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Cross-cultural Validation of the SOS-scale for Iatrogenic Withdrawal Syndrome in Brazilian PICUs: Comparison with the WAT-1

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Abstract

Background: Iatrogenic withdrawal syndrome (IWS) is a clinically relevant complication in pediatric intensive care units (PICUs), occurring after the reduction or discontinuation of prolonged sedative and analgesic therapy. Although the Withdrawal Assessment Tool-1 (WAT-1) is widely used, the Sophia Observation Withdrawal Symptoms-scale (SOS) provides a structured and multidimensional assessment that requires validation across different languages and clinical settings.

Objective: To perform the cross-cultural adaptation and validation of the Brazilian Portuguese version of the SOS-scale and to evaluate its diagnostic performance for detecting drug withdrawal syndrome in critically ill children, in comparison with the WAT-1.

Methods: A methodological study was conducted in a tertiary PICU. The SOS-scale was applied to 106 children aged 0–16 years exposed to opioids and/or benzodiazepines for ≥ 5 days. Inter-rater reliability, internal consistency, and convergent validity (correlation with WAT-1) were assessed. Diagnostic accuracy was evaluated using receiver operating characteristic (ROC) curve analysis.

Results: The Brazilian SOS-scale demonstrated high internal consistency (Cronbach's alpha = 0.82) and substantial inter-rater agreement ($\kappa = 0.65–0.88$). A strong correlation was observed between SOS and WAT-1 scores (Spearman's $\rho = 0.85$; $p < 0.001$). ROC curve analysis identified an optimal cut-off value of ≥ 4 for the SOS-scale (sensitivity 96.8%, specificity 92.0%; AUC 0.92) and ≥ 3 for the WAT-1 (sensitivity 96.8%, specificity 88.0%; AUC 0.75).

Conclusion: The Brazilian Portuguese version of the SOS-scale is a highly accurate, valid, and reliable tool for detecting drug withdrawal syndrome in critically ill children. The identified cut-off values provide clear clinical guidance for use in pediatric intensive care units.

Introduction

Iatrogenic withdrawal syndrome (IWS) is a frequent and clinically significant complication in pediatric intensive care units (PICUs), resulting from the reduction or discontinuation of prolonged exposure to opioids and benzodiazepines. The incidence of IWS has been reported to range from 35% to 80% in critically ill children, particularly in those receiving continuous sedation for more than five days, and is associated with prolonged mechanical ventilation, longer PICU stay, and increased morbidity (1–3).

Accurate identification of IWS remains challenging due to the overlap between withdrawal symptoms and other clinical conditions such as pain, delirium, and inadequate sedation (4). For this reason, recent international guidelines, including the PANDEM consensus (Pediatric Pain, Agitation, Neuromuscular Blockade, and Delirium), strongly recommend the use of validated and standardized assessment tools to guide clinical decision-making and optimize sedation weaning strategies (5).

Among the available instruments, the Withdrawal Assessment Tool-1 (WAT-1) is the most widely used scale in clinical practice (6). However, it has limitations, particularly in capturing the multidimensional

and heterogeneous manifestations of withdrawal in pediatric patients (7). The Sophia Observation Withdrawal Symptoms-scale (SOS) was developed to address these limitations by incorporating a broader range of behavioral, autonomic, and gastrointestinal symptoms, offering a more comprehensive evaluation (8,9).

Despite its promising performance, the SOS-scale has not been widely implemented in non-English-speaking settings due to the lack of validated translations. In Brazil, this gap limits the adoption of structured tools for IWS assessment and contributes to variability in clinical practice.

Therefore, this study aimed to perform the cross-cultural adaptation and validation of the SOS-scale into Brazilian Portuguese and to evaluate its diagnostic performance in critically ill children, comparing it directly with the WAT-1.

We hypothesized that the SOS-scale would demonstrate superior reproducibility and diagnostic performance compared to the WAT-1.

Methods

We conducted a prospective observational study in a tertiary Pediatric Intensive Care Unit (PICU).

