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Clinical Research Ethics Question of the Month: Whom Do You Tell?

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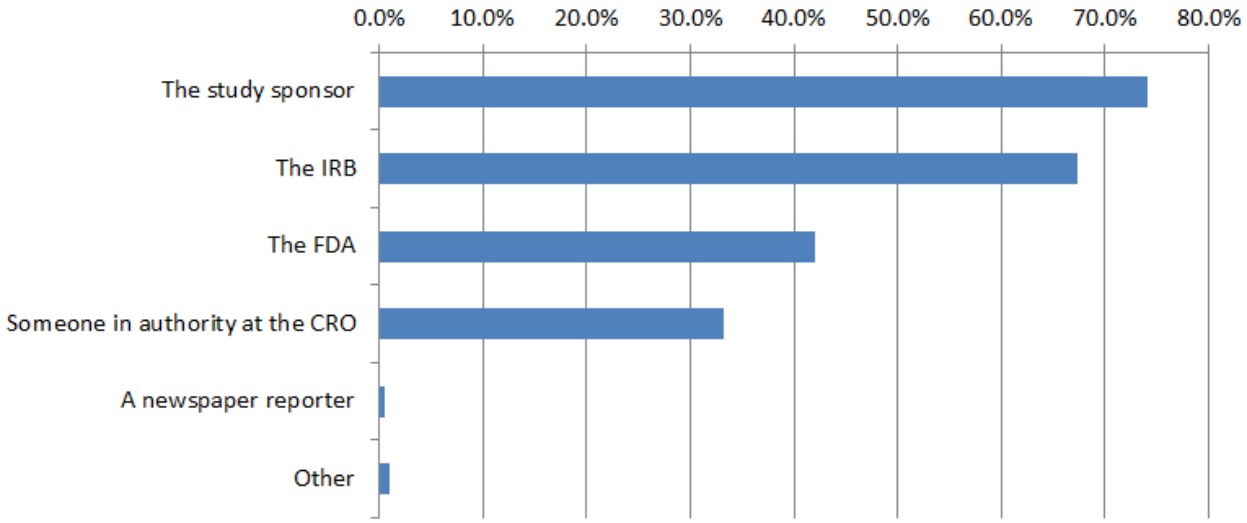
You are the principal investigator/owner at an independent clinical research site that is struggling financially. The first person you enrolled in a cardiology study had a serious stroke after one week in the study. The person had no history of strokes or related conditions. After unblinding, your SAE report to the very large CRO identified the study drug as causation. After a heated discussion, the CRO's medical monitor says he will "overrule" your conclusion and report the SAE (on your behalf) to the IRB and FDA with unknown causation. To prevent further issues, the study will be closed at your site. Should you tell somebody about the situation? You have no other information to make your decision and no clever way to dodge it.

Results

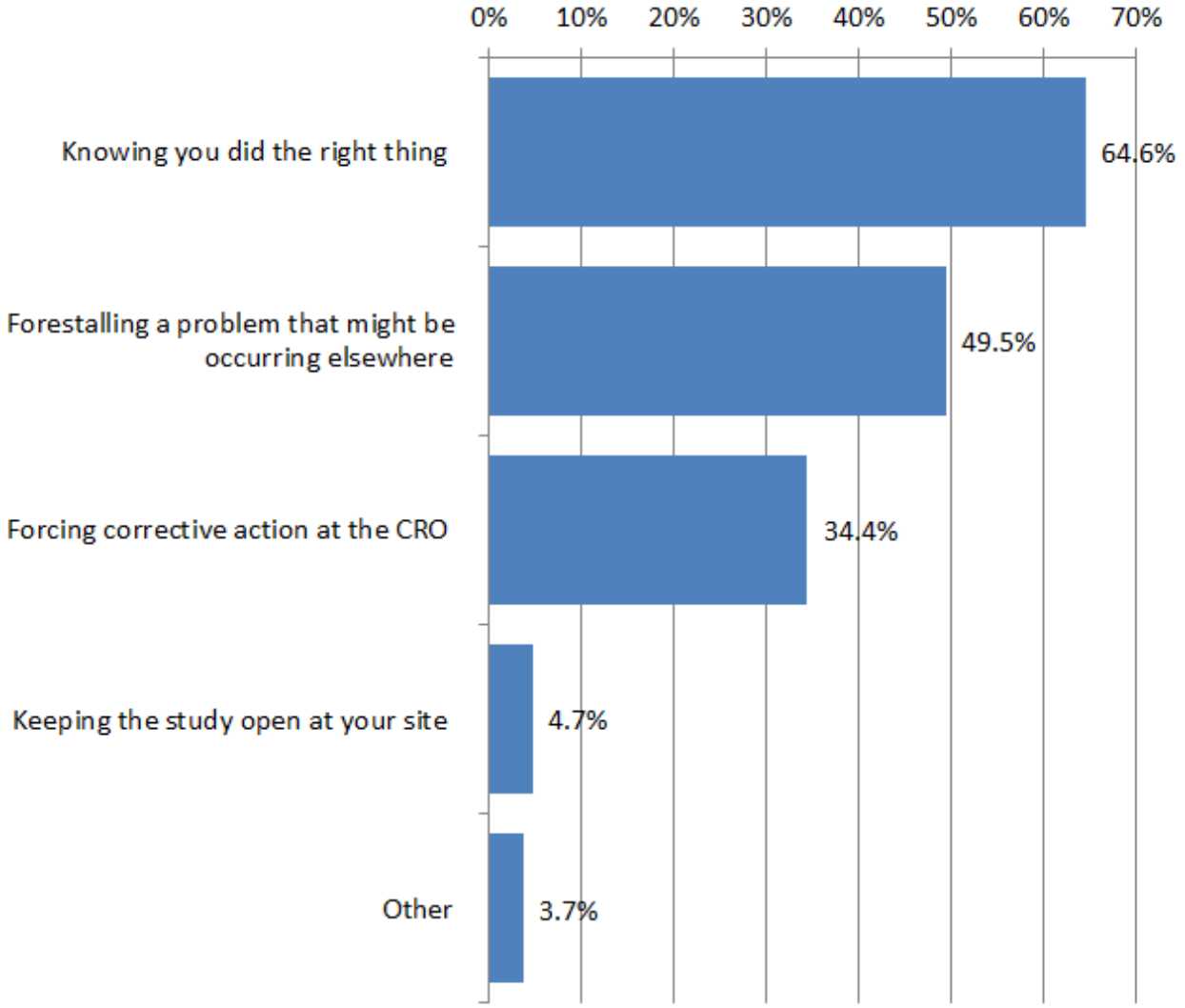
Chart 1. If you would tell somebody about the situation, whom would you tell?



