The Most Important Voice Is Missing: The Case For Including Patient Insights In Protocol Design

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Patient voice isn't an accessory; it's foundational. Patients are key to clinical trials, and relegating them to mere "subjects" diminishes their value. Including the patient voice in study design and development can make an enormous difference in recruitment, enrollment, and retention. Doing so also pleases regulators, who are increasingly putting a premium on patient-focused drug development. It doesn't have to be difficult, but getting it wrong--or not doing it at all--can undermine a trial.

Sponsors and CROs who fail to incorporate the patient voice into study design and execution do so at their own risk. So do those who wait too long to listen to the patient. That's because a patient's insights could fundamentally change design of a study, identify important outcomes and endpoints, or help sponsors understand whether the study is patient-friendly--either in the ease of recruitment or execution.

Sara Ray, MA, Senior Director of Research at Inspire, frequently encounters this concern from pharmaceutical companies and CROs. "One point of hesitancy," she says, "is concern they'll learn something that runs counter to what they want to do with the trial. And that risks throwing everything off."

They're right to worry. "Every little change is going to be a risk." The solution isn't to ignore the patient voice, but to incorporate it earlier, before the protocol is finalized. "Incorporating the patient voice early in the protocol design process gets it right from the start."

Ensuring clients have all the necessary information early is part of Jill Johnston's job as President of WCG Study Planning & Site Optimization, "One of the services we provide at WCG is Study Fast-Start, where we work with pharma and CRO clients to help them do the proper planning before the protocol is written, sites selected, and patients enrolled. Before the study really gets started, we're collecting all that information and data, and providing insights to our customers to help them really plan and mitigate risk from issues they wouldn't have known about otherwise."

Now, by partnering with Inspire, Johnston and her team can give clients access to a new stream of data--patient insights. Inspire, a moderated online health social network, supports more than 3,600 disease conditions reported by over 1.6 million members, providing a wealth of insights.

For instance, would patients mind a visit that lasts four hours or more? Are the patients even able to physically stay at a research clinic location for that long? "Patients diagnosed with hypertension might be totally fine sitting there for four hours. Somebody with cystic fibrosis might find it totally unacceptable," says Ray.

Travel raises similar questions, Ray says. For many patients, travel presents a tremendous burden—enough to keep them from enrolling or even causing them to drop out. However, for some others, especially those with rare diseases, it may still be a burden,

but they are willing to travel for access to new treatments. "They are less concerned about traveling, because they would travel 200 miles to see a specialist. It's a burden they are willing to endure."

Gathering such specific information–not from generic patients, but from precisely the type of patient the sponsor intends to enroll–informs protocol design. By listening to patients and caregivers, sponsors gain insights they'd find no other way. Ray shares a story from before her days at Inspire.