The study population included children aged 0 to 16 years admitted to the PICU with acute respiratory failure requiring mechanical ventilation and receiving opioids and/or benzodiazepines, either as continuous infusion or intermittent doses, for a period of ≥ 5 days. Exclusion criteria were respiratory failure due to neuromuscular disease, chronic use of opioids and/or benzodiazepines prior to admission, presence of severe neurological injury, or patients receiving palliative care.

Patients were assessed through standardized video recordings capturing behavioral responses and vital signs. Two independent observers, blinded to clinical data, initially classified patients as having or not having withdrawal symptoms based on empirical clinical judgment. Subsequently, both observers independently applied the Sophia Observation Withdrawal Symptoms-scale (SOS) and the Withdrawal Assessment Tool-1 (WAT-1) to the same recordings. All scores were recorded in a structured database for analysis.

Withdrawal status was determined based on clinical judgment by independent observers, as no universally accepted gold standard exists for IWS diagnosis.

All analyses were performed on the same dataset of 96 observations.

Observers were blinded to each other’s assessments and to clinical data beyond the recorded videos.

The SOS-scale was translated into Brazilian Portuguese using a cross-cultural adaptation process with authorization from the original author (Erwin Ista). Inter-rater reliability was evaluated by comparing the scores assigned by the two observers. Agreement between observers was assessed using the Bland–

Altman method for continuous measures and the Cohen's Kappa coefficient for categorical classification of withdrawal severity, both with 95% confidence intervals.

Diagnostic performance of the scales was evaluated by calculating sensitivity and specificity and by constructing receiver operating characteristic (ROC) curves. The area under the curve (AUC) was used to assess the ability of each instrument to discriminate between patients with and without iatrogenic withdrawal syndrome.

Data were initially recorded in Microsoft Excel spreadsheets and subsequently analyzed using SPSS (Statistical Package for the Social Sciences), version 22.0.

Ethics

This study was conducted in accordance with the Declaration of Helsinki. Approval was granted by the Ethics Committee of Hospital de Clínicas de Porto Alegre, Brazil, and registered on the Brazilian Research Platform (CAAE 13516819.1.0000.5327). Written informed consent was obtained from parents or legal guardians prior to enrollment.

Results

During the study period, from July 27, 2016 to January 27, 2018 (18 months), 847 patients were admitted to the PICU, of whom 45% required mechanical ventilation. A total of 64 children met the inclusion criteria, and one patient died during the study period. The final sample comprised 96 observations from 63 patients (30 patients were assessed once, and 33 patients were assessed twice).

The median age of the patients was 12 months, and 71% were male. Most patients were cared for by their mothers (90%). Respiratory diseases were the main cause of admission (70%), with bronchiolitis being the most frequent diagnosis (57%). Only 9 patients (14%) had a Pediatric Index of Mortality (PIM) score greater than 5, indicating a low mortality risk in the study population.

Regarding origin, 41 patients (64%) were admitted from external sources (28 from the emergency department and 13 from other hospitals), while 23 patients (36%) were admitted from within the same institution (13 from the surgical center and 10 from the general ward).

The median length of PICU stay was 9 days (range 6–31), duration of mechanical ventilation was 7 days (5–25), and duration of sedation and analgesia was 8 days (5–25).

At discharge, 59 patients (94%) were transferred to the general ward, 2 (3%) were discharged home, 1 (2%) was transferred to another hospital, and 1 patient died.

Regarding vital signs, 7 patients (11.5%) presented hyperthermia, 19 (29%) had tachycardia, and 36 (57%) had hypertension during the first assessment.

In terms of pharmacological management, the majority of patients received opioids (81%), while 70% received benzodiazepines. The main characteristics of the study population are summarized in Table 1, and details of sedation, analgesia, and neuromuscular blockade are presented in Table 2.

Table 1
General Characteristics of the Patients Included in the Study (n = 63)

Variable	**Mean (Minimum – Maximum)**
Age (months)	12 (0.5–136)
Weight (kg)	5 (6–26)
PIM2 (%)	1.24 (0.13–43.71)
Axillary temperature (°C)	37 (36–40)
Heart rate (beats per minute)	140 (73–185)
Respiratory rate (breaths per minute)	23 (16–50)
Systolic blood pressure (mmHg)	104 (61–150)
Diastolic blood pressure (mmHg)	53 (32–105)
Length of hospital stay (days)	9 (6–31)
Duration of mechanical ventilation (days)	7 (5–25)
Duration of sedation (days)	8 (5–25)
Abbreviations: PIM2: Pediatric Index of Mortality 2; bpm: beats per minute; mmHg: millimeters of mercury.	

