In-Trial Interview Sample Size: A Review of the Published Literature

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Key takeaways

> This literature review identified **ten publications of Phase 2 and 3 clinical trials that included in-trial interviews** with a **mean interview sample size of approximately 38 participants** (range=11-90)
> **Three studies confirmed the adequacy of the interview sample size through an evaluation of saturation** (with n=12-28 participants)
> **Interview objectives should be considered in the sampling strategy,** such as whether the experiences of patients across all treatment arms, or a specific subset of patients, are important in achieving study objectives
> **Logistical considerations may impact interview sample size,** particularly for large global trials (i.e., country-specific requirements, and interviews conducted in multiple languages)
> **Planning and discussions with all stakeholders are needed** to ensure that the sample size for the interviews achieve the intended objectives within the logistical limitations of the clinical trial

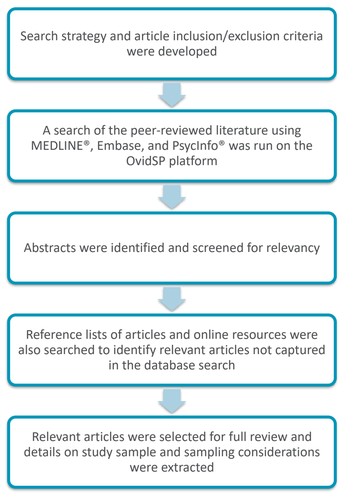
Background and objective

> Patient involvement in drug development is key to ensuring the patient voice informs decision making and is consistently encouraged by regulators.
> Qualitative interviews conducted within clinical trials can provide useful information on patients' trial experience, contribute to understanding of the meaningfulness of changes in disease over the course of the trial, and provide contextual evidence for trial results.[1]
> While in-trial interviews are becoming increasingly popular, guidance and consensus around adequate interview sample sizes are lacking.
> To better understand in-trial interview sampling considerations, the current research was conducted to summarize the sample sizes utilized in published, in-trial qualitative interview studies and considerations for determining sample size and strategy in this context.

Methods

> Qualitative in-trial interview studies published in English between 2012-2022 were identified.
> Selected publications reported on qualitative interview studies conducted within a medical treatment interventional trial (excluding behavioral-based interventions), with trial participants and/or caregivers, and related to patient experiences in the trial (see Figure 1).

Figure 1. Literature review methods



Results

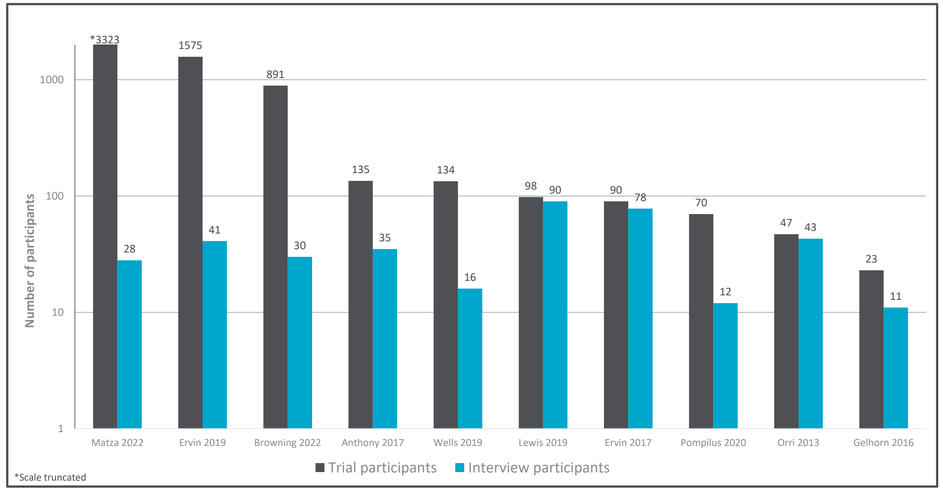
> A total of 168 abstracts were identified from the database search, with ten articles meeting criteria for full-text review.
> Interviews were conducted in Phase 2 or 3 clinical trials across seven different therapeutic areas (i.e., sexual health, mental health, diabetes, inflammatory disorders, oncology, infectious disease, and hematology).
> Interviews aimed to understand changes in disease experience during the trial, understand treatment experience and satisfaction with treatment, and inform measurement strategy (i.e., the appropriateness of patient-reported outcome questionnaires administered in the trial).
  – For one study (Gelhorn, 2016) interview results contributed to the definition of clinically meaningful change that was accepted by FDA
> Clinical trial sample sizes ranged from N=23 to 3,323 and interview sample sizes ranged from N=11 to 90 (mean≈38 and median≈33).
> Most studies (n=6) targeted a subset of trial participants to interview, which made up <1.0%–26% of the total trial population.
> Four studies aimed to interview all trial participants, all of which had trial populations of N<100; 48%–92% of each total trial population ultimately participated in an interview. Missed interviews were reportedly related to trial attrition or lack of interest from the participant or site.
> Three studies reported evaluating and achieving concept saturation to confirm the adequacy of the interview sample size (N=12, N=16, and N=28 interview participants)
> See Table 1 for information on each study's sampling strategy and limitations

Table 1. Summary of publications and sampling data (by article, N=10)

