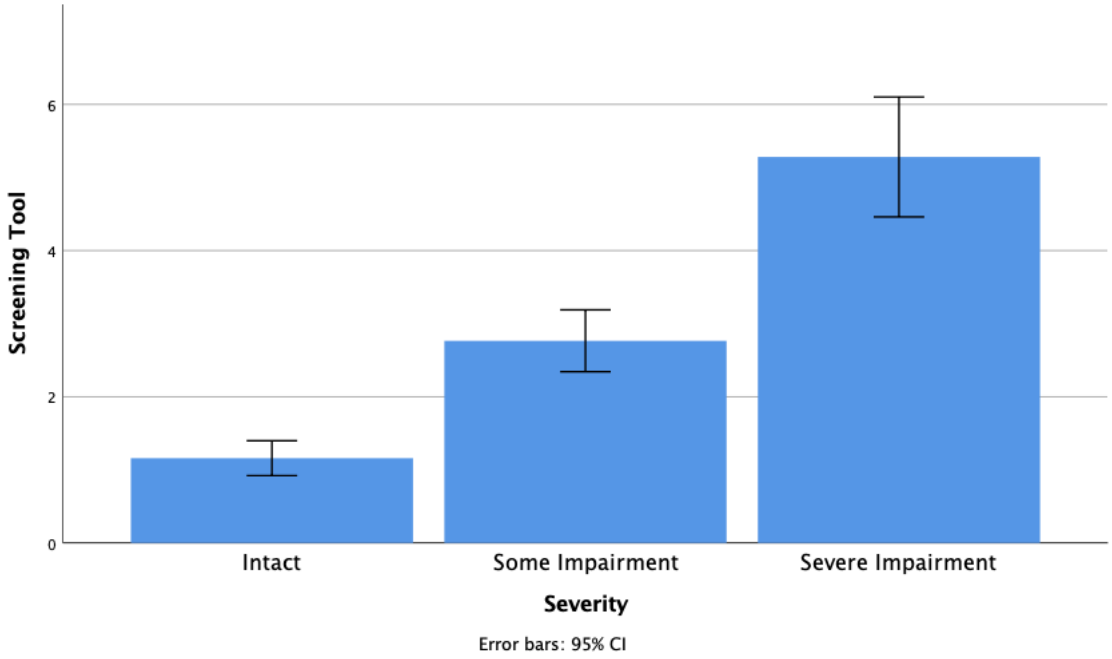

Figure 3. Mean Screening Tool total score for each level of severity of cognitive impairment for the combined sample

Classification statistics

Another aspect of validity is the extent to which a test classifies individuals with a condition of interest versus those that do not have the condition of interest.

Because the some impairment (n=128; 64 SUD and 64 normal control participants) group of the ternary severity variable did not fall into either of these categories, it was eliminated from classification statistics analysis, and only the Intact (n=176; 35 SUD and 141 normal control participants) and Impaired (n=32; 28 SUD and 4 normal control participants) groups were included.

Receiver operating characteristic (ROC) curve analysis between the intact and impaired groups revealed an optimal cut score of ≥3. When this cut score was applied, it resulted in 94% sensitivity and 84% specificity, and explained 92% area under the curve. Negative predictive power was 99% and overall classification accuracy was 86%. See the ROC curve in Figure 4 and classification statistics in Table 5.

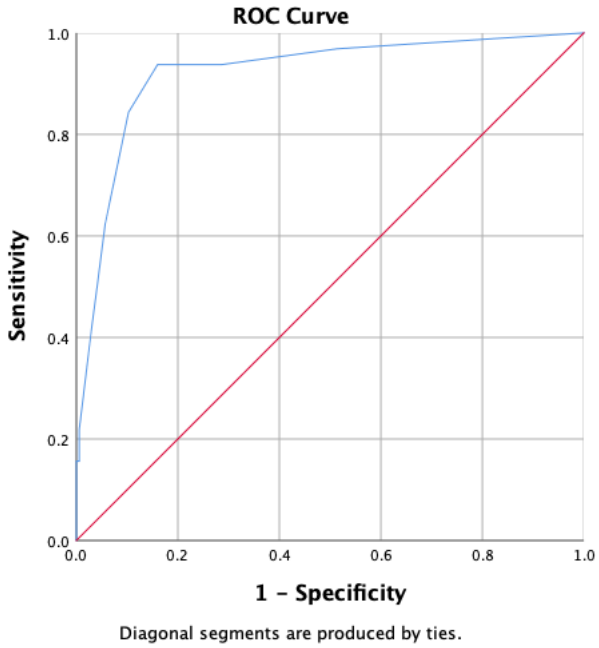

Figure 4. Screening Tool ROC curve for the impaired and intact groups across the whole sample