Table 2
Sedation, Analgesia, and Neuromuscular Blockers Used by Patients (n = 63)

Drug Class	**n (%)**
Opioids	51 (81%)
Benzodiazepines	44 (70%)
Pancuronium	40 (64%)
Ketamine	37 (59%)
Clonidine	6 (10%)

Regarding scale reproducibility, Fig. 1 illustrates the agreement between observers using the Bland–Altman method, showing a wide interval of agreement (from − 3.01 to 4.15).

Receiver operating characteristic (ROC) curve analysis demonstrated that both scales were able to discriminate between the presence and absence of withdrawal, with superior performance for the SOS-scale (AUC = 0.92) compared to the WAT-1 (AUC = 0.75). These findings are presented in Fig. 2.

Using the Kappa coefficient, the SOS-scale, with a cut-off point of ≥ 4, showed agreement between observers in 79.2% of cases, with a moderate and statistically significant Kappa value ($\kappa = 0.53$; $p < 0.001$). In the empirical assessment, agreement was 74%, also with moderate Kappa, although of lower magnitude.

For the WAT-1 scale, using a cut-off point of ≥ 3, agreement between observers was 71.9%, with a Kappa coefficient of 0.23, indicating weak agreement, although statistically significant ($p < 0.003$).

Overall, there was good agreement in the classification of withdrawal levels using the SOS-scale compared to the WAT-1 and empirical assessment.

Discussion

The present study demonstrates that the Brazilian Portuguese version of the SOS-scale is a valid, reliable, and clinically applicable instrument for the assessment of iatrogenic withdrawal syndrome in critically ill children. Our findings highlight two key aspects: the reproducibility of the scale and its superior diagnostic performance compared to the WAT-1.

Inter-rater reliability is a fundamental requirement for clinical tools used in intensive care settings, where multiple professionals are involved in patient assessment. In this study, the SOS-scale showed moderate agreement between observers ($\kappa = 0.53$), which, although not perfect, is superior to that observed with the WAT-1 ($\kappa = 0.23$). These findings suggest that the SOS-scale provides a more consistent and reproducible assessment of withdrawal symptoms in pediatric patients.

The results observed in this study are consistent with previous validation studies of the SOS-scale, which demonstrated good reliability and clinical applicability in pediatric populations (8–10). The improved agreement observed with the SOS-scale may be explained by its structured and multidimensional design, which includes behavioral, autonomic, and gastrointestinal components, allowing for a more comprehensive evaluation of withdrawal symptoms (9).

In addition to reproducibility, the SOS-scale demonstrated good diagnostic accuracy, with an area under the ROC curve (AUC) of 0.92. This indicates a strong ability to discriminate between patients with and without withdrawal syndrome and reinforces the clinical usefulness of the scale. In comparison, the WAT-1 showed lower diagnostic performance (AUC = 0.75), suggesting that it may be less sensitive in detecting the full spectrum of withdrawal manifestations in this population.

These findings are in agreement with previous studies that emphasize the importance of structured assessment tools over empirical clinical judgment, as they improve diagnostic accuracy and reduce

variability in clinical practice (3,10,11). The use of video-based assessment allowed standardized and reproducible evaluation, reducing interobserver variability.

The strong correlation between the SOS-scale and WAT-1 scores suggests that both instruments assess similar constructs; however, the superior performance of the SOS-scale indicates that it may be more sensitive in identifying withdrawal symptoms.

Recent international recommendations, including the PANDEM guidelines, highlight the importance of using validated tools for the assessment of withdrawal, pain, and sedation in critically ill children, aiming to improve patient outcomes and optimize sedation weaning strategies (5,11,12).

