WHITE PAPER

Addressing the Challenges of Conducting Qualitative Interviews within Clinical Trials

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Key Terminology

Embedded (or in-trial) interviews collect patient (and/or caregiver) perspectives through interviews defined as clinical trial activity under the auspices of the clinical trial protocol. They may be conducted at any stage during the clinical trial—as one-time interviews or at multiple time points (longitudinal).

Associated interview studies operate externally to the trial under a separate protocol, but they enroll and interview patients that are enrolled in the clinical trial.

Standalone studies operate externally to the trial under a separate protocol and use a separate population.

Exit interviews are a type of interview, not a study design. They target patients at the end of a treatment experience. They may be conducted as a part of any the three study designs.

Over the past few years, there has been a growing interest in exit interview studies that are conducted within clinical trials. These are known as embedded exit interviews (EEI) studies, or in-trial interviews.

Access to the patient voice through qualitative interviews conducted at study exit or at multiple timepoints during the trial is increasingly valued by regulatory bodies,[1,2] to determine whether treatment-related changes are truly meaningful to patients. Further, these interviews can inform regulatory decision-making and advance patient-centered access to medicines.

EEIs have now been used across a range of medical conditions[3–7] to increase interpretability of the outcome measures that contribute to clinical trial results.[8] Interview results contribute to understandings about patients' experience with their condition, its impacts on their lives, to explore what they can recognize and report as treatment benefit, and to describe their experiences in the trial and identify aspects of burden from their participation.

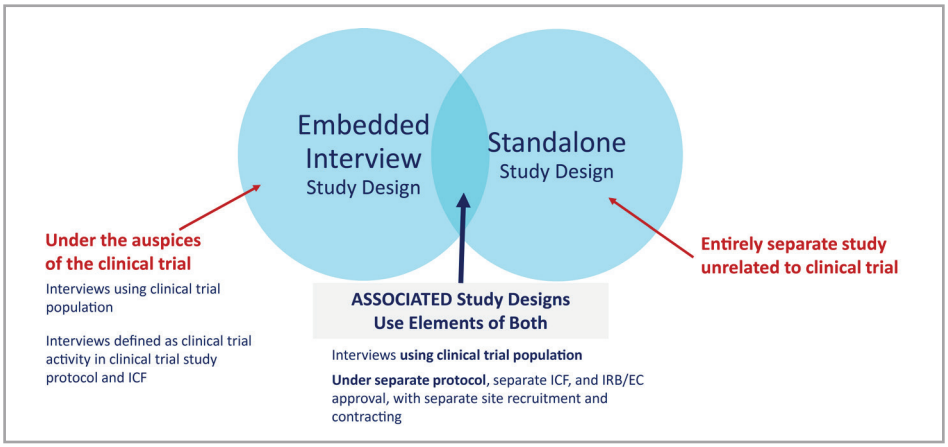

Figure 1: Key differences in study designs

Incorporating qualitative interviews within clinical trials can add meaningful value, but they also pose unique operational and logistical challenges that require careful planning and preparation. This white paper provides insights and recommendations for trial sponsors to successfully address four key areas where significant challenges occur when implementing qualitative research within the context of a clinical trial, and details Evidera's model for conducting interviews within clinical trials.

1. **Trial conduct:** patient and staff burden, confidentiality, and data security
2. **Interview conduct:** transcript cleaning and certification, modifying interview guides, communicating potential adverse events (AEs)
3. **Quality control and training:** interviewer and coder training and monitoring
4. **Operational study management:** defining and timing key activities, creation of interview guides, tracking systems, stakeholder communication

Four Key Challenges and Solutions to Address by Embedding Qualitative Interviews into Clinical Trials

Many sponsors express concerns about the burden of patient interviews on clinical sites and study participants. Additional complexity for operational teams also ranks high on sponsors' list of concerns about conducting embedded interviews. However, potential barriers can be overcome with appropriate interview approaches and proper planning, training, and education.

1. ADDING INTERVIEWS TO CLINICAL TRIAL ACTIVITIES

Sponsors that have not yet conducted qualitative interviews within clinical trials may feel uncertain about the newness, complexity and additional burden it may entail for local clinical site staff. However, because the inclusion of qualitative interviews is becoming increasingly recommended by regulatory agencies, clinical sites gain greater awareness and have more positive experiences.