About three-quarters of the 193 respondents would tell the study sponsor about the situation, 67% would tell the IRB, 42% would tell the FDA, and 33% would tell someone in authority at the CRO. Some respondents would tell multiple people.

One respondent recommended creating a paper trail. One respondent would not want to keep the study open under these circumstances. One respondent suggested that other sites might be seeing the same SAE. One respondent suggested talking to the sponsor to hear its thoughts.

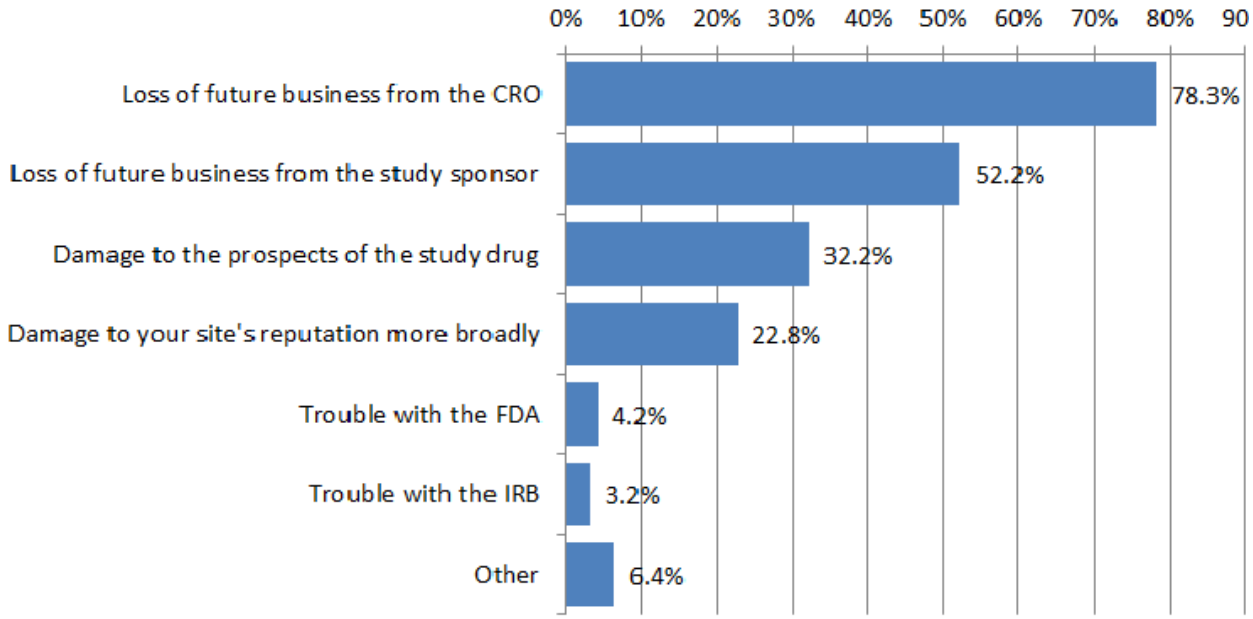
Chart 2. If you tell somebody, what principal benefits do you anticipate?



Ninety percent of respondents would tell somebody in order to avoid potential harm to other study participants, 65% would be motivated to "do the right thing," 50% would want to forestall a problem that might be occurring elsewhere (similar to the first option), and 34% would want to force corrective action on the CRO (also similar). Only 4.7% would tell somebody in order to keep the study open at their site.