Table 5: Classification statistics for the Intact and Impaired groups for the whole and SUD samples

Statistic	Whole sample (n=208)		SUD sample (n=63)	
	Value %	95% CI	Value	95% CI
Sensitivity	93.75	79.19 to 99.23	96.43	81.65 to 99.91
Specificity	84.09	77.83 to 89.16	34.29	19.13 to 52.21
Disease prevalence	15.38	10.77 to 21.02	44.44	31.92 to 57.51
Positive likelihood ratio	5.89	4.15 to 8.37	1.47	1.14 to 1.88
Negative likelihood ratio	0.07	0.02 to 0.28	0.1	0.01 to 0.75
Positive predictive value	51.72	42.99 to 60.35	54.00	47.77 to 60.11
Negative predictive value	98.67	95.08 to 99.65	92.31	62.39 to 98.86
Accuracy	85.58	80.05 to 90.05	61.90	48.80 to 73.85

When the cut score of ≥3 was applied to the SUD sample only, it resulted in 96% sensitivity and 34% specificity, and explained 81% area under the curve. Negative predictive power was 92% and overall classification accuracy was 62%, as seen in Table 5.

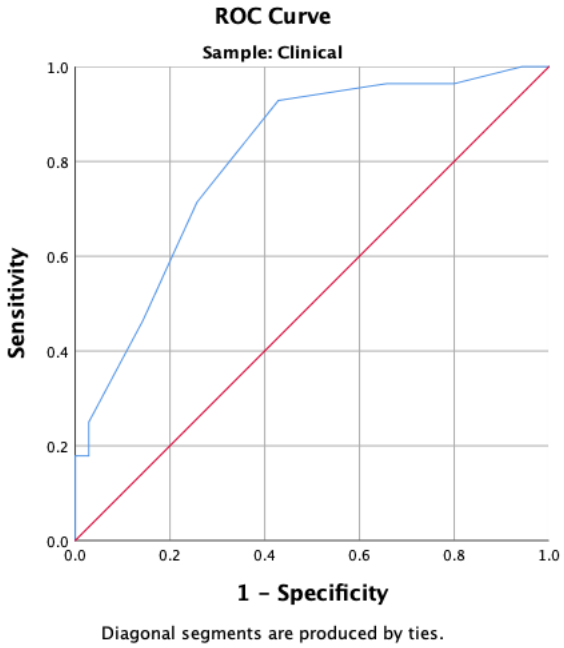

Figure 5: ROC curve for the Screening Tool for the SUD sample

For both the whole and SUD samples, sensitivity and negative predictive power were high, which is desirable for screening instruments.

Outpatient sample validation

The ACE Screening Tool has been validated for use in an outpatient population in the Illawarra Shoalhaven Local Health District with a sample of n=75 clients with SUD. These clients were not required to be abstinent from substances to participate in the study.

Conclusion

The Screening Tool has demonstrated excellent reliability, construct validity and criterion validity. Using a cut score of ≥3, it has excellent sensitivity and negative predictive power, meaning it is likely to detect cognitive impairment when it is present. It is therefore recommended to screen for cognitive impairment within AOD services.

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    - LAMP Opioid Treatment Unit (Nowra)
    - Orana Centre (Wollongong)
    - Shoalhaven Drug and Alcohol Service (Nowra)
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- Kedesh (Wollongong)
- One80TC (Yarramundi)
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- Salvation Army – William Booth (Sydney)
- St Vincent de Paul - Freeman House (Armidale)
- The Glen Centre (Chittaway Point)
- WHOs Hunter (Cessnock)
- WHOs New Beginnings (Rozelle)

Glossary

ADHD	attention deficit hyperactivity disorder
AOD	alcohol and other drug
BRIEF-A GEC	Behavior Rating Inventory of Executive Functioning – Adult version, Global Executive Composite
MoCA	Montreal Cognitive Assessment
ROC	Receiver operating characteristic
SUD	substance use disorder
TBI	traumatic brain injury

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