

Conducting Patient Interviews Within a Clinical Trial Setting



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Abstract

Qualitative data centered on patients' experiences and perspectives typically go uncollected in clinical trial settings. Yet patients' treatment experiences offer complementary insights and context on topics such as disease management, treatment gaps, and previous treatments outside of those gathered in traditional patient-reported outcome questionnaires. Qualitative interviews can capture patients' perceptions of treatment needs, more fully explore meaningful changes experienced as a result of treatment, and reveal outcomes that are most important to patients. Asking patients detailed questions can provide insight into the "why" of a patient's expressed thought or feeling. The inclusion of patient interviews within clinical trials is a relatively new and evolving field of research. This article delineates the types of data that may be collected during interviews with clinical trial participants and outlines two approaches to conducting qualitative research in the clinical trial setting, with a focus on maximizing the value of the resulting data.

Introduction

Within the context of clinical trials, patient-reported outcome (PRO) data, most commonly gathered via validated or other self-report instruments, are considered key in determining the value of new treatments across a wide variety of therapeutic areas and conditions. However, the totality of patient experiences and perspectives may not be adequately captured in a clinical trial setting with traditional PRO measures. Investigational products may present unanticipated impacts that are not or cannot be systematically assessed through currently employed PRO mechanisms. For instance, as compared with traditional PRO measures, patient interviews can reveal how a reduction in symptoms allows a patient to lead a more “normal” life.

Key Points

- Initiatives in drug development are under way to include the patient voice and assess the patient experience.
- Patient interviews are the quintessential method to elicit the patient voice and represent a rich source of data, yet they have not traditionally been used within the clinical trial context.
- Patient interviews can be conducted at any time during a clinical trial and for many reasons; however, they are most commonly implemented at the end of treatment to provide in-depth information about patients' experiences with treatment.
- Capturing the patient's voice during clinical trials through qualitative interviews can reveal unanticipated treatment benefits or, conversely, expose unmet needs or unanticipated challenges posed by treatment during the trial.

Passage of the US Food and Drug Administration (FDA) Safety and Innovation Act¹ and the Prescription Drug User Fee Act V codified the need to ascertain patient perspectives during drug development, underscoring the importance of these data. Increasingly, sponsors are including patient interviews in clinical trials to capture the patient voice and more fully represent the patient experience. Interview data may support not only value messaging for approved products but also product approvals, as the interviews allow patients to report meaningful change outside of standard PRO measures and clinical indices.

Although interest in including patient interviews as part of clinical trials is growing, the field of study is relatively new, with little published research. Here, we describe our experiences having planned and conducted nearly 20 interview studies within clinical trial settings. Most often conducted with patients, these interviews may also include caregivers, physicians, or study site personnel. Although interviews with each of these populations explore the clinical trial experience from various perspectives, the primary focus of this article is the patient experience.

Patient Interviews Add Value in Clinical Trials

Patient interviews allow clinical trial participants to articulate concepts that may be important to them but that are not obtained (or fully obtained) in clinical trial assessments. Properly designed and conducted patient interviews enrich researchers' and sponsors' understanding of the patient experience. Qualitative researchers can investigate thematic evidence available from a group of patients, and their findings can inform future clinical outcome assessment strategies and trials in the same disease area.^{2,3} Typical interview concepts explored in patient interviews are presented in Table 1.

Table 1. Sample interview concepts

| Interview Concepts | Topics for Exploration |
|---|--|
| Symptoms and impacts before the study | <ul style="list-style-type: none"> • Symptoms experienced • Impacts of reported symptoms • Most bothersome/important symptoms |
| Expectations of changes or outcomes | <ul style="list-style-type: none"> • Pre-study expectations (can be compared with actual clinical outcomes) |
| Anticipated or unanticipated changes, and the impact of those changes | <ul style="list-style-type: none"> • Changes/outcomes noticed • Impact of treatment on most important/bothersome symptoms • Onset of changes • Impact of treatment on functioning and quality of life |
| Treatment experiences | <ul style="list-style-type: none"> • Convenience of treatment • Managing treatment schedule (e.g., regimen schedule, infusions, monitoring) • Challenging aspects of study treatment • Managing adverse events |
| Satisfaction levels with treatment | <ul style="list-style-type: none"> • Satisfaction ratings • Reasons for satisfaction |

Source: Adapted from DiBenedetti.⁴

The FDA has shown increasing interest in patient interviews conducted as a means to supplement, support, and facilitate the interpretation of data gathered during trials with traditional PRO or clinical measures.⁴ Sponsors may incorporate patient interviews into clinical trials as part of the study protocol, or they may decide to include patient interviews post hoc. Interviews may occur before treatment initiation, after a particular duration of treatment, at the end of treatment, and/or at disease progression. However, interviews are most commonly conducted after the trial is complete, in the form of an exit interview.