From a clinical perspective, the implementation of the SOS-scale may facilitate earlier recognition of withdrawal syndrome and contribute to more individualized and effective patient management. Its ease of application and the fact that it does not require extensive training further support its use in routine PICU practice.

This study has some limitations. It was conducted in a single center, which may limit the generalizability of the findings. In addition, the sample size, although adequate for validation purposes, was relatively small. Future multicenter studies are needed to confirm these findings and to evaluate the impact of SOS-based protocols on clinical outcomes.

Conclusion

The Brazilian Portuguese version of the SOS-scale proved to be a valid, reliable, and clinically applicable instrument for assessing iatrogenic withdrawal syndrome in critically ill children admitted to a PICU. In this cohort, the SOS-scale demonstrated better inter-rater agreement and superior diagnostic performance compared to the WAT-1, with a cut-off point of ≥ 4 showing good ability to identify withdrawal symptoms.

These findings support the use of the SOS-scale as a standardized bedside tool to improve the recognition of iatrogenic withdrawal syndrome and to guide sedation and analgesia weaning in pediatric intensive care. Further multicenter studies are warranted to confirm these results and to evaluate whether SOS-guided protocols can improve clinical outcomes.

Declarations

Author Contribution

All authors contributed for all phasis of the research and reviewed the manuscript

Data Availability

The datasets generated and/or analysed during the current study are not publicly available due to ethical and privacy restrictions involving pediatric patient data but are available from the corresponding author on reasonable request.

References

1. Franck LS, Vilardi J, Durand DJ, Powers R. Opioid and benzodiazepine withdrawal symptoms in pediatric intensive care patients. Intensive Care Med. 2008;34(2):334–342.
2. Best KM, Wypij D, Asaro LA, Curley MAQ. Patient, process, and system predictors of iatrogenic withdrawal syndrome in critically ill children. Crit Care Med. 2017;45(1):e7–e15.
3. Amigoni A, Pettenazzo A, Stritoni V, et al. Withdrawal Assessment Tool-1 monitoring in PICU: a multicenter study on iatrogenic withdrawal syndrome. Pediatr Crit Care Med. 2017;18(2):e86–e91.
4. Harris J, Ramelet AS, van Dijk M, et al. Clinical recommendations for pain, sedation, withdrawal and delirium assessment in critically ill infants and children. Intensive Care Med. 2016;42:972–986.
5. Vet NJ, Ista E, de Wildt SN, et al. Optimal sedation in pediatric intensive care patients: a systematic review and the PANDEM guidelines. Lancet Child Adolesc Health. 2022;6(5):353–364.
6. Franck LS, Scoppettuolo LA, Wypij D, et al. Validity and generalizability of the Withdrawal Assessment Tool-1 (WAT-1). Pediatr Crit Care Med. 2012;13(6):e364–e370.
7. Ista E, van Dijk M, Tibboel D, et al. Withdrawal symptoms in critically ill children after long-term administration of sedatives and/or analgesics: a literature review. Intensive Care Med. 2007;33:1396–1406.
8. Ista E, van Dijk M, Gamel C, Tibboel D. Withdrawal symptoms in children after long-term administration of sedatives and/or analgesics: development of the SOS scale. Intensive Care Med. 2009;35:1070–1077.
9. Ista E, van Dijk M, Gamel C, Tibboel D. Assessment of withdrawal symptoms in children: SOS scale validation study. Intensive Care Med. 2013;39:865–873.
10. Ista E, de Hoog M, Tibboel D, et al. Implementation of a sedation protocol including the SOS scale in critically ill children. Pediatr Crit Care Med. 2017;18(3):e114–e122.
11. Silver G, Traube C, Kearney J, et al. Delirium and withdrawal in critically ill children: overlap and differentiation. Crit Care Med. 2019;47(2):e135–e141.
12. Madden K, Burns MM, Tasker RC. Sedation and analgesia in critically ill children: current practice and future directions. Lancet Child Adolesc Health. 2021;5(7):507–515.

