Clinical Trial Site Experiences & Attitudes Towards Prospective Assessments of Suicidal Ideation and Behavior (SIB): Results of a Global Internet-based Survey

ISCTM Suicidal Ideation and Behavior Assessment Working Group

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ABSTRACT

Introduction: The International Society for CNS Clinical Trials and Methodology (ISCTM) Suicidal Ideation and Behavior Assessment Working Group conducted an online survey regarding clinical trial site experiences and attitudes towards suicidal ideation and behavior (SIB) data collection following the 2010 release of the FDA draft guidance on prospective assessment of SIB in clinical trials to support the classification of such events. The ISCTM Secretariat sent an email invitation with a link to the 20-item online survey to 6058 sites that had participated in at least one CNS clinical trial in the prior 2 years.

Results: 1004 responses were collected (43% US). Respondents included principal investigators (36%), raters (28%), coordinators (25%), and others (10%). The majority (80%) had conducted SIB assessments. Majority were psychiatrists (43%) and reported using SIB assessments across many indications. Overall, respondents indicated that prospective assessment is "worth the additional burden" (73%), has been "easy to incorporate" (73%) and has "improved subject safety" (74%). The greatest challenge was getting accurate baseline lifetime history (54%), while the greatest benefit was identifying subjects at risk of suicide (85%). Approximately a quarter of respondents reported implementation challenges such as training issues. Differences based on geographical region, respondent's role and responsibility for assessments were observed. Open-ended responses revealed additional challenges, e.g., use in cognitively impaired populations.

Conclusion: Prospective SIB monitoring was generally viewed positively though specific challenges were identified. Study limitations include self-report survey methodology and recruitment of sites based on CNS trial experience. These findings may help guide stakeholders' use of SIB assessments in clinical trials.

INTRODUCTION

- In September 2010 the FDA released a draft guidance recommending the prospective assessment of suicidal ideation and behavior (SIB) in clinical trials.
- The guidance requires SIB monitoring in drug and biological studies in psychiatric and certain other clinical trials to ensure (1) that patients experiencing these events are identified and properly treated, and (2) more timely and complete data collection for these events.
- Since its release, there has been a widespread implementation of SIB assessments in clinical trials conducted at sites worldwide.
- The International Society for CNS Clinical Trials and Methodology (ISCTM) SIB Assessment Working Group (WG) was formed to understand the effects of the guidance on clinical and research practice, and to identify challenges to its implementation.
- The WG held two face-to-face meetings regarding the prospective assessment of SIB involving an array of stakeholders from CNS clinical trials: investigators, raters, and other clinical trial site study staff; pharmaceutical sponsors; and vendors who support these studies. Based on these discussions, the WG developed an anecdotal picture of the implementation challenges and benefits.
- To build a better evidence base on what impact the inclusion of SIB assessments has had on clinical research sites, the WG designed a brief internet-based survey regarding site experiences and attitudes regarding these assessments.