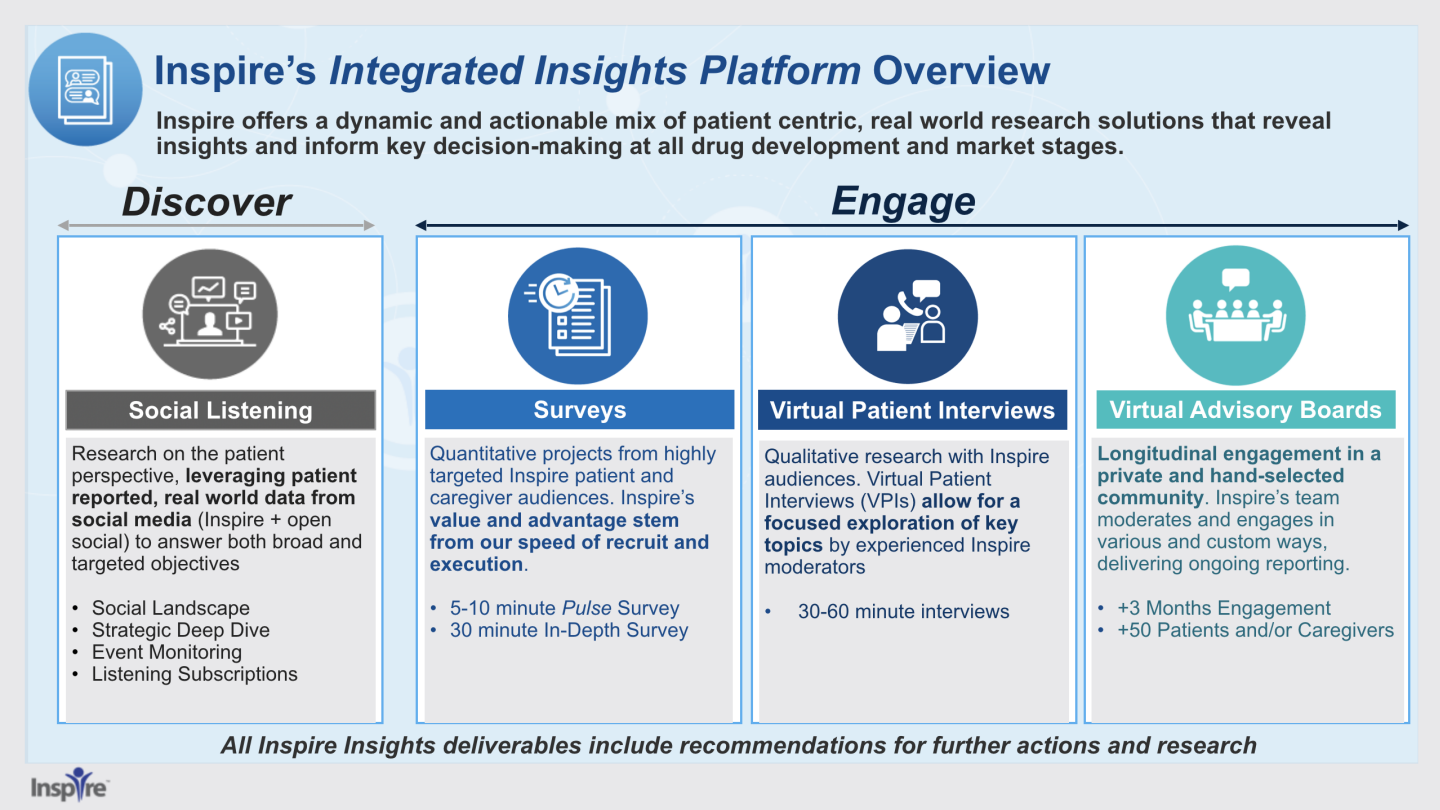
"I was involved in research about HPV vaccination for males. Doctors were, at that, time offering the vaccine to those who were in their mid-to-late teens. Some parents were wary, perceiving that the assumption was that their child was sexually active." After listening to parents, she and her team learned that by offering the vaccine at a much younger age, parents were more receptive–they didn't feel that anyone was suggesting their children were sexually active.

Making Time

So why aren't more sponsors seeking input from patients? One reason is the misperception that it takes too long, Ray says. In response, she explains she can start a survey on Friday and have a finished report in their hands by the following Friday.

"They look at me like I've grown three heads," Ray says. "I'm not saying I'm going to get a hundred-page report in a week. But we can ask targeted questions."

Those reports provide a simple way to get started. "A step up from a short, targeted report would be putting the entire protocol in front of patients–exactly like the ones you're trying to enroll–and see what they think," says Ray. Her favorite approach is to combine a survey with the qualitative insights so sponsors can see what patients are saying and understand why they're saying it.



Social Listening: What's In Your Lexicon?

Another approach to gathering the patient voice is social listening. This can be done early in protocol design and takes about a month. "Gathering organic language from on-line communities, such as Inspire, can help those who are designing the protocol discover what patients and caregivers are naturally saying and concerned about," Ray says.

Inspire has an algorithm that identifies key words and phrases that can answer important questions.