Qualitative interviews are best approached as a core activity within the study, formally described in the study protocol as a part of the design and data collection activities. From the onset, it is also important to set site staff expectations by framing the interviews as non-optional study activities that will drive the collection of critical data points.

Investigators and site staff should receive clear training to clarify:

- The value of giving patients a platform to talk about their experiences and capture their voice to enhance interpretability of the trial results
- That interviews will not be conducted by site staff but rather by a vendor with specific expertise in qualitative interview research methods
- The precise role they will play and all associated processes
- That interviews will add as little burden as possible—for them and for patients

Sites are naturally protective of study participants and may be reluctant to conduct "non-essential" tasks, especially when patients are ill. Staff may also have concerns that the interviews will be burdensome for patients. For example, they may envision patients trapped on the phone for a full hour when they may not have the stamina. It's important for site staff to understand that the interview length is largely determined by how much the patient has to say and, in some cases, they can be quite short. Experienced qualitative interviewers are also sensitive to patients who are struggling with stamina and attention limits and are adept at providing breaks or possibly ending the interview sooner out of concern for the patient's circumstances.

Site staff and investigators often assume this activity presents a higher burden for their patients, but it is not always the case from the perspective of patients. Interviews are typically positive experiences for patients that contribute to their engagement in the study. Most patients want to be heard, and they appreciate the opportunity to discuss their perspectives and experiences with a skilled, non-judgmental, and interested interviewer.

It is also important to convey the importance of the interviews to the patients during the consent process so that they understand why their contribution is valuable. As with any study activity they are consenting to participate in, they have the right to withdraw from the interviews at any time without any negative consequences.

Finally, pilot testing of the interview guide should be conducted to assess the timing and duration of the interviews and to ensure the questions are clear and accessible. Adjustments can then be made if needed.

Concerns also arise related to data safety and the protection of participant confidentiality. Patients will be asked to give permission for their site study team to provide their personal contact information to the interview team so interviewers can contact them directly to schedule and conduct their interview session. These concerns may be raised by a site, an Institutional Review Board (IRB) or ethics committee (EC), a contract research organization (CRO), or study sponsor. It is important to clarify that a vendor conducting qualitative interviews is under the same regulations and laws regarding the treatment of personally identifying information (PII) as anyone else assisting with the conduct of the trial. Using an experienced vendor is the most efficient and lowest burden method for staff, patients and interviewers.

Some country-specific data privacy laws may prevent the transfer of PII to a third-party vendor for the interview activities. In those instances, there are various options that can be used to avoid providing the patient's contact information, but they do pose a higher burden for the sites and less certainty in the outcomes.

To address these concerns, it is necessary to develop clear and comprehensive processes tailored for each study to maintain participant confidentiality in the study documentation submitted to IRBs and ECs. These should include details on how personal contact information will be collected, stored and secured. They should also specify who will have access to this information and how it will be used solely for the purpose of conducting the interviews and analysis.

2. CONDUCTING THE INTERVIEWS

Whether an interview is conducted within a trial or as an associated or standalone interview study, qualitative interviews involve recording and transcribing the interview session. The interviews involve a conversation around specific topics or territories, and it is not possible to control what patients say in their responses. Therefore, these recordings may unintentionally capture various types of PII including family or doctor names, contact details, medical histories, and other sensitive information.

Because the recorded audio files are at risk of containing PII, they cannot be provided to the sponsor as deliverables. However, in a clinical trial, they are technically source documents. Therefore, alternative processes are needed to ensure that the information can be used while protecting patient privacy.

Implementing a standardized transcript certification is a recommended approach as a part of the normal transcript cleaning and redaction step. This involves:

- Listening to the audio file while reading the written transcript.
- Redacting PII and inserting and/or clarifying any missing or erroneous content.
- Inserting a text box at the top corner of the cleaned and corrected transcript to indicate that it has been cleaned of PII and checked and corrected to provide an accurate representation of the interview conversation.

Once these steps are completed, transcripts can act as the official source documents for the study used for coding and qualitative analysis. A PDF version provides the sponsor with a deliverable for the clinical study files.