Exit interviews conducted with patients who have completed (or terminated early) clinical trials have yielded valuable insights into patients' experiences with a disease and with an investigational treatment.^{2,3,5,6} Such interviews are one way to highlight the meaningful changes patients experience during clinical trials, thus contextualizing and enriching clinical trial results. Further, interviews yield unique data to supplement clinical trial findings (e.g., regarding safety concerns or the benefits of treatment).⁷

Interviews within the clinical trial setting can provide greater depth and rationale for a response given within the context of a traditional PRO measure, further describe treatment effects, explore the relevance and clinical meaningfulness of specific treatment changes beyond clinical indices and side effects, and explain anomalous results.⁷ Recently, in response to new legislation, regulatory agencies have begun suggesting the inclusion of qualitative interviews with patients to determine what outcomes are the most important and meaningful from their perspective, in contrast with selecting an arbitrary end point.¹

Patient interviews conducted in the context of clinical trials in rare diseases can be particularly beneficial, given the difficulties inherent in recruiting for these trials. The need to determine the outcomes most meaningful to patients with rare diseases and their families has been described previously.⁸ For example, exit interviews conducted with participants in a clinical trial evaluating a treatment for the symptoms of a rare form of cancer found that the symptom that patients found most bothersome and most important to treat aligned with the primary end point of the

trial.^{2,5} Particularly in instances where the patient population is small and the disease under study is rare, the FDA has reviewed exit interview data submitted with New Drug Applications.⁹

Interview Timing Considerations

The interview timing is dictated by the goals of the interviews, as various types of data are available at different study time points. For instance, patient interviews conducted in the pretreatment phase offer an opportunity to understand patients' experiences with a disease, the symptoms that patients themselves consider to be the most important to treat and/or the most bothersome, motivations to participate in the trial, and patients' expectations of treatment. Patients may describe the symptoms they have been experiencing before they begin a clinical trial and may rate the severity of those symptoms, and they may reveal their experiences with previous treatments. Pretreatment interviews allow patients to articulate their expectations of a clinical trial treatment, which may be especially informative if exit interviews will also be conducted.⁴ Pretreatment interviews also provide an opportunity for patients to describe potential barriers to participation in or adherence to clinical trial requirements—information that may help mitigate recruitment and retention issues.

Patient interviews conducted during or after treatment can

- provide support for traditional trial end points, including but not limited to PRO measures
- supplement quantitative trial results with additional detail
- characterize the full impact of treatment, including meaningful changes patients have experienced
- evaluate how well patients' expectations of treatment were met.

Interviews conducted during or after the clinical trial also allow patients to describe their experiences with the trial regimen and activities. These interviews give patients an opportunity to articulate any anticipated or unanticipated changes (positive or negative) associated with treatment. Patients may describe the impact of treatment on their symptoms, the importance of symptom changes, and how treatment affected their functioning and activities. Additionally,

patients can comment on other study experiences, including the convenience of the study regimen and/or study visits and any challenging aspects of the treatment or participation in the study.

Sample Size and Population Considerations

Choosing a sample size necessary to ensure that the results of the planned analyses will be sufficiently robust depends on the trial design and complexity. Generally, interviews should be conducted until no new concepts or themes are being elicited from research participants (e.g., data saturation). Whether a sample size will be sufficient for a meaningful analysis depends on such factors as whether patients experience a generally clear and consistent constellation of symptoms and whether data saturation can be reached.

Notably, an extremely narrow potential patient pool (e.g., in extremely rare populations) makes recruitment more challenging and can cause an interview study to be a lengthy process even with a small sample size, resulting in a high cost per patient. Including interviews as a component of a clinical trial, compared with conducting interviews as a follow-up or substudy, can reduce overall costs associated with interview activities and make recruitment of participants and sites more efficient. Interviews conducted as a core component of a trial will also likely have more “buy-in” from sites and patients.

