

Columbia-Suicide Severity Rating Scale: Development and Uses

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Statement of Disclosure

- Funding from the FDA to develop and implement the suicidality classification system
- Institution (RFMH) has had research support as part of an effort to help execute the FDA suicidality mandates and requests
- No personal compensation at any time

Co-Investigators....

C-CASA Authors:

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C-SSRS Authors:

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The Problem...

- Field of medicine challenged by lack of conceptual clarity about suicidal behavior and corresponding lack of well-defined terminology
 - In both research and clinical descriptions of suicidal acts
- Variability of terms referring to same behaviors, e.g., threat, gesture. Often negative and based on incorrect notions about seriousness and lethality in methods e.g., manipulative, non-serious

Consequences....

- Negative implications on appropriate management of suicidality and research
 - If suicidal behavior and ideation cannot be properly identified, they cannot be properly understood, managed or treated in any population or diagnosis
- * ***Furthermore, comparison across epidemiological or drug safety data sets is limited, decreasing confidence in rates of suicide attempts***

Consequences...

- Difficulty in interpreting the meaning of suicidal occurrences and hampers precise communication on individual or population basis
 - Occurrences that should be called suicidal may be missed
 - Occurrences may be inappropriately called suicidal
- ***Challenged risk findings and interpretability***

Consequences...

- Difficulty in interpreting the meaning of reported adverse events that occurred in drug trials
 - Adverse Events that should have been called suicidal may have been missed
 - Adverse Events may have been inappropriately classified as suicidal

Challenged risk findings and interpretability

The Need for Consistent Definitions & Data Elements

- “ Research on suicide is plagued by many methodological problems... Definitions lack uniformity,...reporting of suicide is inaccurate...”
Reducing Suicide Institute of Medicine
2002

Alex Crosby, CDC

Examples of The Problem

<u>Original Label</u>	<u>Text</u>
Personality Disorder	10 y.o. male exhibited symptoms of PD of moderate severity and was discontinued, one day later pt. <i>attempted to hang himself w/ a rope</i> after dispute w/ his father. Investigator did not consider this an SAE but rather part of the PD
Accidental Overdose AND Neurosis	The <i>overdose of 6 capsules</i> of study medication was in fact intentional and in response to an argument with the subject's mother.
Medication Error	The patient took 11 tablets impulsively and then went to school...the patient denied that it was a suicide attempt.
Hostility	Age 10: Before his mother's call to the site and again after arguing with his stepfather, <i>he wrapped a cord from the miniblinds around his neck, threatening to kill himself.</i>

More Examples of Difficulties in Adverse Event Labeling

<u>Original Label</u>	<u>Narratives</u>
Emotional Lab./ Suicide Attempt	The patient is reported to have engaged in an episode of "automutilation" where she slapped herself in the face.
Suicide Attempt	Pt. had thoughts of killing self but had no intention of acting on them
Abdominal hernia	41-year old Caucasian male experienced a mild abdominal hernia that led to hospitalization and surgery 1 week later and the patient recovered. The patient experienced eventration after a laparotomy due to an abdominal wound caused by a self-inflicted gun shot .
Trauma	The patient made an attempt to stab himself in the abdomen on day 49 which resulted in minor injury only. This was not considered a true suicide attempt by the investigator and no action was taken...Hence it was not considered to be clinically significant
Suicide Attempt	Hitting his head on the wall... The patient explained it is like my thoughts are about to explode.

**** Note severity goes both ways- labels more severe than¹⁰ they should be as well as less severe than warranted****

“Completed Suicide”

- “...The patient, involved in the federal witness protection program for having testified against mobsters, died by apparent suicide. He made a call to a lawyer and said ‘please help, I’m going to die’. According to primary care physician and Investigator, the patient did not exhibit any signs of depression. There was no sign of despondency or hopelessness. The autopsy report stated the following: ‘cause of death: intra-oral gunshot wound of the head; how injury occurred: shot self; manner of death: suicide’...”

Reason to question labels!

How to Address this Problem?

- Columbia commissioned by FDA
- A common set of guidelines needed to be applied
- Data needed to be examined consistently
- Developed the research supported Columbia-Classification Algorithm for Suicide Assessment (C-CASA¹)
 - Mandated to be used in all antidepressant and anticonvulsant trials as well as other CNS agents, nonpsychotropic drug classes, including cannabinoid 1 receptor (CB1R) inverse agonists, montelukast sodium (Singulair)

¹ Posner et al. American Journal of Psychiatry. 2007;167:1035-1043.₂

Or Else.....

- Critically important to answer question in a careful, thoughtful manner
- Erring in either direction would have adverse consequences:
 - Missing a signal of increased risk of suicidality would result in greater comfort than is warranted in the safety of these drugs
 - “False Signal” A premature decision on the strength of the signal could result in the overly conservative use of these drugs, or their lack of availability entirely for the entire population.

Laughren/FDA

“Drug report barred by FDA

Scientist links antidepressants to suicide in kids”

SF Chronicle 02.01.04

“Expert Kept From Speaking At Antidepressant Hearing”

NY Times 4.16.04

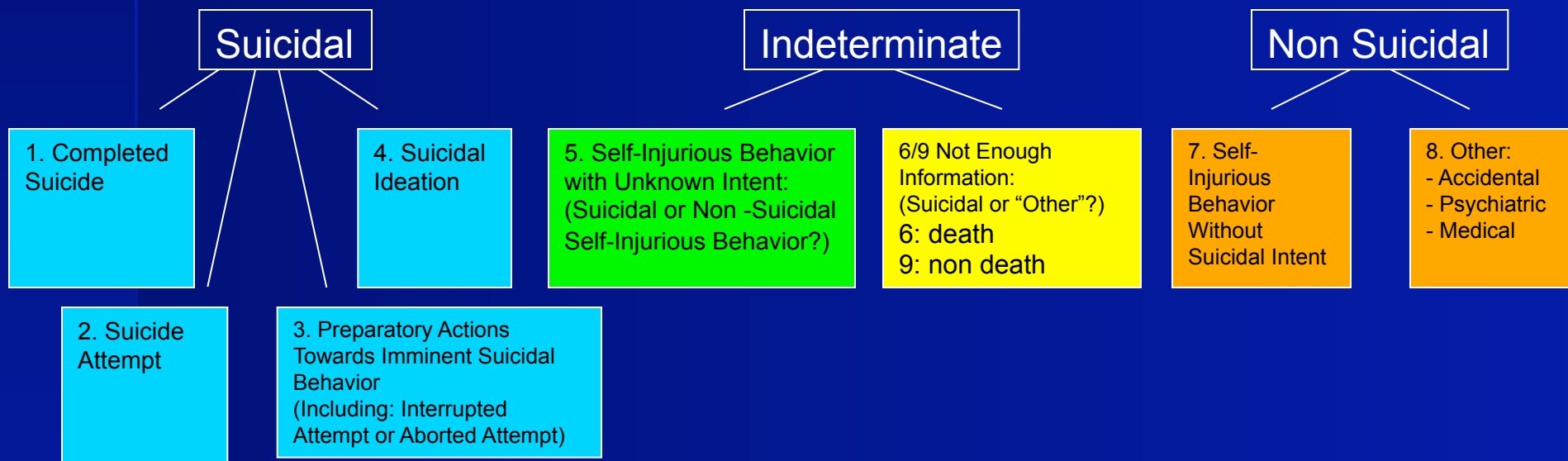
- Press claimed reports were being hidden however, the initial analysis completed by Dr. Mosholder (“FDA Scientist”) was completed with pharmaceutical company rated adverse events e.g. “slap in the face”
- No consistent definitions of suicidal events were used between companies
- Hence, these analyses were considered to be unreliable.
- Findings warranted further examination (e.g., Prozac, Zoloft, Effexor)

C-CASA: How were Suicidal Adverse Events Classified?

Electronic text string search of database for these events

- Search of preferred terms for the following 2 text strings: "suic" or "overdos" "attempt; cut; gas; hang; hung; jump; mutilat; overdos; self damag; self harm; self inflict; self injur; shoot; slash; suic"
- Permitted exclusions for events that represented obvious false positives (e.g., "gas" in "gastrointestinal")
- All accidental injuries, serious adverse events and deaths
- Companies constructed narratives of events according to FDA/C-CASA guidelines and sent them to the Columbia group.

What is the Classification Scheme (C-CASA)?



