Use of the C-SSRS in Clinical Trials: Predicting Short-Term Risk and Detecting Clinical Change

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Objectives

• To describe the predictive validity of the eC-SSRS/C-SSRS in clinical trial research focusing on the assessment of suicidal ideation.

• To describe the sensitivity to change in suicidal ideation as measured by the C-SSRS.

• To discuss possible next steps in suicidal ideation measurement with C-SSRS.
C-SSRS Severity of Ideation Subscale
Convergent Validity

- 6-point ordinal scale: 0=no ideation, 1=wish to be dead
  2=nonspecific suicidal thoughts, 3=suicidal thoughts
  with methods, 4=suicidal intent, and 5=suicidal intent
  with plan.

- Moderately to strongly correlated with Scale for
  Suicide Ideation (worst-point) in TASA study (r=0.52,
  p<0.001; N=472) and ED study (r=0.69, p<0.001,
  N=211).

- Strongly correlated with BDI suicide item (r=0.80,
  p<0.001) and MADRS suicidal ideation item (r=0.63,
  p<0.001) in TASA study.

• Inter-rater reliability for a brief version of the SSRS was excellent (ICC=0.90, p<0.001, N=49) in TORDIA study of depressed adolescents who had not responded to a previous trial with an SSRI antidepressant.

Scale for Suicide Ideation Total Score by Level of C-SSRS Severity of Ideation

\[
F(5,185) = 14.35, \ p < 0.001, \ n = 237
\]

American Foundation for Suicide Prevention
Currier, Brown & Stanley, 2009, unpublished data
C-SSRS Lifetime Severity of Ideation

Predictive Validity

• Lifetime severity of ideation (0 -5) significantly predicted suicide attempts during 24 week follow-up (OR=1.45, 95% CI: 1.07-1.98, p<.001) in TASA study.

• Adolescents who endorsed lifetime ideation, with intent or intent and plan, significantly predicted suicide attempts over 24 weeks compared to those with no intent (OR = 3.26, 95% CI: 1.02-10.45, p = 0.047).

• SSI was not predictive of suicide attempts.

Electronic C-SSRS

• Fully structured ePRO assessment that adheres to the C-SSRS algorithm.
• eC-SSRS has been shown to be comparable to the C-SSRS (Mundt et al., 2010).
• Improves procedural reliability and facilitates disclosure of suicidal ideation and behaviors.
Objective: To evaluate whether lifetime suicidal ideation reported at baseline predicts risk of reporting suicidal behavior during subsequent study participation.
Method

- eC-SSRS assessments were administered to participants in clinical trial research by ERT (September 2009 to May 2011)
- eC-SSRS records from 14 studies
- Treatment for:
  - Major Depressive Disorder
  - Epilepsy
  - PTSD
  - Fibromyalgia

Mundt et al., ISCTM, October 3, 2011, Amelia Island, FL.
## Predictive Validity for Most Severe Level of Suicide Ideation

<table>
<thead>
<tr>
<th></th>
<th>Patients not prospectively reporting suicidal behavior N = 3575</th>
<th>Patients prospectively reporting suicidal behavior N = 201</th>
<th>Odds ratio of prospective suicidal behavior report (95% CI; p-values &lt; .001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Ideation Reported</td>
<td>1757 (99.0%)</td>
<td>17 (1.0%)</td>
<td>--</td>
</tr>
<tr>
<td>Wish to be Dead</td>
<td>737 (95.2%)</td>
<td>37 (4.8%)</td>
<td>5.19 (2.90 – 9.27)***</td>
</tr>
<tr>
<td>Active, no Method</td>
<td>288 (92.9%)</td>
<td>22 (7.1%)</td>
<td>7.90 (4.14 – 15.05)***</td>
</tr>
<tr>
<td>Active, Method, no</td>
<td>375 (91.0%)</td>
<td>37 (9.0%)</td>
<td>10.20 (5.68 – 18.30)***</td>
</tr>
<tr>
<td>Intent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active, Method, &amp;</td>
<td>240 (83.0 %)</td>
<td>49 (17.0 %)</td>
<td>21.10 (11.96 – 37.24)***</td>
</tr>
<tr>
<td>Intent</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Active, Intent &amp; Plan</td>
<td>178 (82.0 %)</td>
<td>39 (18.0 %)</td>
<td>22.65 (12.55 – 40.86)***</td>
</tr>
</tbody>
</table>