To ensure the protection of PII, it is also crucial that project teams are properly trained to follow the standardized approach and the task has accountability and transparency. A consistent, documented process is also needed for the destruction of the audio files after study analysis has been completed.

Another common concern is the duration of the interview. Because qualitative research interviews are largely open-ended conversations, they must be carefully managed to ensure the intended content is covered in a reasonable amount of time. This is always a challenge in conducting interviews, but it can be accomplished with a well-constructed interview guide and well-trained and experienced interviewers.

Pilot testing the interview guide can help to assess the timing and identify any unclear questions. This step is particularly important for global studies that require translations of the interview guide and IRB/EC approval across multiple countries. While it may be possible to adjust the interview guide in standalone studies and to have the revisions approved by the IRBs and ECs, clinical trials tend to be global, and the submissions take a long time to prepare and approve. It is very difficult to make alterations once the translations of the interview guide are submitted, because it affects the IRB/EC status for the clinical trial. Therefore, it is important to conduct any pilot testing of the interview guide before the translations and IRB/EC submissions are made to ensure questions are clear and accessible.

Timing of the interviews is another consideration. Generally, qualitative interviews should be conducted after a targeted study visit for two primary reasons:

1. It is important that the patient mindset is not altered by the interview process prior to completion of any clinical outcome assessments (COAs) that are administered at a visit.
2. The accomplishment of a certain visit (e.g., end of treatment period) is useful as a reference point in the interview process. Interview windows should be tailored to align with the specific study design, and often involves considering the anticipated timeline of treatment effects and selecting appropriate intervals for conducting the interviews. For example, if the treatment is expected to have immediate effects, interviews should be conducted shortly after treatment administration. If the treatment's impact is expected to manifest gradually over time, it is better to conduct interviews at intervals that capture this progression. Timing considerations should also take into account the burden placed on participants, especially for those who may have significant study-related activities.

Two Types of Embedded Interviews

One-time interviews (cross-sectional) ask patients about their recent experience and can include retrospective experience (e.g., before the study, earlier events in the study).

Repeated interviews (longitudinal qualitative research) ask patients for their recent experience and changes since their last interview.

Another common concern that arises when planning for interviews is the potential for artificially inflating AE reporting for the clinical trial. Although interviewers may hear about the same AEs that were reported to the site staff, it is also possible that interviews can reveal AEs previously unknown to the site team.

To address this challenge, it is important to develop methods that supplement the existing AE reporting process established within the clinical trial. These methods should not duplicate or run counter to the standard processes for reconciliation and monitoring already in place. Rather, they should dovetail with existing processes to ensure efficient and accurate AE reporting.

All interviewers should be trained to recognize and properly process the communication of potential AEs that are discovered during the interview process. A small amount of descriptive information should be collected that can be communicated to the site staff. Site investigators can then assess the events and determine the appropriate course of action based on their expert judgment and knowledge of the trial's protocol.

This approach ensures that all potential AEs are properly evaluated and reported in accordance with regulatory requirements using the reporting system and medical training already in place. Unlike standalone and associated interview study designs, the qualitative interviewers in embedded interview studies do not "report" but rather communicate into the existing system.

3. QUALITY CONTROL AND TRAINING

Clinical trials are usually global, and interviews (and sometimes site trainings) must be conducted in native languages. As a result, managing, training, and monitoring site trainers and interviewers from diverse cultures, backgrounds, and experiences can pose challenges. Using well-trained bilingual interviewers with appropriate qualitative interview backgrounds and experience is key. These skilled professionals possess the linguistic proficiency required to clearly communicate with study participants, while also demonstrating expertise in conducting interviews that explore and accurately capture the more complex details of patients' experiences.

Consistency and reliability throughout the interview process is important. While training and monitoring the interviewer team is a standard good practice in any qualitative research, EEIs present additional considerations because the timing of the interview depends on the flow of patients through clinical trial milestones. This can result in long periods of time elapsing between an interviewer's training, the first interview and subsequent interviews. Interviewers may also be from a variety of different countries, and interview staff may change over the duration of the clinical trial. Therefore, more individualized training is needed, ideally close to the time of the interviews. If the trial is extended or if the interview guide is changed, repeat trainings may be required.