Blue boxes = FDA "primary analysis" (includes events deemed suicidal).
Blue + green boxes = FDA "sensitivity analysis" (includes any event that could possibly be suicidal).

C-CASA Key Findings

- From Previous FDA Safety Analyses (Pediatric Antidepressants)
 - Excellent reliability (median ICC=.86)
 - FDA Audit C-CASA “robust and reproducible” excellent transportability.
 - This FDA safety analysis using C-CASA comprised 1/3 different events than earlier analysis relying on pharmaceutical labels (substantial turnover)

Misclassification can lead to over estimation of risk

- More suicidal events overall, but fewer events were labeled suicidal attempts - **50% reduction in attempts** (Posner et al 2007)
- Safety analysis using C-CASA (Hammad et al. 2006) had more precise estimate of risk (tighter confidence interval) compared to a prior analysis relying on an sponsor ratings (Mosholder, 2004).
- This is consistent with previous findings that misclassification leads to overestimation of true risk (Jurek et al. 2005).

C-CASA Singulair: 1/13/09 FDA Update

Company	Merck		Astra Zeneca		Cornerstone Therapeutics	
Medication	Montelukast		Cornerstone Therapeutics		Zileuton	
# Placebo Cntrl'd Trials	41		45		11	
	Active	Placebo	Active	Placebo	Active	Placebo
# Px	9929	7780	7540	4659	1745	1063
Suicidal Ideation Events	1	0	0	1	0	0
Suicidal Behaviors	0	0	0	1	0	0
Completed Suicides	0	0	0	0	0	0
Total	1 (0.01%)	0	0	2 (0.04%)	0	0

Limitations of the Data: *Lessons Learned*

- Studies not designed to assess suicidality
- Association does not mean causality
- Alternative Explanation to Causal Link - Ascertainment Bias
 - Spontaneously generated not systematically elicited
 - Med subjects potentially have more contact with provider consequent to the more common occurrence of physical side effects. (more face-to-face time to hear about suicidal incidents)
 - Possibly accounts for differential rates among subjects receiving drug versus placebo in any safety analysis

Systematic vs. Spontaneous Data: Different Results

- In pediatric antidepressant safety analysis systematically collected data (suicide items from HAM-D, CDRS-R, MADRS, and K-SADS) did not confirm the risk shown by the adverse event data.
 - Worsening: Increase in the suicidality item(s) score of pertinent depression questionnaires relative to baseline, regardless of subsequent change
 - Emergence: Same concept as above, but with normal baseline score
- In Treatment for Adolescents with Depression Study (TADS), C-CASA utilized
 - Systematic assessment (SIQ Jr) did not confirm risk

Many other subsequent analyses show same thing.....

- Large data sets from sponsors, item data shows no risk
- Always same direction, if AE shows nothing, item data shows improvement of suicidality
- 5 year pediatric SSRI (Escitalopram) study using C-SSRS

MSNBC Article 5.7.2008

- "We know that whether or not these drugs actually cause suicidal thought or action is ***a question we have to answer***, but up until now, none of the clinical trials for the drugs were set up to address the question," says Posner. "Either way we have to get the right answers. It's critical to know about drugs that pose risk, but ***debunking false notions of risk is equally important to the public health***."
- "...the FDA hopes that by using Posner's methods, they may be able to find categories of people who might be at risk for suicide on a particular drug... and in whom it can safely be prescribed" says T. Laughren.

C-SSRS Findings: Prospective Adolescent Depression Trial

Number of Pediatric MDD Patients with Increase in Suicidal Ideation and Behavior During Trial by Treatment Group

- 8-Week Trial (N enrolled = 312, N completed = 259)

	Placebo	Active Drug
Suicidal Ideation	13 (10.2%)	12 (9.2%)
Suicide Behavior	3 (2.5%)	2 (1.5%)

- No significant difference between treatment groups.

Emslie et al. AACAP 2008

C-SSRS Findings: Obesity Trial

Comparison of Retrospective and Prospective Data

Trial Phase ²	Retrospective C-CASA ¹ Double-blind	Prospective C-SSRS Extension
Number of Patients ³	8600	~ 5600
Suicidal Ideation	452	12*
Suicidal Behavior	6	4

¹ Stemmed from positive responses on PHQ-9

² Double-blind phase ranged from 12 to 104 weeks; Extension phase was 52 weeks

³ Maximum number of patients entering the extension phase of the trials

* Markedly lower rates of suicidality with systematic monitoring

Columbia-Suicide Severity Rating Scale (C-SSRS)

Posner, K.; Brent, D.; Lucas, C.; Gould, M.; Stanley, B.; Brown, G.; Fisher, P.; Zelazny, J.; Burke, A.; Oquendo, M.; Mann, J.

- Systematic administration of tool designed to track suicidal events and change across a treatment trial
 - In context of multi-site NIMH trial (Treatment of Adolescent Suicide Attempter Study),
 - In response to need for a measure of suicidality severity and change
- **"Prospective counterpart"** of the FDA-commissioned system (indicated in C-CASA article, Posner et al, 2007); C-CASA is retrospective C-SSRS
- Way to get better safety monitoring and avoid inconclusive results
- This is why FDA and other regulatory authorities are often recommending or asking for C-SSRS in ongoing or future studies.

Columbia-Suicide Severity Rating Scale (C-SSRS)

Posner, K.; Brent, D.; Lucas, C.; Gould, M.; Stanley, B.; Brown, G.; Fisher, P.; Zelazny, J.; Burke, A.; Oquendo, M.; Mann, J.

- Developed by leading experts/collaboration with Beck's group U Penn and U Pittsburg/evidence-based
- Feasible, low- burden (typical admin time a few minutes)
- Ages 6 – elderly
- Uniquely assesses *both* behavior and ideation (full range)
- Addresses need for a summary measure of suicidality
- *Comprehensive measure that includes only the most necessary suicidality characteristics (low-burden), i.e., the most essential, evidence-based items needed in a thorough assessment*

Simply.....

- 1-5 rating for suicidal ideation, of increasing severity (from a wish to die to an active thought of killing oneself with plan and intent)
 - Can be two questions;
 - *Have you wished you were dead or wished you could go to sleep and not wake up?*
 - *Have you actually had any thoughts of killing yourself?*

If answer is "No" to both, No more questions on ideation

- There are four behaviors assessed, few questions required
 - Provides definitions and questions to figure out how to classify behaviors

Improved Ascertainment....

Definitions are Important

- All items include **definitions** for each term and **standardized questions for each category** are included to guide the interviewer for facilitating improved identification
 - Behavioral definitions from Columbia Suicide History Form (Oquendo, 2002)
 - Ideation definitions from NIMH Brown, Conwell, Posner, Burke Ideation Project

Additional Features Assessed

- Lethality of Attempts; Compilation of Beck Medical Lethality Rating Scale
- Other Features of Ideation: Intensity
 - Frequency
 - Duration
 - Controllability
 - Reasons for Ideation
 - Deterrents

****All these items significantly predictive of completed suicide (on SSI)/minimum amount of info needed for tracking and severity***

C-SSRS Format and Administration

- Allows for utilization of *multiple sources* of information
 - Any source of information that gets you the most clinically meaningful response (subject, family members, records)
- Semi-structured – flexible format
 - Questions are provided as helpful tools – it's not required to ask any or all questions - just enough to get the appropriate answer
 - Most important: gather enough clinical information to determine whether something should be called suicidal

Suicide Attempt Definition

A self-injurious act committed with at least some intent to die, as a result of the act

- There does not have to be any injury or harm, just the *potential* for injury or harm (e.g., gun failing to fire)
- Any “non-zero” intent to die – Does not have to be 100%
- Intent and behavior must be linked
- Intent can sometimes be inferred clinically from the behavior or circumstances
 - If denies intent to die, but thought that what they did could be lethal
 - “Clinically impressive” circumstances - highly lethal act where no other intent but suicide can be inferred (e.g., gunshot to head, taking 200 pills)

