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# Psychometric Properties of a Novel Vineland™-II 2-Domain Composite Score to Assess Social Communication and Social Interaction in Autism Spectrum Disorder

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## Objectives

- A novel composite endpoint consisting of the arithmetic mean score on the Communication and Socialization domains of the Vineland™-II Adaptive Behavior Scale 2nd Edition (Vineland™-II) could be acceptable as a primary endpoint for phase 3 clinical trials in autism spectrum disorder (ASD)
- To explore the measurement properties of a novel Vineland™-II 2-Domain Composite (2DC) score, which combines these 2 independently validated scales, we conducted a psychometric analysis of this new score using data from the VANILLA phase 2 trial of balovaptan, a 12-week study in adult males with ASD and an intelligence quotient (IQ) ≥ 70 (NCT01793441)

## Methods

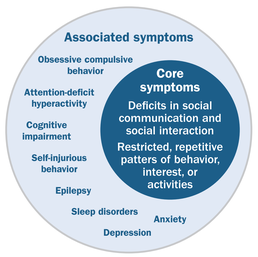
- The 2DC score is calculated as the arithmetic mean of the Vineland™-II Socialization and Communication domain standard scores
- Measure was administered by experienced raters
- Test-retest reliability was assessed using interclass correlation coefficient (ICC) in patients with no change in their clinical status at day 84 on the Clinical Global Impression–Improvement (CGI-I) scale
- Sensitivity to change (baseline to day 84) was assessed by comparing mean scores on Vineland™-II 2DC between subjects with CGI-I scores of "minimally improved" or better versus "no change" or worse using analysis of covariance
- Convergent and discriminant validity, as well as known-group validity, were also explored with baseline Vineland™-II 2DC, age, and IQ as covariates
- All analyses were conducted on the total dataset

## Conclusions

- **In adults with ASD with IQ ≥ 70, the novel Vineland™-II 2DC score shows evidence of reliability, validity and sensitivity to change, and enables a comprehensive assessment of socialization and communication abilities in people with ASD**
- **These findings support the use of the Vineland™-II 2DC score as an outcome measure for assessing the core deficits of socialization and communication in future phase 3 ASD clinical trials**

## Background

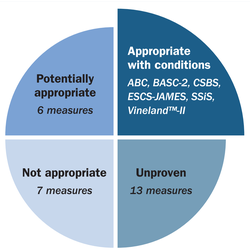
**There is a Lack of Validated Measures for Core Symptoms of ASD Established in ASD Clinical Trials**




- ASD is a complex, heterogeneous neurodevelopmental disorder characterized by impairments in social communication and interaction, as well as repetitive behaviors and restricted interests[1]

Challenges in socialization and communication are among the symptoms that matter most to people with ASD and need to be addressed by new treatments for ASD[2,3]

**There Is a Lack of Consensus on Appropriate Outcome Measures for Evaluating Core Symptoms of ASD[4]**



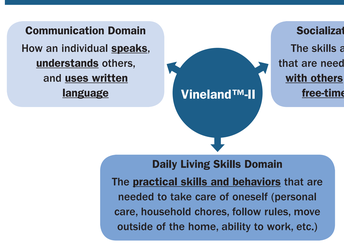

- Readiness of available measures of social communication for use as outcome measures in clinical trials have been evaluated based on their psychometric properties[4]
- Of the 38 measures evaluated, only 6 measures were considered appropriate for use, with some limitations

The Vineland™-II, with strong reliability and validity, was identified as one of the appropriate measures evaluating social communication behaviors

ABC, Aberrant Behavior Checklist; BASC-2, Behavior Assessment System for Children, 2nd Edition; CSBS, Communication and Symbolic Behavior Scales; ESCS-JAMES, Early Social Communication Scales – James; SSiS, Social Skills Improvement System.

### What is the Vineland™-II Adaptive Behavior Scale?

**The Vineland™-II Measures Adaptive Behavior From Birth Through Adulthood**



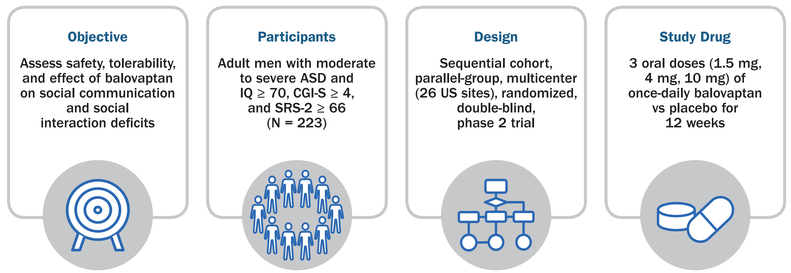

- Semi-structured, clinician-rated, caregiver-reported interview **administered by a trained interviewer**
- Measures adaptive behaviors: **skills that people need to function independently at home, at school, and in the community.** Includes communication and social skills, and daily living skills

- **Vineland™-II characterizes individuals on relevant social and communication skills in the ASD population, with emphasis on actual behavior on a daily basis[4]**
- **Vineland™-II has strong reliability (eg, internal consistency: 0.72–0.90; inter-rater reliability: 0.78–0.80; test-retest reliability: 0.88–0.92) and excellent validity[5]**
- **Vineland™-II Socialization and Communication domain scores are both reliable and valid scales used as endpoints in ASD clinical trials**

Vineland™-II Adaptive Behavior Scale also measures motor skills, administered in children aged ≤ 6 years, and a maladaptive domain that is not part of the composite score.