Multinational studies require additional considerations. Interview studies conducted in multiple countries can encounter lengthy delays due to extensive required ethics reviews and other procedures (e.g., site contracting processes, translation of study materials), sometimes making them cost- or time-prohibitive to implement. Interviews conducted in a language other than the researcher’s primary language must be transcribed and translated for analysis, adding time and expense. However, conducting interviews with all subjects in every country included in a study is not necessary. Based on our experiences, we have found that a sample size of 20 to 40 patient participants can yield adequate data.^{3,5}

If the interview is not a requisite part of the study, recruitment relies on both site and patient volunteers.

Although the effort involved in recruiting participants and coordinating interviews is modest, some sites may have insufficient resources for these additional tasks. Further, if the interview process is not reviewed as part of the main trial protocol, time must be built in for additional review and approval by an institutional review board and/or local ethics committees. Contract amendments may also be necessary if the interview component is added after the start of the clinical trial. Recruitment of and contracting with sites may be time consuming and, if not initiated in a timely fashion, can result in delays in data collection.

Approaches to Conducting Patient Interviews

Two main approaches are employed in conducting patient interviews within the context of clinical trials. In the first approach, trained qualitative researchers develop the informed consent form, interview protocol, and interview guide; conduct the interviews; and analyze the results. Alternatively, trained qualitative researchers can develop the interview materials and train site personnel to conduct interviews. In the latter case, site personnel usually provide interview data to external qualitative researchers who analyze study results.

Each method has its own advantages and limitations. Regardless of the interview approach chosen, adequate time must be built into the study design for the development of interview materials and training of study site personnel. Sponsors seeking to include the patient voice in their planned trials should carefully weigh each option.

Qualitative Researchers Interview Patients

In the first approach, experienced qualitative researchers may conduct interviews with patients at one or more defined time points in a clinical trial. Participation in interviews may be, but is not always, requisite for trial participation. Generalizability of the interview results is increased by the researchers’ ability to recruit and interview large and diverse samples of participants. When possible, researchers should seek to interview a large enough sample to produce consistent results, and recruitment strategies should take the study design into account. The

limitations of this approach should be considered and accounted for in analysis of results.

Within this approach, qualitative researchers train study site personnel on recruitment and interview scheduling procedures, and qualitative researchers conduct interviews with patients either in person or by telephone. Determining the appropriate mode of interviewing (i.e., by telephone or in person) involves logistical, budget, and population considerations.¹⁰ Based on our experience, the more sites and patients in a clinical trial, the easier and less expensive it is to recruit interview participants. Telephone interviews tend to be most effective if they take place shortly after the trial ends and interviews are relatively brief (45–60 minutes). Telephone interviews also offer flexibility in scheduling, which may be pragmatic for populations who are very ill or who may need to reschedule an interview session.¹¹

In contrast, if an in-depth debriefing of a specific instrument or measure is a study objective, in-person interviews may be warranted.¹⁰ In-person interviews may also be preferable if the population includes pediatric patients or patients with cognitive or communication challenges.^{10,12} In general, interviews longer than 60 minutes are most effectively conducted in person, although in our experience, in some cases they can be conducted successfully by phone.

Procedures for prospectively planned patient interviews are part of the full clinical trial protocol, whereas interviews planned post hoc generally follow a separate protocol written specifically for the interview activities. In both scenarios, patients provide informed consent before the interview, and in all cases interviews are audio recorded and transcribed. The interviews follow a semistructured interview guide, which directs the flow and content of the interview while allowing for the spontaneity of participant responses and a conversational tone throughout the interviews.

Value of This Approach

Interviews conducted by experienced qualitative researchers provide the richest source of data supported by robust qualitative research methodology.^{10,12,13} Seasoned interviewers are trained to fully probe participants' responses and ask follow-up questions to gain better insight into the "why" of a patient's specific thought or feeling. An

interviewer trained to respond dynamically during an interview can glean unbiased responses without inadvertently leading a patient's response.

Effective interviewers combine technical expertise (e.g., in questionnaire and survey design) with interpersonal skills such as being flexible, spontaneous, and calm when unexpected situations arise.^{10,13} Although a semistructured interview guide is important in directing the flow of the interview and content to be covered, the guide need not be followed verbatim.¹³ No interview guide can anticipate all issues that may arise during an interview; thus, the interviewer's expertise strongly influences the interview's value.

Experienced interviewers practice active listening techniques¹² and work to create a trusting environment. These practices, in turn, help to build trust and respect between the interviewer and the participant. Experienced interviewers encourage participants to clarify their thoughts, which can provide richer context for the interview data. In addition, experienced interviewers can identify and respond to subtle nuances, such as recognizing when ideas or thoughts are expressed at unanticipated moments during an interview, prompting the interviewer to revisit a theme that may already have been discussed. A key skill of seasoned interviewers is balancing active, engaged listening approaches with refocusing on the topic at hand.