Suicide Attempt? Yes or No

1. The patient wanted to escape from her mother's home. She researched lethal doses of ibuprofen. She took 6 ibuprofen pills and said she felt certain from her research that this amount was not enough to kill her. She stated she did not want to die, only to escape from her mother's home. She was taken to the emergency room where her stomach was pumped and she was admitted to a psychiatric ward. _____
2. Young woman, following a fight with her boyfriend, felt like she wanted to die, impulsively took a kitchen knife and made a superficial scratch to her wrist; before she actually punctured the skin or bled, however, she changed her mind and stopped. _____
3. Patient was feeling ignored. She went into the family kitchen where mother and sister were talking. She took a knife out of the drawer and made a cut on her arm. She denied that she wanted to die at all ("not even a little") but just wanted them to pay attention to her. _____
4. The patient cut her wrists after an argument with her boyfriend. _____
5. Had a big fight with her ex-husband about her stepson. Took 15-20 imipramine tablets and went to bed. Slept all night and until 4-5 pm the next day. States she couldn't stand up or walk. Called EMS – taken to the ER – drank charcoal and admitted to hospital. Unable to verbalize clear intent, but states she was well aware of the dangers of TCA overdose and the potential for death. _____

Suicidal Behavior

SUICIDAL BEHAVIOR <i>(Check all that apply, so long as these are separate events; must ask about all types)</i>	Since Last Visit												
<p>Actual Attempt: A potentially self-injurious act committed with at least some wish to die, <i>as a result of act</i>. Behavior was in part thought of as method to kill oneself. Intent does not have to be 100%. If there is <i>any</i> intent/desire to die associated with the act, then it can be considered an actual suicide attempt. <i>There does not have to be any injury or harm</i>, just the potential for injury or harm. If person pulls trigger while gun is in mouth but gun is broken so no injury results, this is considered an attempt. Inferring Intent: Even if an individual denies intent/wish to die, it may be inferred clinically from the behavior or circumstances. For example, a highly lethal act that is clearly not an accident so no other intent but suicide can be inferred (e.g. gunshot to head, jumping from window of a high floor/story). Also, if someone denies intent to die, but they thought that what they did could be lethal, intent may be inferred.</p> <p><i>Have you made a suicide attempt?</i> <i>Have you done anything to harm yourself?</i> <i>Have you done anything dangerous where you could have died?</i> What did you do? Did you _____ as a way to end your life? Did you want to die (even a little) when you _____? Were you trying to end your life when you _____? Or did you think it was possible you could have died from _____? Or did you do it purely for other reasons / without ANY intention of killing yourself (like to relieve stress, feel better, get sympathy, or get something else to happen)? (Self-Injurious Behavior without suicidal intent) If yes, describe:</p> <p>Has subject engaged in Non-Suicidal Self-Injurious Behavior?</p>	<table border="0"> <tr> <td>Yes</td> <td>No</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> </tr> <tr> <td colspan="2" style="text-align: center;">Total # of Attempts</td> </tr> <tr> <td colspan="2" style="text-align: center;">_____</td> </tr> <tr> <td>Yes</td> <td>No</td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	Yes	No	<input type="checkbox"/>	<input checked="" type="checkbox"/>	Total # of Attempts		_____		Yes	No	<input checked="" type="checkbox"/>	<input type="checkbox"/>
Yes	No												
<input type="checkbox"/>	<input checked="" type="checkbox"/>												
Total # of Attempts													

Yes	No												
<input checked="" type="checkbox"/>	<input type="checkbox"/>												

May help to infer intent

Important: Shows you did the appropriate assessment and decided it should not be called suicidal

Various Uses of C-SSRS Within a Study

- Treatment benefit outcomes
- Safety outcomes
- Clinical safety monitoring
- Coordinated efficiently with other measures
- Epidemiological
- Easily coupled with inclusion/exclusion
 - In past exclusion arbitrary e.g. “serious risk”??
(criteria can be operationalized and assessed by C-SSRS
e.g. past attempt ever -early phases; recent attempt-later phase;
current ideation (intent or plan)
 - Inclusion/exclusion varies/allows you to assess variables

Advantages and Uses....Clinical Safety Monitoring and Management

- Improved Documentation
 - Training on the scale can improve investigators approach to AEs as a whole and documentation of them
- Specify parameters for triggering referrals to mental health professionals
 - Eg., 4 of 5 on ideation item to indicate need for immediate referral
 - Decreases unnecessary referrals, exclusion, and burden – very important for non-psychiatric trials

One Example: FDA Document, How C-SSRS Is Used

Endocrinology-

- C-SSRS to be administered at baseline, then at each visit throughout the duration of the trial
- Baseline:
 - A subject should be excluded from the trial if he/she has any suicidal ideation of type 4 or 5 on the C-SSRS in the last month
- During Study Conduct:
 - A subject should be referred to a Mental Health Professional (MHP) if he/she has any suicidal ideation of type 4 or 5 on the C-SSRS

**See later slides for more details*

Assessment Periods/Time Frames

Flexible, amenable to study or clinical need

- Baseline/lifetime history
- Screening: Recent/Last Week/Past Month/6 months
- Since last assessment (whatever time period that may be)

“Already- Enrolled Subjects” Version

- Some good data better than no good data
- 2 Baseline Periods
 - Prior to Study Entry (lifetime)
 - Study Start to first C-SSRS administration

Baseline Information and Improved Adverse Event Determinations

- Comprehensive baseline history
- Necessary to better determine if adverse event is related to intervention (“new or different”)
 - Investigators asked to make judgments re relationship to treatment
 - If have an event and had something similar prior to study start speaks to relationship to tx or lack thereof

Constellation of Neuropsychiatric Sequelae

- What do we actually need to assess and how?
- Is paired with other psychiatric measures
- Example of “package” to assess key sxS: suicidality, depression, anxiety
 - Depression (e.g., PHQ-9)
 - Anxiety (e.g., GAD-7)
 - Suicidality (C-SSRS)

Baseline:

- A subject should be excluded from the trial if he/she has:
 - A baseline PHQ-9 score of ≥ 15
 - Any suicidal behavior in the last month
 - Any suicidal ideation of type 4 or 5 on the C-SSRS in the last month
 - Type 4 indicates Active Suicidal Ideation with Some Intent to Act, Without Specific Plan
 - Type 5 indicates Active Suicidal Ideation with Specific Plan and Intent
- The GAD-7 score at baseline need not be the basis for exclusion from a trial

Guidance: During Study Conduct

(research-supported cut-points; Williams et al.)

- A subject should be referred to a Mental Health Professional (MHP) if he/she has:
 - A PHQ-9 score ≥ 10
 - A GAD-7 score ≥ 10
 - Any suicidal behavior
 - Any suicidal ideation of type 4 or 5 on the C-SSRS
- A referral to a MHP should also be made if in the opinion of the Investigator it is necessary for the safety of the patient
- If a subject's psychiatric disorder can be adequately treated with psycho- and/or pharmacotherapy, then the patient, at the discretion of the MHP, should be continued in the trial

Why item data isn't sufficient (e.g., HAM-D, PHQ-9, and MADRS)

HAM-D

3. Suicide

0= Absent

1= **Feels life is not worth living**

2= Wishes he were dead or any thoughts
of possible death to self

3= Suicidal ideas or gestures

4= Attempts at suicide (any serious attempt rates 4)

PHQ-9

Thoughts that you would be **better off dead**
or of **hurting yourself** in some way

MADRS

10. Suicidal Thoughts

Representing the feeling that life is not worth living, that a natural death would be welcome, suicidal thoughts, and preparations for suicide. Suicide attempts should not in themselves influence the rating.

0 = Enjoys life or takes it as it comes.

2 = **Weary of life.** Only fleeting suicidal thoughts.

4 = **Probably better off dead.** Suicidal thoughts are common, and suicide is considered as a possible solution, but without specific plans or intention.

6 = Explicit plans for suicide when there is an opportunity. Active preparations for suicide.

Data confirms that when item followed by C-SSRS, eliminate cases that should not have been called suicidal

Can reduce false positives

Feasibility

Iatrogenic

- Asking about suicidality doesn't cause distress or suicidality (Gould et al., JAMA 2005)

■ Feasibility

- Investigators
- Subjects- no withdrawal

■ Who can administer the C-SSRS?

- Need to be trained
- Do not have to be a Mental Health Professional to administer this scale; thousands of health professionals have been trained
- Examples: Any type of physician, psychologist, clinical social worker, mental health counselor, nurse, coordinator

C-SSRS in Clinical Trials- Trials

- Trials in Phases I-IV
- Few thousand sites internationally, psychiatry and non-psychiatry
- Over 90 different languages for all versions
- Drug/placebo; active controls; open maintenance
- Range of interventions: pharmacologic, device, psychotherapy, ECT

Training and Implementation

- Administration Training
 - Approximately 20-30 minutes
 - Trained thousands of health practitioners across world via webex, phone, etc
 - Training DVD for the IM training and supplemental and rater turnover
 - Interactive training tool in development
 - Higher level “Train the Trainer” program
- Various Modalities
 - Paper
 - Centralized Raters
 - Phone
 - Self-report version/IVR

How Do We Think About These Outcomes?