Mundt et al., 2013, unpublished data
### eC-SSRS Lifetime Severity of Ideation by Intensity of Ideation

<table>
<thead>
<tr>
<th>Severity of Ideation</th>
<th>Intensity of Ideation scores</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>No Ideation</td>
<td>1774</td>
</tr>
<tr>
<td>Passive</td>
<td>0</td>
</tr>
<tr>
<td>Active, no method</td>
<td>0</td>
</tr>
<tr>
<td>Active, method, no intent</td>
<td>0</td>
</tr>
<tr>
<td>Active, method, &amp; intent</td>
<td>0</td>
</tr>
<tr>
<td>Active, Intent, &amp; Plan</td>
<td>0</td>
</tr>
</tbody>
</table>

Mundt et al., 2013, unpublished data
Odds Ratios of Prospective Suicidal Behavior Based on Baseline Assessment

Safety Concern Codes (N) | Odds Ratio (95% CI)
--- | ---
None (2792) Negative Baseline Report | 1.00
I - Ideation Only (75) Positive Baseline Report | 5.55 (2.65, 11.59)
B - Behavior Only (479) Positive Baseline Report | 4.32 (2.93, 6.37)
Both - Ideation and Behavior (432) Positive Baseline Report | 9.10 (6.45, 12.84)
All Positive (986) Baseline Reports | 6.40 (4.72, 8.66)
**Lifetime Suicide Behavior at Baseline Predicts Suicidal Behavior During the Clinical Trial**

<table>
<thead>
<tr>
<th>Baseline Reports</th>
<th>Patients not prospectively reporting suicidal behavior</th>
<th>Patients prospectively reporting suicidal behavior</th>
<th>Odds ratio of prospective suicidal behavior report (95% CI; ***p-values &lt; .001)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Actual Attempt</td>
<td>522 (85.6 %)</td>
<td>88 (14.4 %)</td>
<td>4.56 (3.40 – 6.11)***</td>
</tr>
<tr>
<td>Interupted Attempt</td>
<td>349 (82.7 %)</td>
<td>73 (17.3 %)</td>
<td>5.28 (3.88 – 7.18)***</td>
</tr>
<tr>
<td>Aborted Attempt</td>
<td>461 (84.7 %)</td>
<td>83 (15.3 %)</td>
<td>4.75 (3.53 – 6.40)***</td>
</tr>
<tr>
<td>Preparatory Behavior</td>
<td>177 (81.2 %)</td>
<td>41 (18.8 %)</td>
<td>4.92 (3.38 – 7.16)***</td>
</tr>
</tbody>
</table>

*Posner, NCDEU, June 2012, Boca Raton, FL*
Sensitivity to Change of C-SSRS Severity of Ideation (0-5) and SSI

Treatment of Adolescent Suicide Attempters (TASA)

Visit Week

C-SSRS Severity

SSI Total (Current)

N = 124

Conclusions

• The C-SSRS Severity of Ideation has been shown to be sensitive to changes in ideation for adolescent suicide attempters.
Conclusions

• Both C-SSRS/eC-SSRS demonstrate convergent and predictive validity in clinical trial research.

• Suicide behavior risk increases with each increase of level of severity (1-5) of lifetime suicidal ideation.

• Patients with lifetime suicidal ideation with intent to act were ~20 times more likely to report suicidal behavior during the trial.