Quality control and interviewer monitoring—involving a senior interviewer or trainer evaluating the audio of an interview session against a defined set of core competencies—is another key step to ensure global consistency and adherence throughout the data collection process. With active monitoring systems, variations can be swiftly identified and interviewers can be counseled. Monitoring helps overcome challenges associated with cross-cultural diversity and facilitates reliable and high-quality data collection while respecting cultural norms and contextual differences within participating countries.

Consistency and quality control concerns also extend to coders. Due to the variability of when patients reach milestones and participate in interviews, long periods of time may lapse between training and a coder's work on a transcript. The volume of data generated by EEI studies requires multiple coders to work over extended periods of time, which may result in inconsistencies. Training and individually monitoring each coder is necessary to foster a uniform approach and ensure accuracy and consistency over time. This requires a person skilled in qualitative data management to train, monitor and periodically assess coding quality. During the monitoring process, individual feedback sessions can provide tailored guidance to resolve any discrepancies, clarify misunderstandings, and optimize coding accuracy. Metrics, such as inter-coder agreement, can be assessed at the end of the coding process to evaluate the degree of consensus among coders.

4. OPERATIONAL STUDY MANAGEMENT

To minimize the risk of issues and disruptions, EEIs must be designed with the end in mind and key interview activity elements detailed in the clinical protocol. When key elements are missing or too strictly defined, some embedded studies have faced the need to amend the protocol, and some have had key interview activities truncated in unintended ways. An experienced qualitative research vendor needs to be brought online and ready to start work before the clinical trial protocol and consent forms (or amendment documents) are finalized to provide input on the protocol. A few examples of important elements to build flexibility around include:

- The number of patients to be interviewed: the participation rate varies from study to study and depends on many factors that are difficult to predict in advance.
- The interview window: some participants may cancel the interview at the last minute and may need to be excluded or rescheduled after the defined interview window; this requires discussion with the sponsor.
- The conduct of the interview: the protocol must clearly specify that non-participation in the interview study does not constitute reporting of a protocol violation.

The next critical activity is interview guide development, allowing sufficient time for reviews, pilot testing, and revisions before translation work begins. Timelines and expectations between the qualitative interview team, the sponsor and the CRO should be clear so that the translations can be provided in time for IRB/EC submissions.

Collaboration with the CRO is also necessary to set up the tracking systems. This activity should start when patients begin to enter the study, even if their interview window comes months later at the end of their treatment. The site training slides should be developed and reviewed by the sponsor and the CRO so early statements can be made as appropriate during site activation. Specific training on how sites can connect their patients to the interview team is completed later, but before the first patients come to their interview window. Good communication is essential to ensure the right activities are accomplished at the right moment so that patients don't miss their interview windows.

Overview of the Evidera Model

Qualitative interviews play a crucial role in capturing patient experiences and perspectives, thereby enhancing the understanding of treatment efficacy and patient-reported outcomes. These interviews offer additional unique benefits when conducted within the context of a clinical trial.