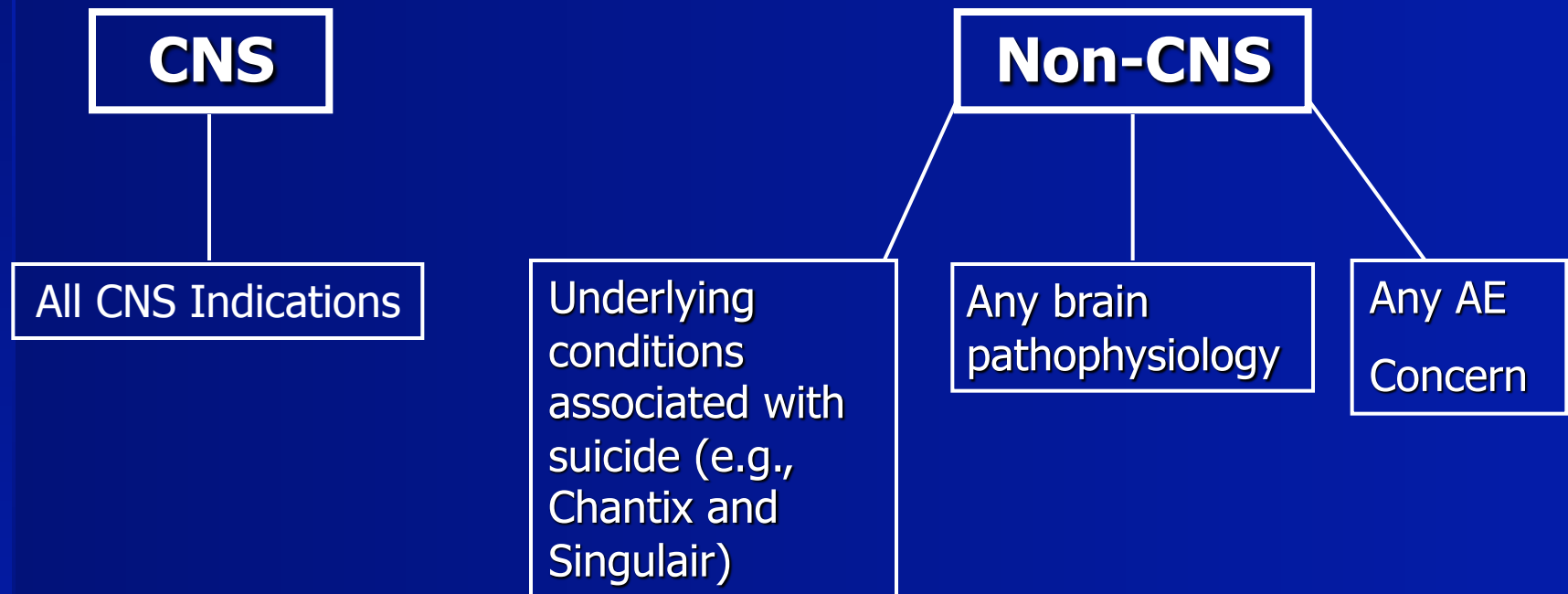
- Association with underlying condition (shouldn't vary across groups)
- A suicidality instrument for RCTs primarily needs to systematically collect info to determine if an occurrence meets criteria for a nosological category; it is not to predict future behavior or characterize state/trait
- To provide between group differences
- Also has risk assessment features

Tailored for Population Specific Data Collection

- For Example - Huntington's Disease, Bereavement, Epilepsy, Suicide Clusters

SUICIDAL IDEATION					
<i>Ask questions 1 and 2. If both are negative, proceed to "Suicidal Behavior" section. If the answer to question 2 is "yes," ask questions 3, 4 and 5. If the answer to question 1 and/or 2 is "yes", complete "Intensity of Ideation" section below.</i>		Since Last Visit	Postical		
1. Wish to be Dead Subject endorses thoughts about a wish to be dead or not alive anymore, or wish to fall asleep and not wake up. <i>Have you wished you were dead or wished you could go to sleep and not wake up?</i> If yes, describe:		Yes <input type="checkbox"/>	No <input type="checkbox"/>	Yes <input type="checkbox"/>	No <input type="checkbox"/>
2. Non-Specific Active Suicidal Thoughts General non-specific thoughts of wanting to end one's life/commit suicide (e.g. "I've thought about killing myself") without thoughts of ways to kill oneself/associated methods, intent, or plan during the assessment period. <i>Have you actually had any thoughts of killing yourself?</i> If yes, describe:		Yes <input type="checkbox"/>	No <input type="checkbox"/>	Yes <input type="checkbox"/>	No <input type="checkbox"/>
3. Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act Subject endorses thoughts of suicide and has thought of at least one method during the assessment period. This is different than a specific plan with time, place or method details worked out (e.g. thought of method to kill self but not a specific plan). Includes person who would say, "I thought about taking an overdose but I never made a specific plan as to when, where or how I would actually do it.....and I would never go through with it". <i>Have you been thinking about how you might do this?</i> If yes, describe:		Yes <input type="checkbox"/>	No <input type="checkbox"/>	Yes <input type="checkbox"/>	No <input type="checkbox"/>

What drugs should be prospectively evaluated?



C-SSRS used in Government, Industry, & Foundation sponsored intervention studies

Psychiatric

- MDD
- Major Depressive Episode Associated with Bipolar I Disorder
- Refractory Depression
- Bipolar
- GAD
- OCD
- ADHD (w/ and w/o Dyslexia)
- Schizophrenia
- Personality Disorders
- Alcohol Dependence
- Bereavement
- Tardive dyskinesia
- Tourette's
- Psychedelic drug therapy

**Basically All Psychiatric Disorders*

Non-Psychiatric

- Healthy Volunteers
- Overweight patients
- Obesity
- Diabetes
- Interstitial Cystitis/ Painful Bladder Syndrome
- Eczema
- Smoking Cessation (w/ and w/o Schizophrenia/Schizo Affective Disorder)
- Cancer Survivors
- Insomnia
- Cardiovascular Disease
- Non-alcoholic Steatohepatitis
- Overweight with Type 2 Diabetes
- Group Intervention for OEF/OIF TBI Survivors and Families
- Metabolic disorders
- Traumatic Brain Injury
- Alzheimer's
- Dementia
- Huntington Study Group
- Fibromyalgia
- Epilepsy
- Epileptic patients with renal impairment
- Chronic Headaches
- Neuropathic Pain due to Multiple Sclerosis
- Diabetic Peripheral Neuropathic Pain
- Peripheral Naturopathic pain
- Osteoarthritis pain
- Lower Back Pain
- Restless Leg Syndrome

What we are seeing.....

- MDD: adults approx. 10%
- GAD: 3%
- Non-alcoholic Chronic Liver disease: < 1%
(liver disease associated with depression & suicidality; no referrals triggered)
- ADHD: ages 6-12, 0% ideations & behaviors
- Cardiovascular: 1-2% (no referrals triggered)
- Obesity: <1% (no referrals triggered)
- Obesity with Depressed Patients: 1.25%
ideation or behavior

C-SSRS Data from Blinded GAD Trial

Lifetime History of Suicidal Ideation and Behavior Obtained at Baseline and Incidence Rates During Trial

C-SSRS Item	Lifetime (N=908)	During Trial (N=908)
<i>Ideation</i>		
Wish To Be Dead	113	
Non-Specific Active Thoughts	49	
Active Thoughts Without Intent To Act	23	3%
Active Thoughts With Some Intent—No Plan	15	
Active Thoughts With Plan And Intent	11	
<i>Behavior</i>		
Actual Attempt	33	0
Total Number of Attempts	40	0
Interrupted Attempt	4	0
Aborted Attempt	8	0
Preparatory Acts Or Behavior	9	0
Suicidal Behavior	13	0
Subjects with One or More Positive Responses on C-SSRS	12.4% (N=113)	3%

C-SSRS Findings: Prospective MDD Clinical Trial (N=376)

