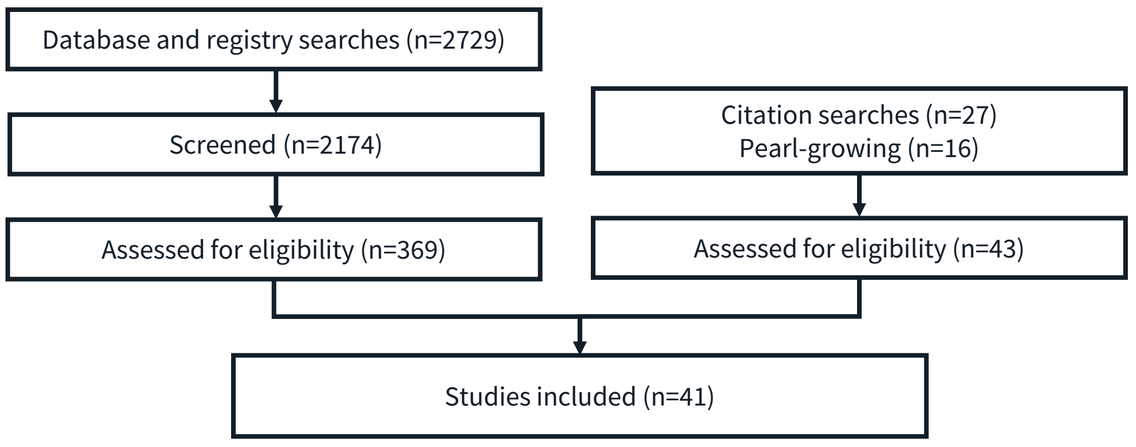
Qualitative research methods and Bayesian elicitation for evaluating the effect of treatment in clinical trials for rare diseases: a scoping review

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Qualitative methods and expert elicitation enrich rare disease trials but managing participant and expert bias pose ongoing challenges.

Figure 1: PRISMA Flow Diagram



Introduction

Collecting qualitative information in clinical trials has the potential to provide rich insights into treatment effects that quantitative outcomes can fail to capture[1]. This is of particular value in rare diseases with heterogeneous symptoms, limited clinical knowledge, lack of validated disease-specific outcome measures, and constrained numbers of potential participants[2].

Expert elicitation captures prior beliefs regarding efficacy – which is typically qualitative information[3] and may be facilitated by qualitative methods. When combined with patient health data using Bayesian methods, these insights can reduce sample size requirements and improve trial feasibility[4].

This scoping review identifies (1) qualitative research methods used to evaluate treatment efficacy and (2) how prior beliefs are currently elicited for efficacy analysis, in rare disease trials.

Box 1: Quotes from studies

On bias of participant outlooks:

"***Increased healthcare interactions and the novel nature of the treatment might contribute to more positive outlooks. It is important to consider this context when interpreting the findings of this study[5]***

On regulatory demand for qualitative research:

"***Regulatory authorities requested qualitative data to further understand the neurocognitive changes observed by the investigators through the clinical trials[6]***

On the relevance of expert elicited priors:

"***Experts will have clinical experience of using both drugs and observational data sources exist to inform prior opinion[7]***

Methods

A scoping review of medical literature was conducted by searching databases (Medline, Web of Science and the Cochrane Library) and clinical trial registries (clinicaltrials.gov, EU CTR and ISRCTN). Protocols, results papers and Statistical Analysis Plans were included if they reported the use of qualitative or Bayesian elicitation methods for rare disease clinical trials evaluating treatment efficacy. A two-stage selection process was applied by first reviewing titles and abstracts and then full text for eligibility. Data on study characteristics and methods were extracted from eligible articles after the full review. Screening and data extraction was performed by two reviewers. Extracted data were synthesized using descriptive statistics for quantitative data and content analysis for qualitative data.

Early results

Most eligible studies were conducted in Europe, about a pharmaceutical intervention and for a rare genetic condition. Preliminary results are presented on 7/30 qualitative studies and 5/11 elicitations:

- Primary motivations for qualitative research were to capture individualised outcomes, address the lack of disease-specific measures, regulatory demand and to interpret and triangulate trial findings.
- Qualitative research captured meaningful improvements, positive and negative treatment impacts and information quantitative measures missed.
- Studies identified how patient outlook potentially influences their responses.
- Qualitative research contributed to improved understanding of treatment, validated quantitative results and further research recommendations.
- Primary motivations for elicitation were to incorporate existing knowledge, inform trial design and were often guided by similar trials.
- Expert consensus was commonly achieved, but uncertainty remained about absolute treatment effects.
- Researchers used elicitation to inform sample sizes, though targets frequently remained infeasible or elicited priors represented unachievable sample sizes.
- While not all studies transparently specified their elicitation, robust elicitation provides an exemplar for future trials, methodological insights and highlights remaining uncertainties.

Discussion

These preliminary findings show qualitative research and elicitation bridge data gaps in rare disease trials by leveraging insights on experience and expertise that quantitative outcomes often lack. The approaches have been used to address challenges of small sample sizes, heterogeneity and lack of existing data. A shared caveat highlighted in this work is their vulnerability to subjective factors – the influence of outlook and overconfidence on patient and clinician responses – which demonstrates a need for frameworks to address the unique challenges of rare disease trials.

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