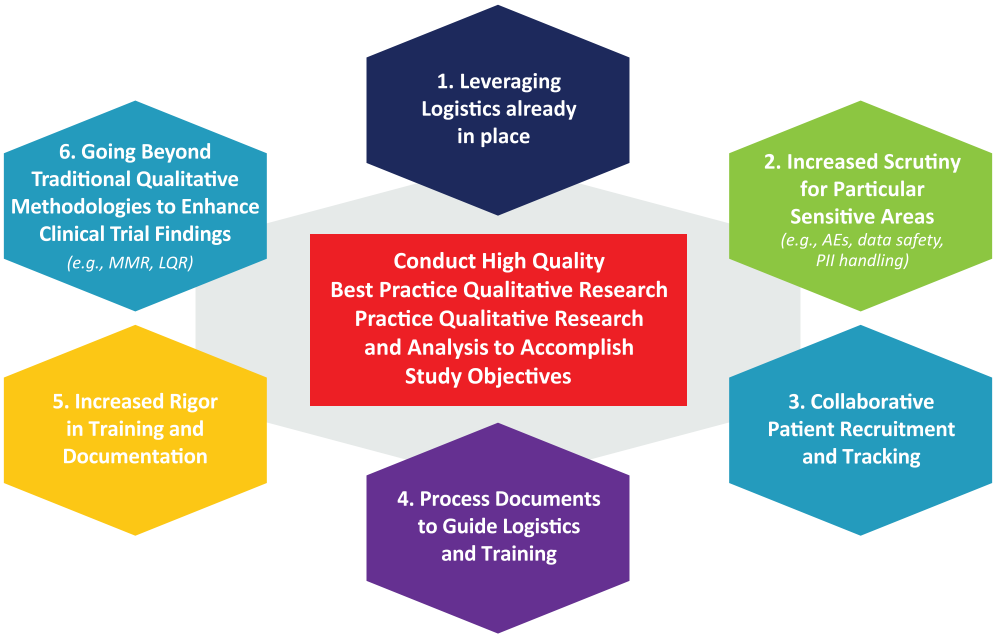

Figure 2: Model for EEI Implementation

Evidera's model encompasses six key EEI implementation elements to help ensure successful execution of interview studies within a clinical trial program.

1. **Leveraging logistics already in place**
   By leveraging existing clinical trial logistics, such as the study protocol and forms, IRB/EC submissions, and site recruitment and contracting, time and resources are optimized and redundant activities minimized.
2. **Increased scrutiny for particularly sensitive areas**
   To ensure the privacy and security of PII, applying strict management protocols including restrictions on access, secure storage, and documented destruction is recommended. It is important to collaboratively develop agreements about AE communication for each study to avoid any artificial inflation of AE reporting.
3. **Collaborative patient recruitment and tracking**
   Collaboration between the study sponsor, CRO and research sites is essential to enable a synchronized approach to planning for interview windows as patients progress through the study at each site. Rigorous tracking in concert with existing sponsor and/or CRO tracking systems is necessary to ensure patients do not miss their interview window.
4. **Process documents to guide logistics and training**
   Process documents are critical for guiding the logistical aspects of EEIs that are not explicitly outlined in the clinical trial protocol. This is especially important for unusual elements, or where multiple stakeholders have concerns about the process and how it will impact the trial procedures and sponsor's SOPs (e.g., communication about AEs, handling of identifying information for patients). Process documents provide information, clarity on expectations and agreements, and directives for training the project team and site staff. Gaining sponsor's agreement to the process ensures that everyone involved in the study is on the same page. These documents can then be added to the clinical trial files to maintain a record of how particular study activities were carried out, and how confidentiality and compliance was achieved.
5. **Increased rigor in training and documentation**
   Rigorous training programs are essential to ensure data quality and reliability. Training programs are conducted for sites, interviewers, simultaneous interpreters, and coders, and ensure that all are proficient in conducting the interviews and emphasize the importance of accurate documentation. Training logs are maintained to document training completion.
6. **Advanced methodologies to enhance clinical trial findings**
   Analytic methods such as mixed methods research (which combines qualitative data from the interviews with quantitative data from the clinical trial) are used to enhance study findings and provide supporting evidence for the study endpoints. When a more comprehensive understanding of evolved experiences and perspectives between two timepoints are helpful, longitudinal mixed methods analysis, which combines the standard longitudinal quantitative analysis approach with a longitudinal qualitative analysis approach, can also be considered. Quantitative data provides numerical change data (e.g., change in a COA score based on statistical significance), and qualitative data provides the patients' narratives explaining the context, the nature of the change, and if the change is meaningful to them.

Conclusion

Embedding qualitative interviews into clinical trials has its difficulties, but these can be managed.

Embedding qualitative interviews within clinical trials presents a valuable opportunity to capture patient perspectives and enhance the understanding of treatment outcomes—insights that regulatory bodies value to enhance their decision-making process. However, this integration also brings forth unique challenges related to trial conduct, interview conduct, quality control and training, and operational study management.

While there are challenges associated with conducting qualitative research within the context of a clinical trial, there are also ways these challenges can be met with minimal interference to the clinical trial or the qualitative research process. Evidera's model for EEIs is designed to carry out our qualitative research using best practices while respecting the demands of the clinical trial environment and causing the least amount of interference possible to the clinical trial research program. By employing Evidera's model for conducting interviews within clinical trials, sponsors and sites can navigate and overcome these challenges, and generate meaningful insights to help foster a more patient-centric approach to health care.

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