• C-SSRS Severity subscale, specifically lifetime suicidal ideation with intent to act, is a strong predictor of suicidal behavior during the trial and is an indication for further clinical evaluation.
• Psychometric properties of the C-SSRS need to be further studied:
  – for predicting suicide
  – over briefer time intervals using ecological momentary assessment technologies
  – for cultural and contextual factors that may influence the reporting of ideation
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http://www.cssrs.columbia.edu

All collaborators have a financial interest in the C-SSRS and eC-SSRS
Selection of Assessments and Cases

35,224 All Assessments

217 (0.6%) Excluded
- 201 uncompleted assessments
- 10 programming error of eC-SSRS algorithm
- 6 fibromyalgia records

6,308 Baseline Assessments

28,669 Follow-up Assessments

3,778 Cases

Mundt et al., ISCTM, October 3, 2011, Amelia Island, FL.
eC-SSRS Administration

- For all eC-SSRS assessments
  - Responded to an average of 10.3 (SD = 4.8) queries
  - Mean completion time was 3.8 (SD = 1.9) minutes
- Mean # Follow-up Questions
  - Positive Reports: 22.7 (SD = 5.8)
  - Negative Reports: 9.4 (SD = 3.4), p.<.001
- Mean Time Required to Complete Report (minutes)
  - Positive Reports: 7.7 (SD = 2.7)
  - Negative Reports 3.5 (SD = 1.5), p.< .001
- Completion rate 99.89%

Mundt et al., ISCTM, October 3, 2011, Amelia Island, FL.
Severity of Suicidal Ideation by Type of Assessment

Mundt et al., 2013, unpublished data
Classification of Cases for Lifetime Suicidal Ideation and Behavior

POSITIVE CASE

Lifetime suicidal ideation
With intent to act
(severity of 4 or 5)

Or suicide attempt

Or aborted attempt

Or interrupted attempt

Or behavior preparatory for making an attempt.

n = 3,778

26%

NEGATIVE CASE

NO lifetime suicidal ideation with intent to act

Or suicide attempt

Or aborted attempt

Or interrupted attempt

Or behavior preparatory for making an attempt.

Mundt et al., 2013, unpublished data
# Lifetime Suicidal Ideation and Behavior by Diagnosis

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Negative Lifetime</th>
<th>Positive Lifetime</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDD</td>
<td>3890 (71.6 %)</td>
<td>1541 (28.4 %)</td>
</tr>
<tr>
<td>PTSD</td>
<td>177 (60.0 %)</td>
<td>118 (40.0 %)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>348 (95.3 %)</td>
<td>17 (4.7 %)</td>
</tr>
<tr>
<td>Epilepsy</td>
<td>167 (77.0 %)</td>
<td>50 (23.0 %)</td>
</tr>
<tr>
<td>Complete data set</td>
<td>4582 (72.6 %)</td>
<td>1726 (27.4 %)</td>
</tr>
</tbody>
</table>

Mundt et al., 2013, unpublished data
C-SSRS Intensity of Ideation Subscale

• 5-point ordinal scale: frequency, duration, controllability, deterrents, and reason for ideation.

• Moderately correlated with the SSI (worst-point) in TASA study ($r=0.56$, $p<0.001$; $N=487$) and modestly correlated in the ED study ($r=0.34$, $p<0.001$; $N=193$).

• Moderately to strongly correlated with BDI suicide item ($r=0.51$, $p<0.001$; effect size=1.19) and MADRS suicidal ideation item ($r=0.69$, $p<0.001$; effect size=1.93) in TASA study. Modestly correlated with SSI ($r=0.34$, $p<0.001$; $N=193$) in ED study.

• Internal consistency reliability was high (Cronbach’s alphas 0.937 to 0.946) in TASA study and moderate (Cronbach’s alpha of 0.73) in ED study.

Lifetime Suicidal Ideation
Severity by Intensity of Ideation

• Generally, the eC-SSRS intensity of suicidal ideation increases as a function of the severity of the eC-SSRS suicidal classification levels.

• Pearson’s correlations
  – .77 for participants with no lifetime ideation
  – .31 for participants with lifetime ideation

Mundt et al., 2013, unpublished data