### The VANILLA Study

**VANILLA (NCT01793441) is the first phase 2 clinical study of balovaptan in adult men with ASD**




- **Balovaptan treatment was not associated with a significant change from baseline compared with placebo at 12 weeks in the primary efficacy endpoint (SRS-2)**
- **SRS-2 is a caregiver-rated scale that may not measure social constructs alone and can be influenced by factors such as age, expressive language, cognitive level, and problem behaviors[1]**

Dose-dependent, significant, and clinically meaningful improvements on the Vineland™-II, driven mainly by improvements in the Vineland™-II Socialization and Communication domains, were observed for participants treated with balovaptan 4 mg or 10 mg compared with placebo

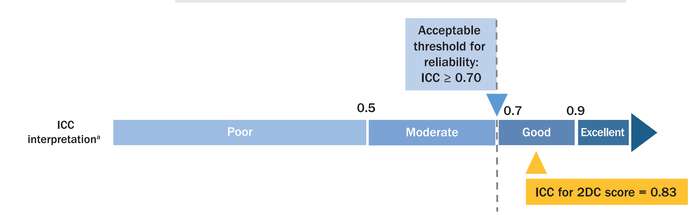
CGI-S, Clinical Global Impression–Severity; SRS-2, Social Responsiveness Scale, 2nd Edition.

## Results

### Test-Retest Reliability

**The Vineland™-II 2-Domain Composite Demonstrated Very Good Test-Retest Reliability**

The Vineland™-II-2DC Demonstrated Very Good Test-Retest Reliability Between Baseline and Day 84[a]

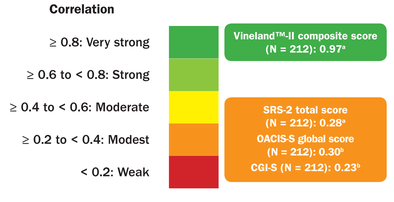



The Vineland™-II 2DC has robust reliability, as demonstrated by exceeding the threshold for acceptable reliability

N = 88; Patients who did not change in their clinical status during the study (CGI-I).
[a] ICC interpretation according to Koo TK, Li MY. *J Chiropr Med*. 2016;15(2):155-163. Erratum in: *J Chiropr Med*. 2017;16(4):346.
ICC, interclass correlation coefficient.

### Concurrent Validity

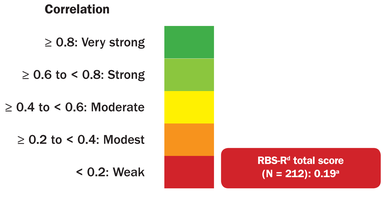
**The Vineland™-II 2-Domain Composite Correlates Highly With Vineland™-II, a Scale That Measures Similar Attributes**




- The 2DC score correlated with and demonstrated similarly robust psychometric properties to the Vineland™-II Composite score[c]
- Correlations with scales that measure related attributes were weak to modest

### Discriminant Validity

**The Vineland™-II 2-Domain Composite Correlates Weakly With RBS-R, a Scale That Measures Different Attributes**




Correlations with symptom-oriented scales that measure attributes different than those measured by 2DC were weak, as hypothesized

[a] Pearson correlation coefficient.
[b] Spearman rank *r*. OACIS Verbal score = 0.18; OACIS Nonverbal score = 0.24; and OACIS Social score = 0.25.
[c] High correlation is expected due to considerable overlap.
[d] RBS-R measures spectrum of repetitive behaviors, including stereotyped, self-injurious, compulsive, routine, sameness, and restricted.
OACIS-S, Ohio Autism Impression Scale–Severity; RBS-R, Repetitive Behavior Scale–Revised.

### Known-Groups Validity

**The Vineland™-II 2-Domain Composite Has Strong Known-Groups Validity**

| CGI-S Group at Screening (Severity Score) | n | Result: LS Mean (95% CI) |
|---|---|---|
| 4: Moderately ill | 118 | 62.01 (59.27–64.76) |
| 5: Markedly ill | 65 | 56.19 (52.49–59.89) |
| 6: Severely ill | 7 | 42.13 (30.89–53.37) |

The Vineland™-II 2DC has strong known-groups validity, with significant difference (nominal *P* value < 0.05) and evidence of monotonic decrease in scores between CGI-S groups

Analysis of covariance. Adjusted for baseline Vineland™-II 2DC score, age, and IQ.
LS, least squares.

### Sensitivity to Change

**The Vineland™-II 2-Domain Composite Is Sensitive to Change**

| Change From Baseline to Day 84 in CGI-I Scores | n | Result: LS Mean (95% CI) |
|---|---|---|
| "Minimally improved" or better | 98 | 6.58 (4.61–8.56) |
| "No change" or worse | 92 | 2.01 (–0.03, 4.06) |
| Difference between means | | 4.57 |

Sensitivity to change for the 2DC score was significant between groups (nominal *P* value < 0.05)

Analysis of covariance. Adjusted for baseline Vineland™-II 2DC score, age, and IQ.
LS, least squares.

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Balovaptan is not approved by Health Canada.

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