C-SSRS Item	Total Events/Subjects	%
<i>Ideation (N Events)</i>		
(1) Wish To Be Dead	322	86%
(2) Non-Specific Active Thoughts	55	15 %
(3) Active Thoughts Without Intent To Act	35	9 %
(4) Active Thoughts With Some Intent—No Plan	3	1 %
(5) Active Thoughts with Plan and Intent	4	1 %
<i>Behavior (N Events)</i>		
Preparatory Acts or Behavior	1	<1%
Interrupted Attempt	1	<1%
Aborted Attempt	1	<1%
Actual Attempt	1	<1%
N Subjects with >=1 Positive Ideations	163	43%
N Subjects with >=1 Positive Behaviors	4	1%

Canada, Belgium, Bulgaria, Estonia, Finland, France, Germany, Poland, Slovakia, Australia, India, South Africa

Baseline from Fibromyalgia Trial

- Based on 496 patients
- Wish to be dead - 8.67%
- Suicidal Thoughts - 4.23 %
- Ideation w/out Intent - 3.23%
- Ideation w/out plan - 2.22%
- Ideation plan intent - 2.42%
- Actual Baseline - 0%
- Nonsuicidal baseline - 0.4%
- Interrupted baseline - 0%
- Aborted baseline - 0%
- Prep acts baseline - 0.4%
- Behavior present
 baseline period- 1.41%
- Completed suicide – 0%

Total: 22.98%

Fibromyalgia Trial

- Based on 1888 CSSRS forms
- Wish to be dead - 0.64%
- Suicidal Thoughts - 0.21 %
- Ideation w/out Intent - 0.16%
- Ideation w/out plan - 0.11%
- Ideation plan intent - 0.05%
- Actual Baseline - 0%
- Nonsuicidal baseline - 0%
- Interuupted baseline - 0%
- Aborted baseline - 0%
- Prep acts baseline - 0%
- Behavior present
- baseline period- 0.05%
- Completed suicide - 0%

Total: 1.22%

Events During Pain Trial

■ Wish to be dead -	0.72%
Suicidal Thoughts -	0.34%
Ideation w/out Intent -	0.12%
Ideation w/out plan -	0.06%
Ideation plan intent -	0.03%
Actual -	0%
Nonsuicidal -	0%
Interuupted -	0%
Aborted -	0%
Prep acts -	0%
Behavior -	0.03%
Completed suicide -	0%

C-SSRS Requests/Uses

- World Health Organization-Europe: *100 Best Practices for Adolescent Suicide Prevention*
- AMA Best Practices Adolescent Suicide
- U.S. Army
- Health Canada
- A county-wide Suicide cluster in New York
- Japanese National Institute of Mental Health and Neurology
- Israeli National Suicide Prevention Program
- Korean Association for Suicide Prevention
- Planned statewide dissemination in Victoria, Australia – Health and Law Enforcement agencies
- National multi-site clinical trials [e.g., Preschoolers with Attention-Deficit/Hyperactivity Treatment Study (PATS)]
- Drug and Alcohol Addiction Centers
- National Institute on Alcohol Abuse and Alcoholism: NIAAA
- Commissioned by VA to do online training for clinical trials
- Center of Excellence for Research on Returning War Veterans
- Hospitals and Community Clinic Settings
 - Inpatient and ERs; general medical and psychiatric, Crisis services, Special Needs Clinics, VA's
- Primary care
- Surveillance Efforts; CDC Definitions are Columbia Defns
- AFSP/Developing Centers Registry Project
- NIH-medically ill
- Suicide Section of **SCID**
- Clinical Practice, nationally and internationally
- Schools (Middle Schools, High Schools, and College Campuses)

“F.D.A. Requiring Suicide Studies in Drug Trials ” New York Times 1.24.08

- Most Profound Change in Drug Development Regulation in 16 Years
- “Researchers at Columbia University have developed a questionnaire to help systematically assess suicidal thoughts and behavior. The Food and Drug Administration is now requiring that drug companies adopt the methodology in their clinical trial.”

Correspondence from the EMEA to the London Times

- "European legislation for both clinical trials and marketing authorization of medicines has established clear procedures to report and evaluate any suicidal event. **The use of the Columbia University Questionnaire to systematically assess suicidal thoughts and behaviors has been required for a number of ongoing developments in the context of the EMEA Scientific Advice procedure.** In addition, the issue of suicidality is regularly addressed during pre-authorization evaluation of new medicines (centralized procedure and also referrals in the context of mutual recognition and decentralized authorization procedures), usually at the time of the initial assessment report (Day 80) of the Agency's Committee for Medicinal Product for Human Use (CHMP) and when specific questions are issued to the Applicant at Day 120. **Suicidality may be addressed by reports, as mentioned above, but also during the evaluation of new medicinal products based on: a Central mechanism of action; for example a Central Nervous System active substance like a new anti-epileptic,** a target population, like patients suffering from major depression, bipolar disorder, or frequent concomitant conditions in the target population, like depression/anxiety during smoking cessation.

From New England Psychologist (April 2008)

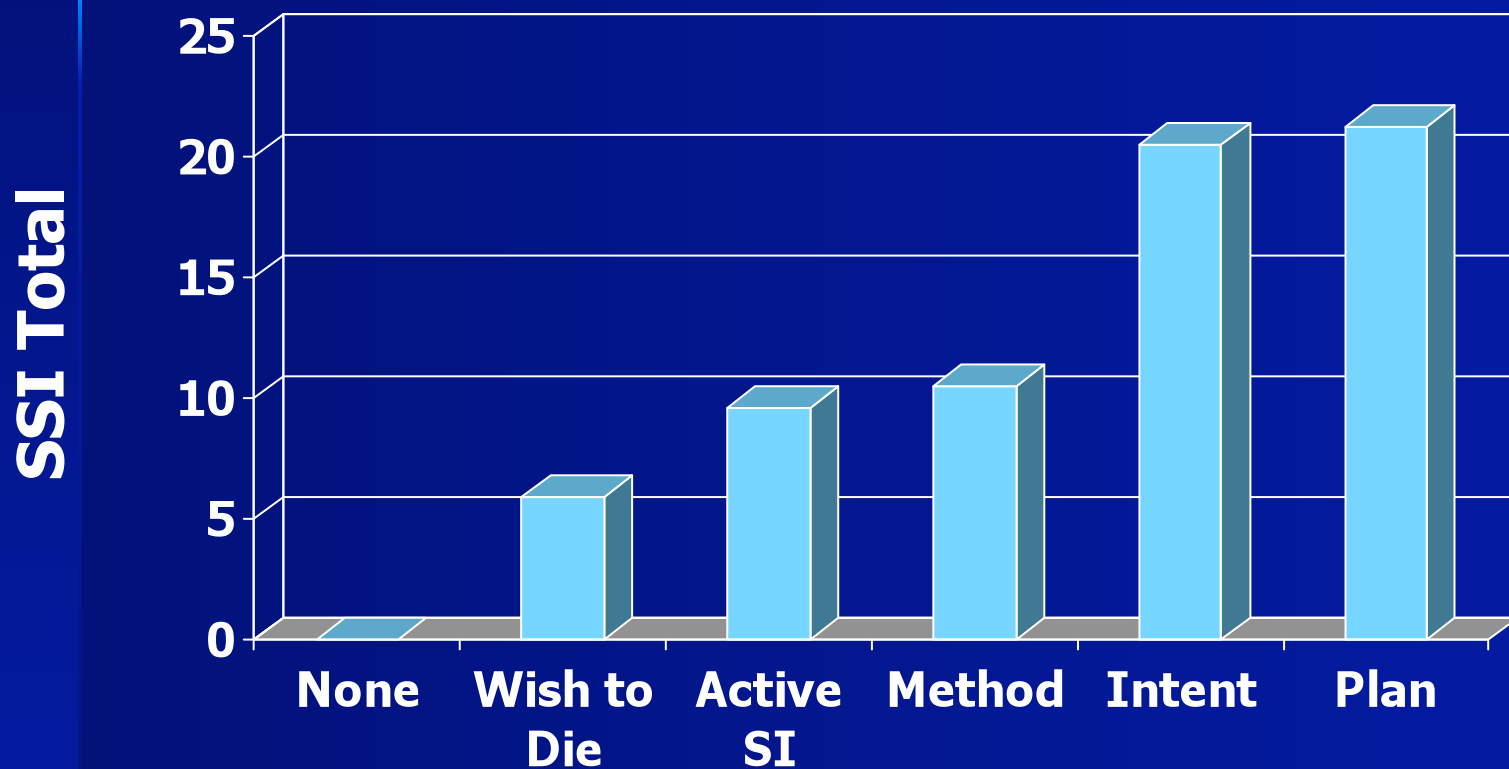
- "We give the scale at every session as part of best practice," Toll says. "We are not predicting that they are suicidal, but if they are, we will attend to it. I'm pleased to say we've not found anyone suicidal."
- Benjamin Toll goes onto say "The community-at-large benefits from this type of screening when its citizens are appropriately and adequately treated"