For example:

- What are patients and caregivers saying about other clinical trials?
- What are patients and caregivers saying about their current treatments? What makes their current treatments particularly burdensome?
- What are patients and caregivers saying about their measures of efficacy or success for treatment?
- What do patients and caregivers value in the treatments? Is it length of life? Quality of life? Something else?

Beyond that, Ray notes, sponsors need to understand, "What is their lexicon? This is something really important that is overlooked."

- How do patients and caregivers describe treatments?
- How do patients and caregivers describe experiences?
- What words do patients and caregivers use and prefer? What terms do they dislike or shy away from?

"By learning their lexicon, you can find out what words resonate with patients and caregivers. In this way, sponsors show solidarity with the community that they are going to be involved with for months or possibly years."

Having access to a patient community dramatically improves recruitment and enrollment. Knowing what those patients want is the key to site feasibility and retention.

The Golden Site

Johnston's goal is to develop a golden investigational site profile for each client. That means thinking about the patient population being investigated. "Along with inclusion/exclusion questions from the protocol, I need to get a sense of what kind of patient will be enrolled." Does the patient have a mild or severe version of the disease? What type of physicians would typically see that particular patient? A family physician? A specialist? What sort of specialist? Do they see other providers in addition to a primary one?

"What I'm trying to get an understanding of is, who do those patients typically go to see at that point of time

in their disease progression? If they received a relatively new diagnosis, they might go to see one type of physician, and if they're pretty far along their disease progression, they could be seeing a totally different type of physician."

Without this information, "I might find out I was fishing in the totally wrong pond, if you will, because I made the wrong assumption about where the patient receives care." And that's an assumption that can devastate enrollment.

"Having that insight and combining that data to help me develop a 'golden site profile' can make a world of difference between whether I have picked the right type of site or the wrong type for a clinical trial."

Everything rests on site selection, including recruitment, enrollment, and retention.

Wisdom Of The Crowd

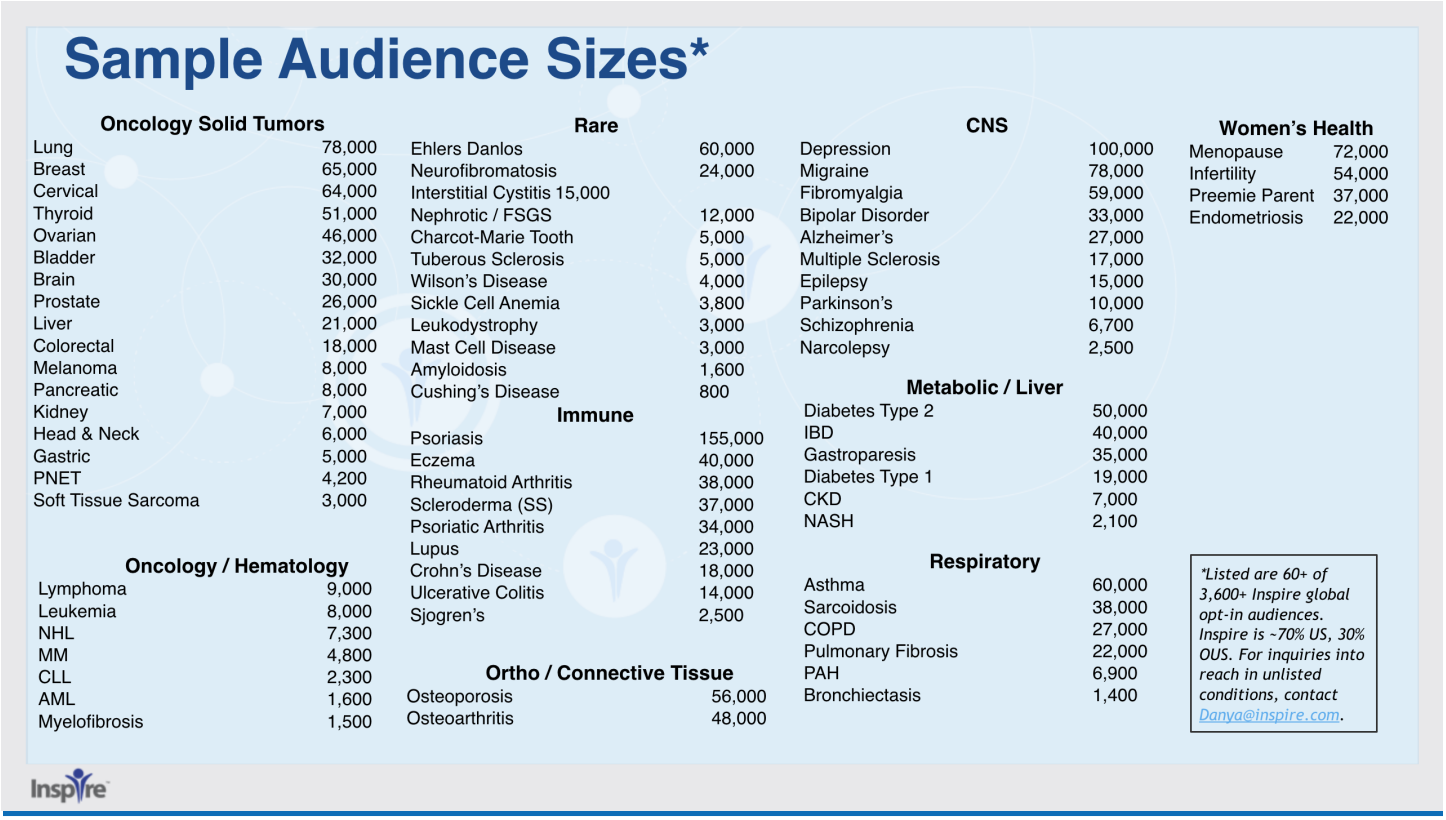
Sponsors and CROs typically can't do something like this on their own. Or at least, not in short order. For one thing, we often see they lack a way to access patient insights quickly, Johnston explains. "If you had to do this on your own as a pharma company, you might be able to just reach out to a couple patients you know, but that's just two individual voices."