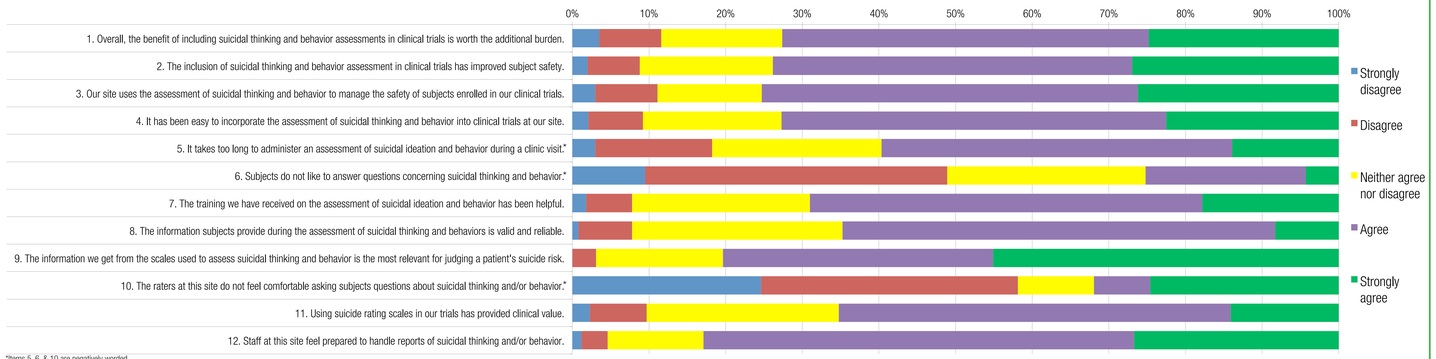
METHODS

- Summaries of the face-to-face meetings were used to generate 20 items, including 5 demographic questions.
- A list of 6058 study sites that had participated in at least one CNS clinical trial in the prior two years was obtained from an independent vendor's contact database.
- An email invitation to participate from the ISCTM Secretariat with a link to the online survey was distributed to a list of 6058 sites that had participated in at least one CNS clinical trial in the prior two years.
- Instructions encouraged respondents to speak with others at their site about their experiences implementing the assessment of SIB and to provide one response from the site that reflected the broader experience.
- Responses were collected over a 3-week period using SurveyMonkey™ and summarized descriptively.

RESULTS

- 1004 responses were collected (16.6% response rate); 25 sites that had not conducted SIB assessments were excluded for a total of 979 evaluable responses.
- Respondents reflected a wide coverage of geographic regions with surveys returned from 61 countries. (Figure 2)
- Respondents held a variety of roles at the sites and had a wide variety of training backgrounds (Table 1)
- The majority (80.1%) had personally conducted prospective SIB assessments.
- In general sites had extensive experience with SIB assessments, predominantly in CNS indications though non-CNS indications were also represented. (Table 2)
- The majority of sites indicated (agreed/strongly agreed) that SIB assessment has been "worth the additional burden" (73%), that it has been "easy to incorporate" (73%) and has "improved subject safety" (74%). (Figure 1)
- Identifying subjects at risk of suicide was endorsed by 84.1% of sites as the most important benefit; the greatest challenge was getting accurate baseline lifetime history (51.1%). (Tables 3 & 4)
- Open-ended responses revealed positive comments along with specific challenges to the use of these assessments, such as in cognitively impaired populations. (Table 5)
- Respondents from outside the US agreed more strongly with most opinion items, including that raters in general do not feel comfortable asking about SIB but were less likely to identify the accuracy of baseline SIB history assessments as an issue
- US PIs expressed less concern over the accuracy of baseline SIB history assessments than other roles at the site.

Figure 1: Opinion Items From the Survey for Entire Sample



*Items 5, 6, & 10 are negatively worded.

Table 1: Respondent Characteristics

	Entire Sample	U.S.	Outside U.S.
Role at the Site	(N=977)	(N=404)	(N=549)
Principal investigator	35.9%	27.7%	41.3%
Site Coordinator	25.0%	37.6%	15.9%
Rater	28.7%	21.8%	34.2%
Other Role[a]	10.4%	12.9%	8.6%
Background	(N=973)	(N=402)	(N=547)
Psychiatrist	42.8%	18.2%	60.5%
Neurologist	10.4%	5.7%	13.5%
Physician, other specialty	9.2%	13.7%	5.7%
Nurse/social worker	13.6%	23.4%	6.8%
Psychologist	8.8%	10.7%	7.7%
Other	14.8%	27.6%	5.5%
Responsible for SIB assessments			
	(N = 968)	(N=404)	(N=545)
Yes	80.1%	80.1%	79.6%
No	19.9%	19.9%	20.4%

[a]Sub-investigators were included under "Other." Sample sizes do not sum to total due to missing data.

Table 2: Therapeutic Experience by Respondents

	% of trials conducted in Therapeutic Area			
	None	1-10 trials	11-25 trials	> 25 trials
Affective disorders	32.1%	49.1%	10.8%	8.0%
Schizophrenia / Schizoaffective disorder	40.8%	46.0%	8.9%	4.2%
Neurodegenerative (e.g.,Alzheimer's, Huntington's, Parkinson's)	42.9%	44.9%	7.0%	5.2%
Epilepsy	80.7%	16.8%	1.7%	0.8%
Pain	62.0%	32.7%	2.8%	2.5%
Other CNS Diagnoses	45.0%	40.9%	7.5%	6.6%
Other non-CNS diagnoses	66.9%	23.6%	3.2%	6.3%