C-SSRS Psychometric Properties

Reliability and Validity: Adults

- Pilot registry study NIMH Developing Centers and AFSP
- Multi-site trial at 3 psychiatric EDs (N=121)
- **100% sensitivity and 98% specificity** for correctly classifying attempts versus no attempts compared to classifications by hospital staff
- Convergent validity:
 - Severity of ideation ***highly correlated*** with severity of ideation on the SSI ($r=.69, p<.001$)
 - Intensity of Ideation total score moderately correlated with the SSI total score ($r=.55, p<.001$)
 - Actual Lethality score was moderately correlated with the Beck Lethality Scales score ($r=.55, p<.001$)
- Reliability:
 - Moderate internal reliability of the Intensity of Ideation 5-item measure (Cronbach's alpha=.59)

SSI Total Score by Highest Level of Ideation on the C-SSRS



American Foundation
for Suicide Prevention

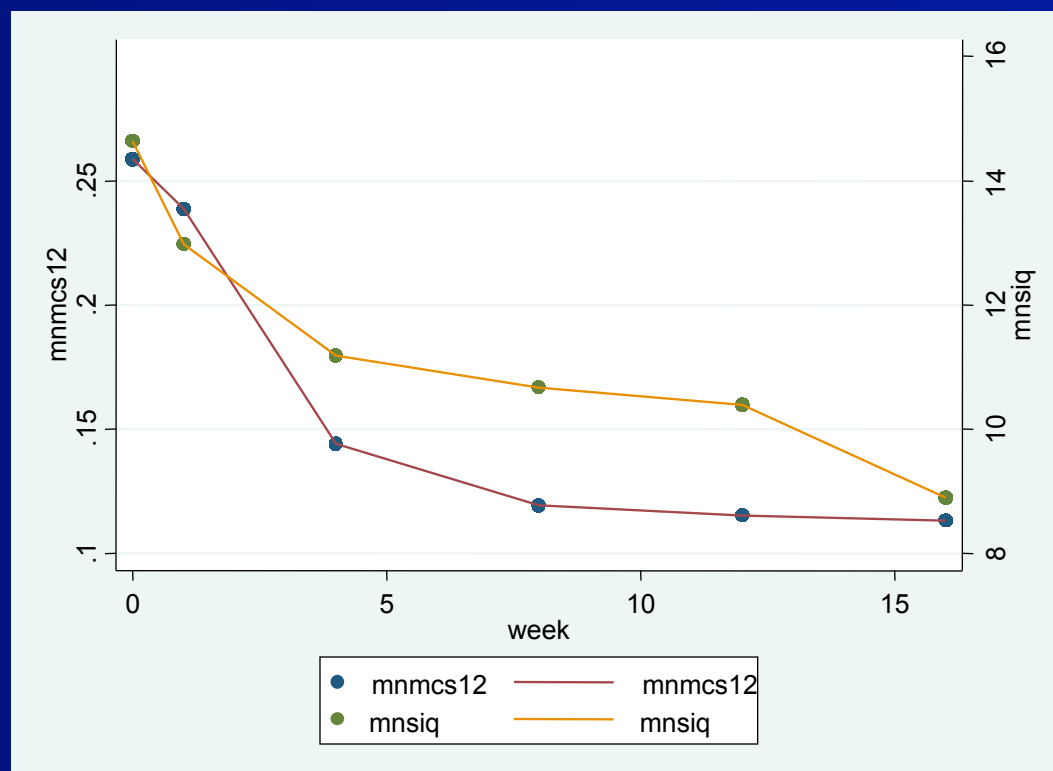
$F(5,185) = 14.35, p < .001$
Currier, Brown & Stanley (2009)

C-SSRS Psychometric Properties: Adolescents – Convergent & Discriminant Validity

- Convergent validity:
 - Strong positive relationship between C-SSRS and SIQ-Jr over time, $p < .001$
 - Baseline C-SSRS suicidal ideation severity item & suicidal ideation intensity scale significantly correlated with SIQ-Jr and CDRS-R suicide item (r 's range from .52 - .57, $p < .001$)
- Discriminant validity:
 - Baseline C-SSRS suicidal severity ideation item NOT correlated with CDRS-R change in appetite item $r = .07$, difficulty sleeping item $r = .06$, fatigue item $r = -.08$, or somatic item $r = -.07$.

C-SSRS Psychometric Properties: Adolescents – Sensitivity to Change

- As the severity of suicidal ideations on the C-SSRS decreased over the trial, the SIQ-Jr scores decreased in a similar pattern, $p < .001$



Sample (n=259) of pediatric patients (ages 12 to 18) in an RCT evaluating escitalopram relative to placebo to treat MDD

C-SSRS Psychometric Properties: Adolescents – Predictive Validity & Reliability

- Predictive validity:
 - Reporting lifetime suicidal ideation on C-SSRS at screening associated with increased chance of reporting **suicidal behavior**, Fisher's exact test $p = .0008$, during the trial.
- Reliability:
 - Internal consistency reliability of intensity of ideation subscale (for lifetime ideation) = .74.

Inter-Rater Reliability

- Treatment of SSRI-Resistant Depression in Adolescents
- N=49
- 100% for Behavior
- 90% for Ideation ($p < .001$)

(Brent, Emslie, Clarke et al. AJP, 2009)

Conclusions

- Intervention trials using prospective and systematic measurement of suicidality would more clearly delineate the relationship between suicidal adverse events and medication treatment.
- Consistent and systematic assessment (e.g. C-SSRS) can provide more meaningful data within a study, as well as across studies, improving pooled analyses
- Improved assessment of suicidal events is necessary to better inform risk benefit analyses.
- ***Decreasing false positives and debunking false notions of risk are as important as knowing about risks that exist***



Columbia-Suicide Severity Rating Scale (C-SSRS)

Posner, K.; Brent, D.; Lucas, C.; Gould, M.; Stanley, B.; Brown, G.; Fisher, P.; Zelazny, J.; Burke, A.; Oquendo, M.; Mann, J.

- Systematic administration of a tool designed (in a NIMH Trial) to track suicidal **events across a treatment trial**
- ***Prospective version*** of the system we developed for the FDA
- Designed to collect better safety monitoring data and avoid inconclusive results
- This is why the FDA and other regulatory authorities are often recommending or asking for C-SSRS in ongoing or future studies

**Different Sources
of Input**

=

**Same Output
(e.g., eC-SSRS)**

SUICIDAL IDEATION		
1. Wish to be Dead	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>
2. Non-Specific Active Suicidal Thoughts	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>
3. Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>
4. Active Suicidal Ideation with Some Intent to Act, without Specific Plan	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>
5. Active Suicidal Ideation with Specific Plan and Intent	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>
INTENSITY OF IDEATION		
Frequency (1-5)		
Duration (1-5)		
Controllability (0-5)		
Deterrents (0-5)		
Reasons for Ideation (0-5)		
SUICIDAL BEHAVIOR (Check all that apply, so long as these are separate events; must ask about all types)		
Completed Suicide	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>
Actual Attempt	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>
	Total # of Attempts: _____	
Interrupted Attempt	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>
	Total # of interrupted: _____	
Aborted Attempt	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>
	Total # of aborted: _____	
Preparatory Acts or Behavior	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>
Any Suicidal Behavior	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>
Non-Suicidal Self-Injurious Behavior	Yes	No
	<input type="checkbox"/>	<input type="checkbox"/>
Answer for Actual Attempts Only (Lethality Section)		Most Lethal Attempt
		Date: / /
Actual Lethality/Medical Damage (0-5)		
Potential Lethality: Only Answer if Actual Lethality=0 (0-2)		

How to Make Sense of the Data

- Most Important/Primary Data
 - Identification of suicidality: Ideation and Behavior
 - Categorical distinctions
- Treatment emergent ideation – need to account for baseline level of ideation
- Important to evaluate changes –worsening &/or improvement in ideations and behaviors
- Secondary Data/Used for Clinical Monitoring/Descriptive
 - Operationalize changes – Severity and intensity of ideations and nature and lethality of behaviors

C-SSRS: Prospective C-CASA

C-CASA

1. Completed Suicide

2. Suicide Attempt

3. Preparatory Actions
Towards Imminent
Suicidal Behavior

4. Suicidal Ideation

7. Non-Suicidal Self-Injurious
Behavior

C-SSRS

Completed Suicide

Actual Attempt

-Interrupted Attempt
-Aborted Attempt
-Preparatory Acts or Behavior

1. Wish to Die
2. Active Suicidal Thought
3. Active Suicidal Thought with
Method
4. Active Suicidal Thought with Intent
5. Active Suicidal Thought with Plan
and Intent

Non-Suicidal Self-Injurious
Behavior

Other Categories Become Obsolete with Prospective data collection

C-CASA

C-SSRS

5. Self-injurious Behavior, Intent Unknown
6. Not Enough Information: Death
9. Not Enough Information: Non-Death



Not Applicable - Unknowns are eliminated with Prospective Data Collection (These C-CASA categories created ONLY to make sense of limitations of retrospective adverse events.)