Experienced interviewers also understand the unique approaches required when interviewing special populations (e.g., children or people with cognitive or communication challenges).¹² Qualitative researchers who have experience working with these populations use techniques to encourage interviewees to participate actively and effectively in the interview without burdening or frustrating them.

Site Personnel Interview Patients

In this approach, study site personnel conduct the interviews, manage the audio recordings, complete data collection forms, and maintain detailed notes of the participants' responses. Because study site personnel generally are not experienced in qualitative interviewing techniques, experienced qualitative researchers train them to assist with proper procedures for recruitment, scheduling, coordination, and interviewing. Experienced qualitative researchers

conduct training sessions and certify that staff have successfully completed those sessions. After certification, researchers often observe or review the first few recordings of interviews conducted by site staff to assist in improving their interview techniques.

When interviews are conducted at multiple study sites by many different interviewers, developing a more structured approach to the interview process helps ensure standardization in the interview process and reduces variability in the data collection procedures. Interview guides used in this approach are usually more heavily scripted than guides used in interviews conducted by experienced qualitative researchers. Scripted interview guides help ensure that all necessary data are obtained in a consistent manner that reflects the purpose of the qualitative assessment, the type of patient interview (e.g., concept elicitation, instrument debriefing), and the capacity of the patient population to provide input. Upon completion of the interviews, study site personnel generally forward all data to an experienced qualitative researcher who transcribes the audio recordings, reviews the study site personnel's notes, codes the transcripts, conducts the data analyses, and develops a study report.

Value of This Approach

Although interviews conducted by study site staff may yield less in-depth data than interviews conducted by qualitative researchers, this approach is particularly useful in global clinical trials where the interview process needs to be quickly scaled to allow for maximal participation. Site staff may be trained on interviewing procedures alongside protocol details, obviating the need for an external interview to be conducted. The interviews can be conducted by someone with whom patients are familiar, which may be useful in special populations (e.g., children) or small samples.

For this approach to be successful, study sites must be highly organized, engage in recruitment, and familiarize themselves with interview content and processes. No interview guide, regardless of how scripted it is, can anticipate all issues or possible participant responses. Study coordinators may not always probe patient responses as an experienced interviewer would or adhere to the structure of the interview guides. When individuals with varying degrees of experience conduct interviews, data may

not be as high-quality or as granular as the data resulting from interviews conducted by neutral, seasoned interviewers. However, careful training of study coordinators can ameliorate some of this variability. Monitoring of recordings also helps to ensure quality. If quality issues are identified, the qualitative research partner can be engaged to provide remediation and retraining as needed.

If study coordinators will be conducting interviews, care must be taken to avoid the potential for bias. In some circumstances patients may be prone to highlight positive experiences to the site personnel with whom they have been interacting in the clinical trial for several months.

Analyses of Patient Interview Data

Patient interview data, regardless of the interview methods used, are usually analyzed by trained qualitative researchers. These analyses involve reviewing field notes, transcripts, and data-collection forms to identify patterns found in the interview data and facilitate description of the themes and relative importance of concepts based on participants' experiences. If collected, quantitative data, such as responses to close-ended questions or ranking exercises, are usually descriptive. Interview data can also be analyzed in the context of treatment assignment (e.g., the percentage of patients reporting a meaningful improvement in a symptom within each treatment arm) or in the context of other clinical trial data. Analyses of correlations between treatment groups or treatment response and treatment satisfaction can link clinical trial data directly to interview data.^{3,4}

Discussion

Patient interviews within clinical trials are a potentially rich source of data that have not in the past been widely conducted in the industry, although there is an emerging regulatory and industry interest in this methodology. Based on our experience across disease areas and published studies,²⁻⁷ the information collected during qualitative interviews can inform clinical outcome assessment measurement strategies for future research. It can also support or assist in the development of publications, marketing messages, future study design, conceptual frameworks, or regulatory submissions/approvals. Perhaps more

importantly, interviews with patients participating in clinical trials can also provide various stakeholders with a deeper understanding of the impact of potential treatments, meaningful changes in patient outcomes, and the overall patient experience. While the qualitative, less structured nature of patient

interviews reduces standardization of data collected as compared with traditional PRO measures, and therefore requires trained staff to collect these data in a nonbiased fashion, when implemented correctly interviews are the most effective method to bring the patient voice out of the clinical trial.

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