Study and patient population*	Interview/trial sample size (%)†	Sampling strategy	Sampling results and limitations§
Matza 2022[2] Type 2 diabetes	**n=28/3,323 (<1.0%)‡** • All participants on treatment, dosing for participants not specified	• 20-30 participants were targeted from six US-based clinical sites • Only those on the active treatment were considered for inclusion	• Key demographic and clinical characteristics were comparable to full trial sample • **Saturation was considered to have been achieved**
Ervin 2019[3] Type 1 Diabetes	**n=41/1,575 (2.6%)‡** • Placebo: n=14 • Treatment group 1: n=11 • Treatment group 2: n=16	• Targeted English-speaking participants from US, Canada, and UK (20 out of 82 sites) • Sample size based on precedent set by Anthony et. al. 2017 • Proportion of interview participants in each treatment group was comparable to trial (i.e., 1:1:1)	• 43 out of 72 eligible patients (59.7%) agreed to participate (two participants subsequently did not attend interview) • Key demographic and clinical characteristics were comparable to full trial sample • Results stratified by treatment group after unblinding
Browning 2022[4] Mulluscum contagiosum (MC)	**n=30/891 (3.4%)** • Placebo: n=15 • Treatment group: n=15	• Targeted English-speaking participants from a subset of sites (16 out of 55) • Only participants with less than complete lesion clearance at end of study were eligible • Equal representation of both treatment groups	• Small sample size and no racial diversity considered to be study limitations
Anthony 2017[5] Diarrhea	**n=35/135 (25.9%)** • Placebo: n=9 • Treatment group 1: n=9 • Treatment group 2: n=10	• Targeted in a subset of countries (5 out of 12) in an effort to minimize personnel and languages required (i.e., English and German languages) • Proportion of interview participants in each treatment group was comparable to trial (i.e., 1:1:1)	• Results were stratified by treatment group • Key demographic and clinical characteristics were comparable to full trial sample
Wells 2019[6] Hemophilia A	**n=16/134 (11.9%)** • All participants on prophylaxis treatment	• Targeted three countries with the greatest proportion of eligible patients	• Interviews were conducted as a separate study from the trial which may have limited participation by sites and patients • Small sample size and limited ethnic and geographic diversity considered to be study limitations • **Saturation was considered to have been achieved**
Lewis 2019[7] Depression	**n=90/98 (91.8%)‡** Trial 1: n=29/30 • Placebo group 1-2: n=9 • Treatment groups 1-3: n=20 Trial 2: n=61/68 • Placebo group 1-2: n=25 • Treatment group 1: 17 • Treatment group 2: 18	• Targeted all sites/trial participants	• Results were stratified by treatment group • Due to small sample size, data from the two active treatment groups were combined for analysis
Ervin 2017[8] Type 1 and 2 diabetic gastroparesis (DGP)	**n=78/90 (86.7%) (pre-treatment)** **n=51/90 (56.7%) (end of treatment)** • Participant treatment groups not reported	• Targeted all sites/trial participants	• Smaller sample size at timepoint 2 due to attrition (failure to meet randomization requirements, loss to follow-up) • Several interviews not included in analysis due to low level of English proficiency • Results were pooled across treatment arms • Saturation was anticipated but not specifically monitored
Pompilus 2020[9] Ankylosing spondylitis, Crohn's disease, PsA psoriatic and rheumatoid arthritis	**n=12/70 (17.1%)** • All participants on treatment, dosing regimen for participants not specified	• Targeted a sub-sample of patients who agreed to participate • Targeted mix of demographic characteristics	• **Saturation was considered to have been achieved**
Orri 2013[10] Female sexual arousal disorder (FSAD)	**n=43/47 (91.5%)** • All participants received placebo and three separate doses of the trial treatment (crossover study with four treatment periods)	• Targeted all sites/trial participants	• Interviews conducted after all treatment periods and participants reported on each treatment period; results stratified by treatment period after unblinding • Small sample size in some categories (defined as the positive responses by treatment period), considered a limitation to data interpretation
Gelhorn 2016[11] Carcinoid syndrome and diarrhea	**n=11/23 (47.8%)** • Participant treatment groups not reported	• All sites invited to participate; 2 out of 8 agreed • Participants needed to be proficient in English • Participants with an impairment that would interfere with participation (e.g., cognitive) were not eligible	• 11 out of 16 eligible patients (68.7%) agreed to participate • Small sample size considered a limitation in drawing conclusions of treatment efficacy • Saturation was evaluated but results not reported

*Articles presented descending order of trial sample size;
†Number of patients interviewed out of the number of patients randomized
‡As reported by the authors;
§The combined N from two trials

Figure 2. Clinical trial sample size versus interview sample size



*Scale truncated

Conclusions

> In-trial interviews can be incorporated into clinical trials of any sample size, across a wide variety of therapeutic areas
> It is not always necessary to include the full trial participant sample in interviews to obtain sufficient qualitative data, particularly when the trial sample size is large (i.e., >100). In these instances, the following factors should be considered to help determine appropriate interview sample size:
  – **Interview objectives**: Interviews aimed at exploring treatment experience across treatment arms will require a robust sampling strategy to ensure adequate representation of each arm, particularly when the study is blinded. Conversely, for studies aimed to evaluate content validity of a questionnaire or to understand a specific aspect of a disease (e.g., symptom concepts) a more limited number of interviews can be sufficient. In addition, if interview objectives focus on specific experiences of a certain patient subgroup in the trial, this would impact sampling strategy and, ultimately, sample size.
  – **Trial sample characteristics**: The ethnic, demographic, health, and geographic diversity of the trial sample should be considered in the sampling approach to ensure results can be generalizable to the full trial sample; for example, targeting a sample of participants from select sites that represent patient ethnicities and geographic regions of the trial.
  – **Study methodology**: Whether the interviews are embedded within the clinical trial itself or as a separate study from the trial will affect interview participation. If interview participation is sought from a larger proportion of trial participants it is more ideal to include interviews in the trial protocol and have them conducted within a short time frame of the last study visit, to help minimize patient (or site) dropout due to lack of interest or loss to follow up.
> Stakeholders need to plan an in-trial interview sampling strategy that will be robust enough to address the interview objectives and generalizable to the target patient population, while also weighing any methodological and logistical challenges to participation.

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