8. Other (Accident; Psychiatric; Medical)



N/A: No Indication of Suicidal Ideation or Behavior

Clinician Screen Not Adequate

- “Structured Interview May Better Detect Adolescent Suicidality: Simpler 2-Question Screening Approach by Trained Clinicians Falls Short” (Medscape Medical News, 2008)
- Screening method (without a measure) over-detected suicidal ideation & under-detected suicidal acts



Structure and Scaling

- **Screening Questions:** 2 for ideation, 4 for behavior (if answer is no to 2 ideation questions, go to behavior)
- **Approx 17 items**
- **No global score; some categorical and some severity information, specified for behavior and ideation**
 - Categorical-types of ideation and behavior, total # of occurrences
 - Scaling component, several continuous scale variables
 - Lethality
 - intensity
- **Categorical responses do not require narrative description: optional** (training includes how, more important in non-psychiatric areas where it can serve as a QA mechanism; and facilitates AE descriptions)

Blinding of Event Narratives to Avoid Bias

- Received from Company blind to all potential drug identifying information:
 - Drug name
 - Company/sponsor name
 - Patient identification numbers
 - Active or placebo arm
 - *Any and all* medication names and types (e.g. tx with other meds may be associated with a particular antidepressant side effect profile and thus could potentially bias)
 - Primary Diagnosis/Indication of study
- Additional Blinding of potentially biasing information:
 - Original label of event given by investigator or sponsor
 - “serious” or “non-serious” labels

Columbia- Classification Algorithm for Suicide Assessment: Codes

Suicidal

1. Completed Suicide
2. Suicide Attempt
3. Preparatory Actions Towards Imminent Suicidal Behavior
4. Suicidal Ideation

Indeterminate

5. Self-injurious Behavior Intent Unknown
6. Not Enough Information: Death
9. Not Enough Information: Non-Death

Non
Suicidal

7. Self-Injurious Behavior Without Suicidal Intent
8. Other (Accident; Psychiatric; Medical)

Children's Depression Rating Scale

— SUICIDAL IDEATION —

- | | |
|---|---|
| Understands the word <i>suicide</i> , but does not apply the term to himself/herself. | 1 |
| <i>Sharp</i> denial of suicidal thoughts. | 2 |
| Has thoughts about suicide, or of hurting himself/herself (if he/she does not understand the concept of suicide), usually when angry. | 3 |
| | 4 |
| Has recurrent thoughts of suicide. | 5 |
| | 6 |
| Has made a suicide attempt within the last month or is actively suicidal. | 7 |

- Posner K, Oquendo MA, Gould M, Stanley B, Davies M (2007). Columbia Classification Algorithm of Suicide Assessment (C-CASA): Classification of Suicidal Events in the FDA's Pediatric Suicidal Risk Analysis of Antidepressants. *Am J Psychiatry*; 164:1035-1043
- Brent, Emslie, Clarke et al. (2009). Predictors of spontaneous and systematically assessed suicidal adverse events in the Treatment of SSRI-Resistant Depression in Adolescents (TORDIA) study. *American Journal of Psychiatry*, AiA:1-9.
- Brown, G. K., Currier, G., & Stanley, B. (September, 2008). Suicide Attempt Registry Pilot Project. Invited presentation for the National Institute of Mental Health annual meeting of the Developing Centers for Intervention and Prevention of Suicide, Canandaigua, NY.
- Posner, K. (2008) Suicidality Across Drug Indications: Columbia Suicidal Adverse Event Identification and FDA Safety Concerns: The Issues and the Answers, From Outcomes to Feasibility. Invited presentation to the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration, Silver Spring, MD

SUICIDALITY TRACKING SCALE (STS)

(From MINI Tracking, Module C. Copyright Sheehan et al 2006 revision)

RATING INSTRUCTIONS:

1. **Over the past week did you suffer any accident?** NO YES

IF NO, SKIP TO QUESTION 2.

IF YES, ASK:

1a. to what extent did you plan or intend to hurt yourself
in that accident (either passively or actively)?

not at all	a little	moderately	markedly	extremely
<input type="text" value="0"/>	<input type="text" value="1"/>	<input type="text" value="2"/>	<input type="text" value="3"/>	<input type="text" value="4"/>

IF THE ANSWER TO QUESTION 1a IS 0, SKIP TO QUESTION 2.

IF IT IS SCORED ≥ 1 , ASK:

1b. Did you intend to die as a result of this accident? NO YES

3. want to harm yourself or to hurt or to injure yourself?	<input type="text" value="0"/>	<input type="text" value="1"/>	<input type="text" value="2"/>	<input type="text" value="3"/>	<input type="text" value="4"/>
4. think about suicide?	<input type="text" value="0"/>	<input type="text" value="1"/>	<input type="text" value="2"/>	<input type="text" value="3"/>	<input type="text" value="4"/>
5. plan for a suicide?	<input type="text" value="0"/>	<input type="text" value="1"/>	<input type="text" value="2"/>	<input type="text" value="3"/>	<input type="text" value="4"/>
6. take active steps to prepare for a suicide attempt in which you expected or intended to die?	<input type="text" value="0"/>	<input type="text" value="1"/>	<input type="text" value="2"/>	<input type="text" value="3"/>	<input type="text" value="4"/>
7. Over the past week did you injure yourself intentionally? IF NO, SKIP TO QUESTION 8. IF YES, ASK:	<input type="checkbox"/> NO <input type="checkbox"/> YES				
Over the past week, how seriously did you:					
7a. deliberately injure yourself without intending to kill yourself?	<input type="text" value="0"/>	<input type="text" value="1"/>	<input type="text" value="2"/>	<input type="text" value="3"/>	<input type="text" value="4"/>
8. attempt suicide?	<input type="text" value="0"/>	<input type="text" value="1"/>	<input type="text" value="2"/>	<input type="text" value="3"/>	<input type="text" value="4"/>

TOTAL

SUICIDAL IDEATION

Ask questions 1 and 2. If both are negative, proceed to "Suicidal Behavior" section. If the answer to question 2 is "yes," ask questions 3, 4 and 5. If the answer to question 1 and/or 2 is "yes", complete "Intensity of Ideation" section below.

Lifetime:
Time He/She
Felt Most
Suicidal

1. Wish to be Dead

Subject endorses thoughts about a wish to be dead or not alive anymore, or wish to fall asleep and not wake up.
Have you wished you were dead or wished you could go to sleep and not wake up?

Yes No

If yes, describe:

2. Non-Specific Active Suicidal Thoughts

General, non-specific thoughts of wanting to end one's life/commit suicide (e.g. "I've thought about killing myself") without thoughts of ways to kill oneself/associated methods, intent, or plan.
Have you actually had any thoughts of killing yourself?

Yes No

If yes, describe:

3. Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act

Subject endorses thoughts of suicide and has thought of at least one method during the assessment period. This is different than a specific plan with time, place or method details worked out (e.g. thought of method to kill self but not a specific plan). Includes person who would say, "I thought about taking an overdose but I never made a specific plan as to when, where or how I would actually do it.....and I would never go through with it".
Have you been thinking about how you might do this?