Table 3: Benefits Endorsed by Respondents

Benefit	Total sample %	US (%)	Outside US (%)
Helps identify subjects at risk of suicide	84.1%	81.3%	86.4%
Makes running clinical trials safer	61.2%	51.4%	66.9%
Provides subjects with a sense that their safety is important and is being monitored	58.8%	58.9%	59.2%
Helps educate site staff on the importance of suicide-related issues in clinical trials	57.6%	55.4%	59.2%
Can help identify drugs that may cause patients to become suicidal	55.5%	53.9%	57.2%
Improves our ability to provide care	49.5%	42.6%	54.6%
Helps identify patients who may benefit from treatment	42.4%	39.7%	43.9%
Reduces the stigma associated with suicidal thinking and behavior	35.8%	33.9%	37.1%
Will provide important prescribing information for prescribers	28.2%	26.4%	29.0%
Other	2.0%	3.0%	1.3%

Note: Respondents endorsed all that applied so the total >100%.

Table 4: Challenges Endorsed by Respondents

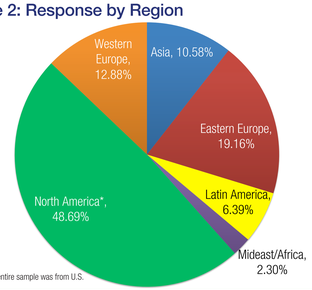
Challenge	Total sample % N = 979	US % N = 405	Outside US% N = 550
Difficulty getting accurate information on a subject's lifetime history of suicidal thoughts and behaviors at baseline	51.1%	56.6%	47.0%
The amount of time it takes to do an assessment	26.1%	23.4%	27.0%
Lack of a referral network for subjects with suicidal issues	25.6%	17.7%	31.0%
Finding the correct version of the scale to use	23.6%	15.8%	29.1%
Difficulty getting the correct language translations needed for our site	22.1%	5.2%	33.9%
Difficulty fitting this assessment into a typical clinic visit	20.9%	14.9%	24.9%
Lack of adequate training to conduct these interviews and assessments	20.0%	12.2%	25.2%
Uncertainty about what to do if a subject has suicidal thoughts/behaviors	17.3%	17.4%	17.1%
Other	11.9%	19.8%	6.6%

Note: Respondents endorsed all that applied so the total >100%.

Table 5: Responses to Open-Ended Question

Number responses	Topic	Sample response
15	Comment on specific scale	Kelly Posner PhD designed the CSSRS for non-clinicians yet sponsors won't allow non-MD's to administer the scale. The makes visits less efficient and takes time from the MD.
14	General comments that scales are clinically relevant; important to assess suicidality in clinical trials	Assessment of suicidality is simple and important tool to safety in clinical trials
13	General comments about SIB assessments (e.g., too long/complicated/convoluted)	We need better and more reliable scales!
11	Problems with use in cognitively impaired populations	The use of "scales" in dementia trials is a fig leaf and provides meaningless information.
7	Training issues	There needs to be more training of site staff on how to correctly perform this type of testing.
5	Rater issues	Allowing trained coordinators who are not MDs to use the scales may improve reporting as subjects have the most comfort with the coordinator
4	Patients self-report of symptoms is problematic/unreliable/difficult to obtain	It is unclear how truthful the patients are regarding their symptoms, however, there is value in at least, asking the question
4	Patients benefit directly from assessing SIB	Benefit that subjects have better awareness & understanding that suicide ideation may occur as a side effect & that this should be reported as it can be addressed.
2	Issues related to the use of these scales across different cultures	The assessment should be differed based upon country to country. It should be depend upon depression level of different people of different origin.
2	Predicting suicidality	The scales provide a systematized approach to asking patients about suicidal thoughts, this does not translate to an adequate or reliable assessment of the patient's risk for self harm.

Figure 2: Response by Region



*42.41% of entire sample was from U.S.

CONCLUSIONS

- This study, the first to look at this topic, found that the inclusion of prospective SIB assessment is generally viewed positively.
- Nevertheless, approximately a quarter of respondents reported important implementation challenges.
- Study limitations include internet-based survey methodology (self-report with no independent verification), recruitment of sites based on CNS trial experience, and no comparison to previous standard practice.
- These findings may help guide stakeholders' use of SIB assessments in clinical trials.

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