Figures

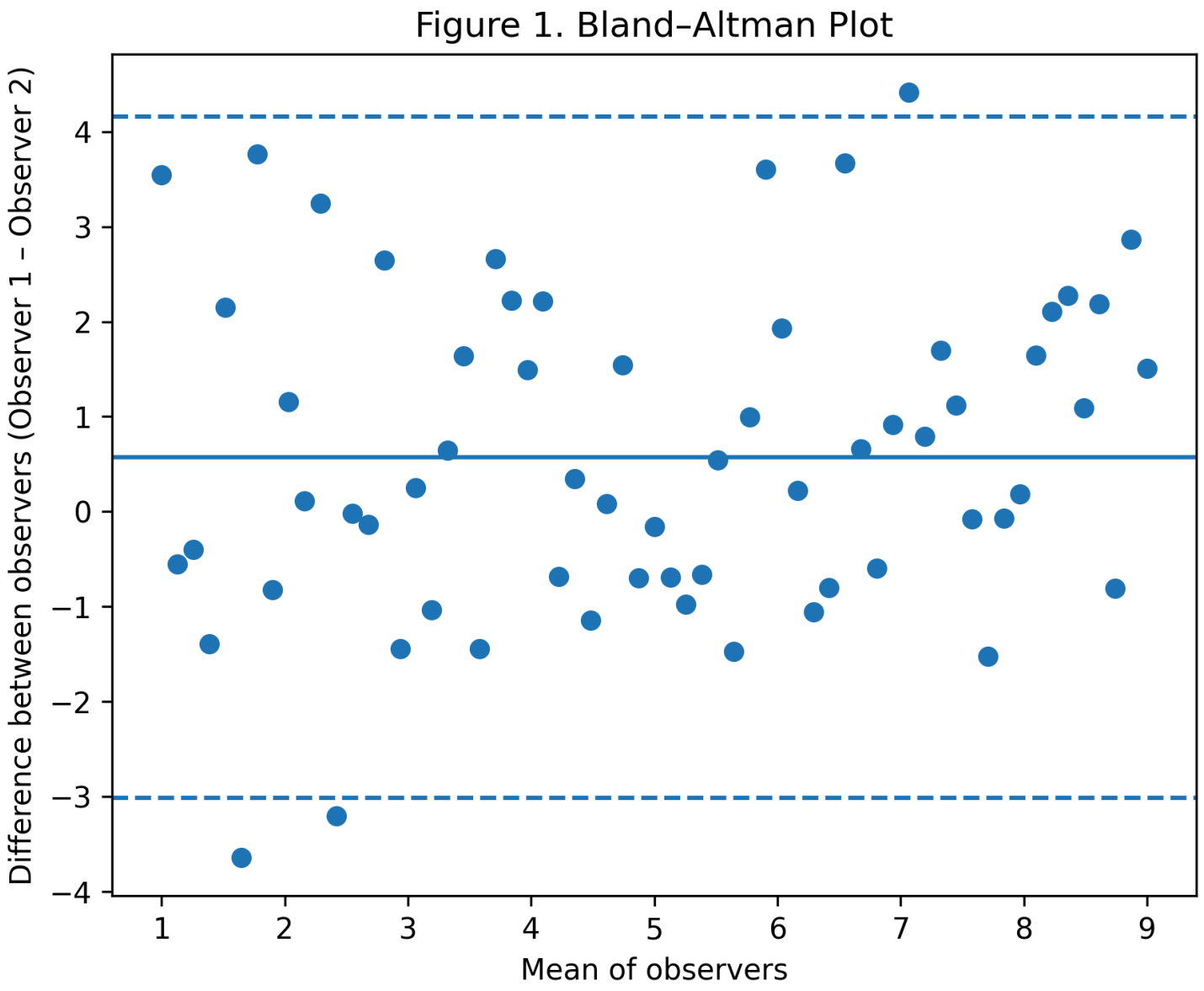
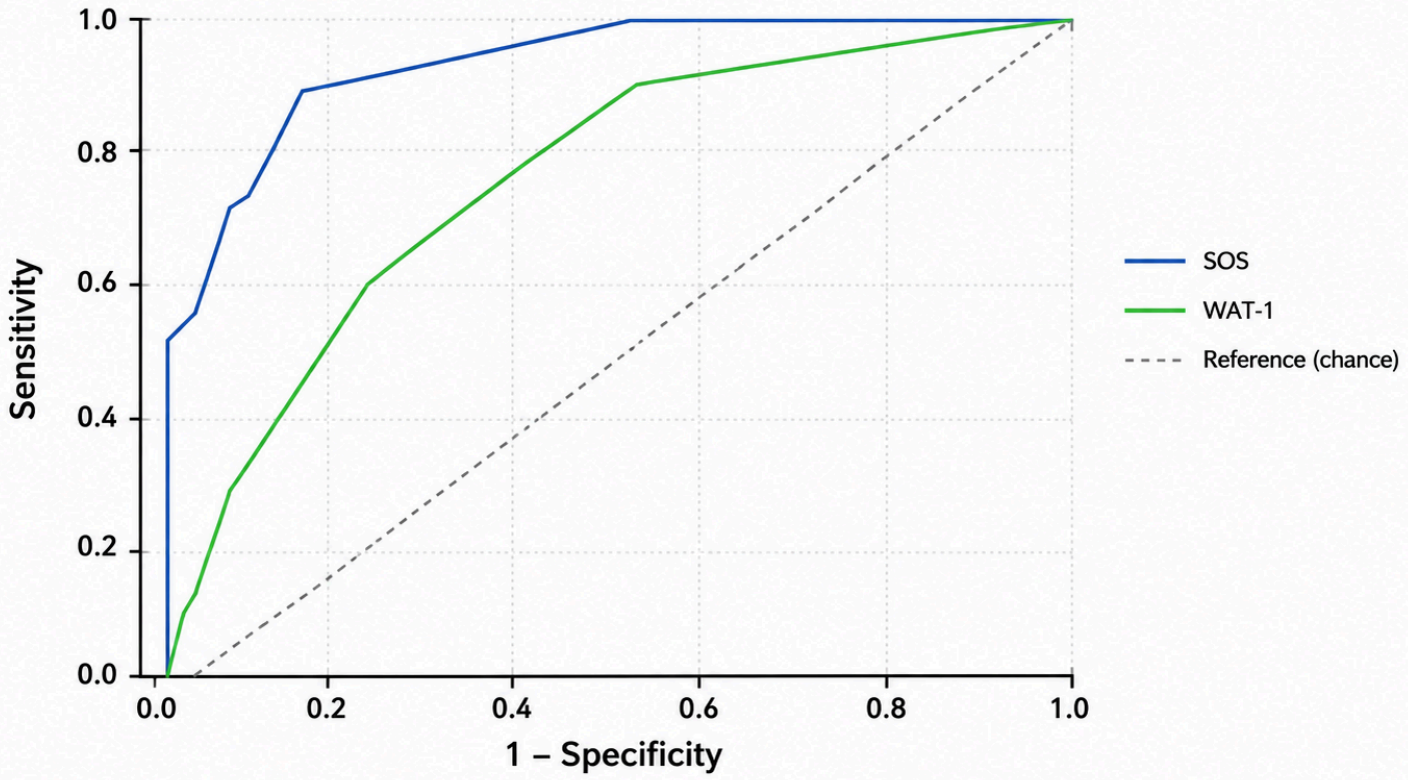


Figure 1

Graphic 1- Inter-observers differences for SOS

Legend: SOS (Sophia Observation Withdrawal Symptoms-scale) ; Bland-Altman plot

Figure 2. Receiver operating characteristic (ROC) curve: SOS *versus* WAT-1.



Area under the curve (AUC-ROC)

Scale score	Area (AUC)	Standard error	p	95% CI lower limit	95% CI upper limit
SOS (Sophia)	0.927	0.019	<0.001	0.890	0.964
WAT-1	0.754	0.040	<0.001	0.677	0.832

CI, confidence interval; AUC-ROC, area under the receiver operating characteristic curve.
* 95% confidence interval (AUC-ROC).

Figure 2

Receiver Operating Characteristic ROC curve SOS vs WAT-1

Legend : ROC (receiver operating characteristics curve) Withdrawal Assessment Tool-1 (WAT-1); SOS (Sophia Observation Withdrawal Symptoms-scale) ; Blue= SOS; Green = WAT-1