One respondent said that following the regulatory guidelines for reporting should protect the site from regulatory consequences. One respondent said that reporting the incident would likely lead to an audit, which would not be a bad thing.

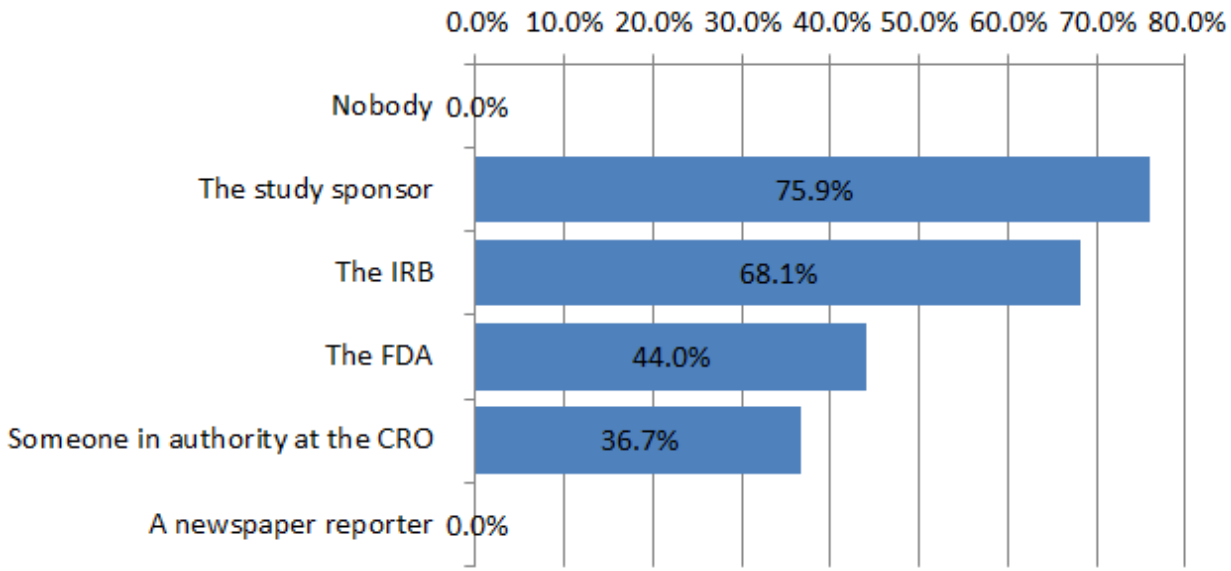
Chart 3. If you tell somebody, what principal risks do you anticipate?



If they tell somebody, 78% of respondents would be concerned about losing future business from the CRO, 52% would be concerned about losing future business from the study sponsor, 32% would be concerned about the impact on the prospects of the study drug, and 23% would be concerned about damage to the site's reputation more broadly. Small percentages would be concerned about trouble with the FDA or IRB.

Several respondents would not want to do business with the CRO again, so that risk would be irrelevant for them. One respondent would make sure all the study documentation was correct and complete, especially for the subject who had the stroke. One respondent expressed concern about receiving continuing communications from the sponsor that would be important to other subjects.

Chart 4. So, whom would you tell?



All respondents would tell *somebody*.

After considering the questions above, slightly more respondents would tell the study sponsor (+1.8%), the IRB (+0.7%), the FDA (+2.0%), and somebody in authority at the CRO (+3.5%).

Question 5. If you tell somebody, what are the chances something bad will happen to your site?

Thirty-two percent of respondents — all of whom would tell somebody — would expect something bad to happen to their site as a result.

Question 6. Other than possibly telling somebody about the situation, is there something else you would do?

Three respondents would document all communications with the CRO's medical monitor. Two respondents would contact other sites to find out if they had seen the same SAE. Two respondents would ask the sponsor or the IRB to consider adding stroke to the study's list of risks (if other sites had also seen them). One respondent would write a letter to the sponsor, CRO, IRB and FDA presenting its perspectives on the situation. One respondent would ask that the data and safety monitoring board (DSMB) review the SAE. One respondent would inform the study participant of the situation. One respondent would hold a meeting with study staff to brief them on the situation.

Discussion

Every respondent would tell somebody about the situation, even though 32% believed it would cause bad things to happen to the site. After considering the risks and benefits, the number of different people that would be contacted increased.

This is a hypothetical situation and respondents are anonymous, so it's easy to be courageous, but it is still a remarkable result.

The respondents' primary motivations were to protect study participants, the integrity of the study, and probably the integrity of clinical research more broadly. While there were a number of significant risks and potential benefits, 65% of respondents simply wanted to do the right thing.

Next Month's Question

You are a member of an IRB reviewing a study protocol for a new artificial heart that, if approved by the FDA, will likely save many lives. The study sponsor, a very small company, plans to test the device in patients who will probably die without the device. It cannot afford to test the device with an adequate sample size, so it proposes to increase the sample size with funds raised by auctioning off the right to participate. Any delay in approval will likely cost lives. Will you vote to approve the study?

Read the full question and give us *your* answer at:
https://www.surveymonkey.com/r/YFLGPQC

Please send your ethical conundrums to ngoldfarb@firstclinical.com.

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