Anecdotal insights could do more harm than good, leading sponsors down the wrong path. Even if the pharma company has a robust patient advisory council, only a couple patients on that council are likely to have the specific indication being studied.

That's why having access to a community of patients who have that particular condition is so important, Johnston adds. "You aren't dealing with one or two voices. You might be dealing with 10 or 20 or 30." You're getting directionally more accurate information.

Working with Inspire, WCG can draw from any of the 235-plus condition-specific online communities.

In some cases, says Ray–such as Wilson's Disease–"There is no other online community where a sponsor can obtain rich user-generated content or access these rare patients for virtual patient interviews, virtual advisory boards or surveys."



Patients, Not Proxies

There's no shortage of experts who'll try to tell you what patients want, Ray says. "Research panels may advertise that they provide 'health literacy' services, but as a linguist I have seen some recommendations from these panels that are not grounded in research." In one example, a panel told her she needed to change "oncologist" to "cancer doctor" because "oncologist" was too difficult a word for stage 4 cancer patients. "A patient with stage 4 cancer knows what an oncologist is. That is not a weird word to them."

Many sponsors who think they are incorporating the authentic patient voice aren't. "The operational staff will often say, 'I'm going to rely on my key opinion leader to provide the voice of the patient,'" Johnston explains. Unfortunately, that KOL is looking at that patient population from a provider perspective. They cannot fully put themselves in the patient's shoes–or head.

She relates a discussion about a clinical trial for Parkinson's disease. The key opinion leaders were adamant that gait was the key measure. But the patients themselves focused on having use of their hands and their arms for a longer period of time, because they want to be able to care of themselves longer.

"They know, they've already realized they're probably going to have trouble walking. While gait's important to them, the most important thing is that they're able to be independent and have that use of their arms, hands, and fingers," Johnston says.