Yes No

If yes, describe:

4. Active Suicidal Ideation with Some Intent to Act, without Specific Plan

Active suicidal thoughts of killing oneself and subject reports having some intent to act on such thoughts, as opposed to "I have the thoughts but I definitely will not do anything about them".
Have you had these thoughts and had some intention of acting on them?

Yes No

If yes, describe:

5. Active Suicidal Ideation with Specific Plan and Intent

Thoughts of killing oneself with details of plan fully or partially worked out and subject has some intent to carry it out.
Have you started to work out or worked out the details of how to kill yourself? Do you intend to carry out this plan?

Yes No

If yes, describe:

INTENSITY OF IDEATION

The following features should be rated with respect to the most severe type of ideation (i.e., 1-5 from above, with 1 being the least severe and 5 being the most severe). Ask about time he/she was feeling the most suicidal.

Most
Severe

Most Severe Ideation: _____

Type # (1-5)

Description of Ideation

Frequency

How many times have you had these thoughts?

- (1) Less than once a week (2) Once a week (3) 2-5 times in week (4) Daily or almost daily (5) Many times each day

Duration

When you have the thoughts, how long do they last?

- (1) Fleeting - few seconds or minutes (4) 4-8 hours/most of day
(2) Less than 1 hour/some of the time (5) More than 8 hours/persistent or continuous
(3) 1-4 hours/a lot of time

Controllability

Could/can you stop thinking about killing yourself or wanting to die if you want to?

- (1) Easily able to control thoughts (4) Can control thoughts with a lot of difficulty
(2) Can control thoughts with little difficulty (5) Unable to control thoughts
(3) Can control thoughts with some difficulty (0) Does not attempt to control thoughts

Deterrents

Are there things - anyone or anything (e.g. family, religion, pain of death) - that stopped you from wanting to die or acting on thoughts of committing suicide?

- (1) Deterrents definitely stopped you from attempting suicide (4) Deterrents most likely did not stop you
(2) Deterrents probably stopped you (5) Deterrents definitely did not stop you
(3) Uncertain that deterrents stopped you (0) Does not apply

Reasons for Ideation

What sort of reasons did you have for thinking about wanting to die or killing yourself? Was it to end the pain or stop the way you were feeling (in other words you couldn't go on living with this pain or how you were feeling) or was it to get attention, revenge or a reaction from others? Or both?

- (1) Completely to get attention, revenge or a reaction from others. (4) Mostly to end or stop the pain (you couldn't go on living with the pain or how you were feeling).
(2) Mostly to get attention, revenge or a reaction from others. (5) Completely to end or stop the pain (you couldn't go on living with the pain or how you were feeling).
(3) Equally to get attention, revenge or a reaction from others and to end/stop the pain. (0) Does not apply

SUICIDAL BEHAVIOR <i>(Check all that apply, so long as these are separate events; must ask about all types)</i>				Lifetime
Actual Attempt: A potentially self-injurious act committed with at least some wish to die, as a result of act. Behavior was in part thought of as method to kill oneself. Intent does not have to be 100%. If there is <i>any</i> intent/desire to die associated with the act, then it can be considered an actual suicide attempt. <i>There does not have to be any injury or harm</i> , just the potential for injury or harm. If person pulls trigger while gun is in mouth but gun is broken so no injury results, this is considered an attempt. Inferring Intent: Even if an individual denies intent/wish to die, it may be inferred clinically from the behavior or circumstances. For example, a highly lethal act that is clearly not an accident so no other intent but suicide can be inferred (e.g. gunshot to head, jumping from window of a high floor/story). Also, if someone denies intent to die, but they thought that what they did could be lethal, intent may be inferred. Have you made a suicide attempt? Have you done anything to harm yourself? Have you done anything dangerous where you could have died? <i>What did you do?</i> <i>Did you _____ as a way to end your life?</i> <i>Did you want to die (even a little) when you _____?</i> <i>Were you trying to end your life when you _____?</i> <i>Or did you think it was possible you could have died from _____?</i> Or did you do it purely for other reasons / without ANY intention of killing yourself (like to relieve stress, feel better, get sympathy, or get something else to happen)? (Self-Injurious Behavior without suicidal intent) If yes, describe:				Yes No <input type="checkbox"/> <input type="checkbox"/> Total # of Attempts _____ Yes No <input type="checkbox"/> <input type="checkbox"/>
Has subject engaged in Non-Suicidal Self-Injurious Behavior? Interrupted Attempt: When the person is interrupted (by an outside circumstance) from starting the potentially self-injurious act (<i>if not for that, actual attempt would have occurred</i>). Overdose: Person has pills in hand but is stopped from ingesting. Once they ingest any pills, this becomes an attempt rather than an interrupted attempt. Shooting: Person has gun pointed toward self, gun is taken away by someone else, or is somehow prevented from pulling trigger. Once they pull the trigger, even if the gun fails to fire, it is an attempt. Jumping: Person is poised to jump, is grabbed and taken down from ledge. Hanging: Person has noose around neck but has not yet started to hang - is stopped from doing so. Has there been a time when you started to do something to end your life but someone or something stopped you before you actually did anything? If yes, describe:				Yes No <input type="checkbox"/> <input type="checkbox"/> Total # of interrupted _____
Aborted Attempt: When person begins to take steps toward making a suicide attempt, but stops themselves before they actually have engaged in any self-destructive behavior. Examples are similar to interrupted attempts, except that the individual stops him/herself, instead of being stopped by something else. Has there been a time when you started to do something to try to end your life but you stopped yourself before you actually did anything? If yes, describe:				Yes No <input type="checkbox"/> <input type="checkbox"/> Total # of aborted _____
Preparatory Acts or Behavior: Acts or preparation towards imminently making a suicide attempt. This can include anything beyond a verbalization or thought, such as assembling a specific method (e.g. buying pills, purchasing a gun) or preparing for one's death by suicide (e.g. giving things away, writing a suicide note). Have you taken any steps towards making a suicide attempt or preparing to kill yourself (such as collecting pills, getting a gun, giving valuables away or writing a suicide note)? If yes, describe:				Yes No <input type="checkbox"/> <input type="checkbox"/>
Suicidal Behavior: Suicidal behavior was present during the assessment period?				Yes No <input type="checkbox"/> <input type="checkbox"/>
Answer for Actual Attempts Only				
	Most Recent Attempt Date:	Most Lethal Attempt Date:	Initial/First Attempt Date:	
Actual Lethality/Medical Damage: 0. No physical damage or very minor physical damage (e.g. surface scratches). 1. Minor physical damage (e.g. lethargic speech; first-degree burns; mild bleeding; sprains). 2. Moderate physical damage; medical attention needed (e.g. conscious but sleepy, somewhat responsive; second-degree burns; bleeding of major vessel). 3. Moderately severe physical damage; <i>medical</i> hospitalization and likely intensive care required (e.g. comatose with reflexes intact; third-degree burns less than 20% of body; extensive blood loss but can recover; major fractures). 4. Severe physical damage; <i>medical</i> hospitalization with intensive care required (e.g. comatose without reflexes; third-degree burns over 20% of body; extensive blood loss with unstable vital signs; major damage to a vital area). 5. Death	Enter Code _____	Enter Code _____	Enter Code _____	
Potential Lethality: Only Answer if Actual Lethality=0 Likely lethality of actual attempt if no medical damage (the following examples, while having no actual medical damage, had potential for very serious lethality: put gun in mouth and pulled the trigger but gun fails to fire so no medical damage; laying on train tracks with oncoming train but pulled away before run over). 0 = Behavior not likely to result in injury 1 = Behavior likely to result in injury but not likely to cause death 2 = Behavior likely to result in death despite available medical care	Enter Code _____	Enter Code _____	Enter Code _____	

Other Categories Become Obsolete with Prospective data collection

C-CASA

C-SSRS

5. Self-injurious Behavior, Intent Unknown
6. Not Enough Information: Death
9. Not Enough Information: Non-Death



Not Applicable - Unknowns are eliminated with Prospective Data Collection (These C-CASA categories created ONLY to make sense of limitations of retrospective adverse events.)

8. Other (Accident; Psychiatric; Medical)



N/A: No Indication of Suicidal Ideation or Behavior

Example: Item data versus C-SSRS – Use C-SSRS rates of ideation lower

- Large scale obesity drug program
- PHQ-9: 452 suicidal ideations reported (8600 subjects) over 12 to 104 weeks (during RCT phase)
- C-SSRS: 12 suicidal ideations reported (5600 subjects) over 52 weeks (during extension phase)