Study Site Experiences & Attitudes Toward Prospective Assessments of Suicidal Ideation and Behavior in Clinical Trials: Results of an Internet-based Survey

ISCTM Suicidal Ideation and Behavior Assessment Working Group

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INTRODUCTION

- In September 2010 the FDA released a draft guidance requiring the prospective assessment of suicidal ideation and behavior (SIB) in clinical trials.
- The guidance requires that SIB be monitored 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) that there is 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 ISCTM SIB 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; regulators; 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 of 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.
- An invitation to participate from the ISCTM Secretariat and a link to the online survey were distributed via email to a list of 6,058 investigators, raters, and site staff with valid email addresses obtained from a vendor database.
- SurveyMonkey was used to collect responses. Sites had a three week deadline to respond.
- Instructions encouraged respondents to speak with others at their site about their experiences implementing SIB assessments and to provide one response from the site that reflected the broader experience.
- Responses were summarized descriptively.

RESULTS

- A total of 1,004 responses were collected over 3 weeks.
- Respondents reflected a wide cross-section of geographic regions (Figure 2).
- Respondents held a variety of roles at the sites and had a wide variety of training backgrounds (Figures 3 and 4).
- The majority (79.2%) 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 1).
- The majority of sites indicated that assessment of SIB has been “worth the additional burden” (72%), has been “easy to incorporate” (72%) and has “improved subject safety” (74%) (Figure 1).
- Identifying subjects at risk of suicide was endorsed by 85% of sites as the most important benefit. Other benefits were endorsed by 42-61% of the sample (Table 2).
- The greatest challenge was getting accurate baseline lifetime history (54.5%), yet other important challenges were endorsed by nearly a quarter of the sample (Table 3).
- Open-ended responses revealed specific challenges with the use of these assessments, particularly in cognitively impaired populations (Table 4).

FIGURE 1
Survey on Assessment of Suicidality

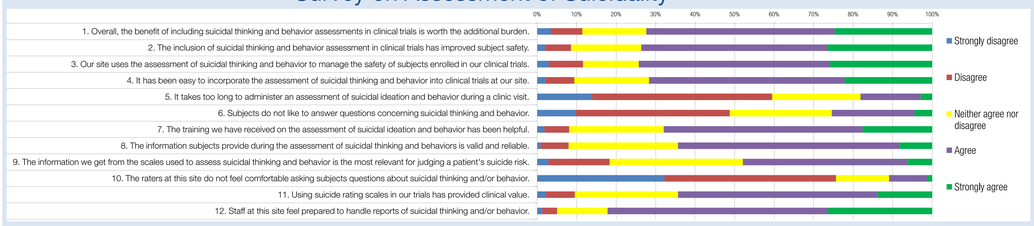


FIGURE 2
Responses by Region

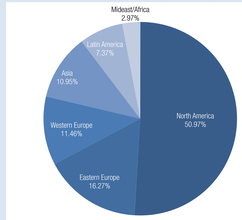
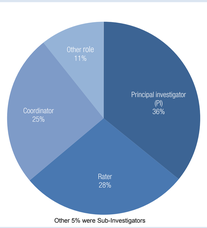


FIGURE 3
Role at Site



Other 5% were Sub-Investigators

FIGURE 4
Training Background

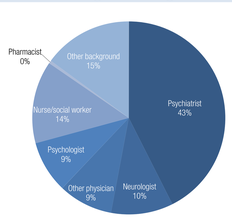


TABLE 1

	% 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 2

Most Important Benefits Associated with Implementing SIB Assessments in Clinical Trials	
Helps identify subjects at risk of suicide	84.5%
Makes running clinical trials safer	61.4%
Provides subjects with a sense that their safety is important and is being monitored	58.8%
Helps educate site staff on the importance of suicide-related issues in clinical trials	57.5%
Can help identify drugs that may cause patients to become suicidal	55.7%
Improves our ability to provide care	49.9%
Helps identify patients who may benefit from treatment	42.3%

Note: Respondents marked all that applied so total exceeds 100%.

TABLE 3

Most Challenging Problems in Implementing SIB Assessments in Clinical Trials	
Difficulty getting accurate information on a subject's lifetime history of suicidal thoughts and behaviors at baseline	54.5%
The amount of time it takes to do an assessment	27.9%
Lack of a referral network for subjects with suicidal issues	27.1%
Finding the correct version of the scale to use	25.5%
Difficulty getting the correct language translations needed for our site	24.0%
Difficulty fitting this assessment into a typical clinic visit	22.4%
Lack of adequate training to conduct these interviews and assessments	21.7%
Uncertainty about what to do if a subject has suicidal thoughts/behaviors	18.7%
Other	9.2%

Note: Respondents marked all that applied so total exceeds 100%.

Other responses included specific issues with SIB scales such as training/repetitious/wording; problems using with specific populations such as cognitively impaired; difficulty with relying on subject self-report; rater issues; and uncertainty whether scales adequately predict risk.

TABLE 4

Responses To Open Ended Questions		
Number of responses	Topic	Sample verbatim 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. This 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.
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	Use of scales cross-culturally causes issues	The assessment should be differed based upon country to country. It should be depend upon depression level of different people of different origin.

CONCLUSIONS

- This study, the first to look at this topic, finds that the inclusion of prospective SIB assessment is generally viewed positively.
- Approximately a quarter of respondents report important implementation challenges.
- Study limitations include internet-based survey methodology (*e.g.*, self-report with no independent verification), participating sites were drawn from a pool of sites with CNS trial experience (potential selection bias as sites may have more experience with SIB assessments), responses may not fully capture the sites' total experiences, and no comparison to what SIB assessment practices were routinely used prior to the guidance.
- These findings may help guide stakeholders' use of SIB assessment in clinical trials.
- Additional analysis is warranted, e.g., how results may differ geographically or among sites with different demographics or training.

DISCLOSURE: ISCTM supported the implementation of the survey with staff time and funding; the affiliations of all authors are given above; the authors report no other conflicts of interest.