Drawing directly from the patient is a relatively new approach, Ray acknowledges. Sponsors aren't necessarily comfortable with qualitative research, and many continue to lean on "old-school methods, such as focus groups," she says.

That isn't enough. "If you want the most authentic patients–phone interviews or virtual advisory boards or social listening or surveys–that's a way to include a wider range of patient types." For example, a patient who's living in Idaho, has a full-time job and three kids doesn't have the time to fly to Atlanta for a focus group.

"By drawing from the real patients and caregivers on Inspire communities, you're actually touching the pool of people from whom you'll–ideally--be recruiting," Ray says.

The advocacy community has its place but may have different experiences and things to share.

"For instance, in recent research with the FDA, Inspire compared transcripts of a Voice of the Patient event held in Washington, D.C. to user-generated content on Inspire. We found that the patient advocates at the VOP event were farther along in their journey, many years post diagnosis. Their focus was on the disease being discussed at the event."

In contrast, she says, many Inspire members who were at the beginning of their journey, did not understand their diagnosis and did not realize how the severity of this new diagnosis compared to other comorbidities. "Being able to access patients from all backgrounds and experiences creates more robust findings."

Partners, Not Subjects

Incorporating actual patient insights makes patients part of the research, not merely subjects. And patients very much want to be part of the research, says Ray. Engagement lasts beyond the trial. Too often, she says, a patient leaves the study and never hears from the sponsor or site team again, except for an impersonal survey six months later.

There's a better way: She tells of one sponsor who connected with the participants in a trial. It sent them the trial results, a picture of a little girl and a note that said something like, "This is 'Janie.' She's undergoing the treatment you helped test, and today, 'Janie' is in remission." Learning about 'Janie' reinforces that they made the right decision and makes them feel more positive about clinical trials in general, Ray says.

"The ways in which patients talk and interact with each other is important." This won't lead to instant changes in recruitment and retention, she acknowledges. "But over time it's a small step that can provide real value."

Industry And Regulators Muddling Through

Everyone talks about "patient-centricity," but many sponsors aren't sure how to ensure it's incorporated into study design. "As study teams are starting their projects, they have a thousand things, a thousand tasks they have to worry about," Johnston says. "So sometimes, the operations team will decide it's not worth the energy."

What's interesting is that these same people know the industry is clearly moving toward patient-centricity. But for many sponsors, it's more concept than execution. The attitude, Johnston says, is this: "It's impacting the industry, but that doesn't have anything to do with my study. We're not going to do that on my study. It will be too distracting or take too much time to incorporate the feedback. We're under time pressure as it is now."

Even though they know the industry is moving in that direction, they would prefer to be a late follower than an early adopter. "There's this real challenge between the patient-centricity folks who are trying to incorporate the voice of the patient and the people who are operationally focused to try to get things done in the most efficient way possible," she explains.

"We have to be able to do it in such a way that satisfies both parties, and do it in the most efficient, cost-effective manner possible. That's why I think

the Inspire methodology, the way that they have it set up, makes it easier and more accessible to pharma companies and CROs to incorporate that patient voice throughout the study-planning stage in a very cost-effective, meaningful way."

And now is the time to do it, says Ray. The industry is moving in that direction, and so are the regulators. The FDA's patient-focused drug development (PFDD) initiative will ultimately transform how the pharmaceutical industry develops drugs by calling for patient experience to be included across the research continuum. The goal is to ensure patient-centricity, but like many on the industry side, the FDA is working out just what patient-centricity involves, she adds.

This provides an opportunity for sponsors that take patient engagement seriously to help set the agenda.

PFDD criteria are loosely defined, but the FDA is also receptive to questions, Ray says. When she and her team develop a survey, set up patient interviews or develop virtual advisory boards, they're able to obtain guidance from the PFDD staff. "I have found the FDA is extremely willing to help."

Moreover, because PFDD efforts are still evolving, it's a chance to shape the criteria, Ray says. "Rather than agonizing over the regulatory issues around drug development, sponsors should be at the forefront, helping define ways to include the patient experience in drug development."

Authors

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