PCR101

Patient-Centric Approach and Personalized Clinical Trials to Increase Patients Engagement in Drug Development: Insight from a Targeted Literature Review

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Background

- In recent years, the process of conducting clinical trials for drug development has undergone significant changes for three main reasons:
  - Inefficiency and high cost of classic drug development process (i.e., Phase I, II, III clinical trials) has become unsustainable.[1, 2]
  - Several biomedical discoveries such as biomarkers or genetic markers have forced a change in the classic ways of conducting and designing clinical trials.
  - The growing emphasis on patient-centered drug development has led to important changes in the conduct of trials, including the development of personalized outcomes and the integration of patient perspectives into all stages of trial design.
- Researchers are seeking input from patients and their caregivers and using their insights to guide the decision-making process.
- Patient-centric trials refers to a research approach that prioritizes patients in their design and execution.[3]
- The aim of patient-centric trials is to improve the overall experience for participants and ultimately advance healthcare by producing more meaningful and applicable results.[3,4]

Objective

- To identify factors that could enhance implementing patient-centric approaches and personalized clinical trials in drug development.

Methods

Study Selection

- Relevant studies published in the last 10 years were identified by searching Embase (via OvidSP) from January 1, 2013 to February 28, 2023 using predefined search strategies. Additionally, hand searches were conducted on selected websites and Google Scholar.
  - **Inclusion Criteria**
    - Publications describing novel trial designs or novel methods of conducting clinical trials as potential alternatives to the traditional approach of designing and conducting clinical trials.
    - Publications focused on the benefits of using novel designs and how they can improve clinical drug development programs.
    - Publications reporting strengths and limitations for inclusion of such trials in clinical drug development programs.
    - Publications describing perceptions of regulatory bodies (i.e., United States Food and Drug Administration [FDA] and European Medicines Agency [EMA]) on the results of these novel methodologies.
  - **Exclusion Criteria**
    - Records published more than 10 years ago (pre-2013). These publications were considered too dated to discuss “novel” or “innovative” trial designs in rapidly evolving research space.
    - Publications describing methods for very novel, “home-grown” study designs that have not been commonly reported in the literature (i.e., less than three publications have described them).

Evidence Synthesis

- The findings of this review are presented descriptively. Based on the studies included, we categorized factors into the following categories:
  - **Patient Engagement and Trial Planning**
  - **Novel Trial Design**
  - **Innovations in Biotechnology and Information Technology**
  - **Special Contexts**
- Within each category, relevant studies were described, compared, and discussed in context to the aim of the review. Links were made between the results of included studies and their conclusions in relation to the objectives of the review.

Results

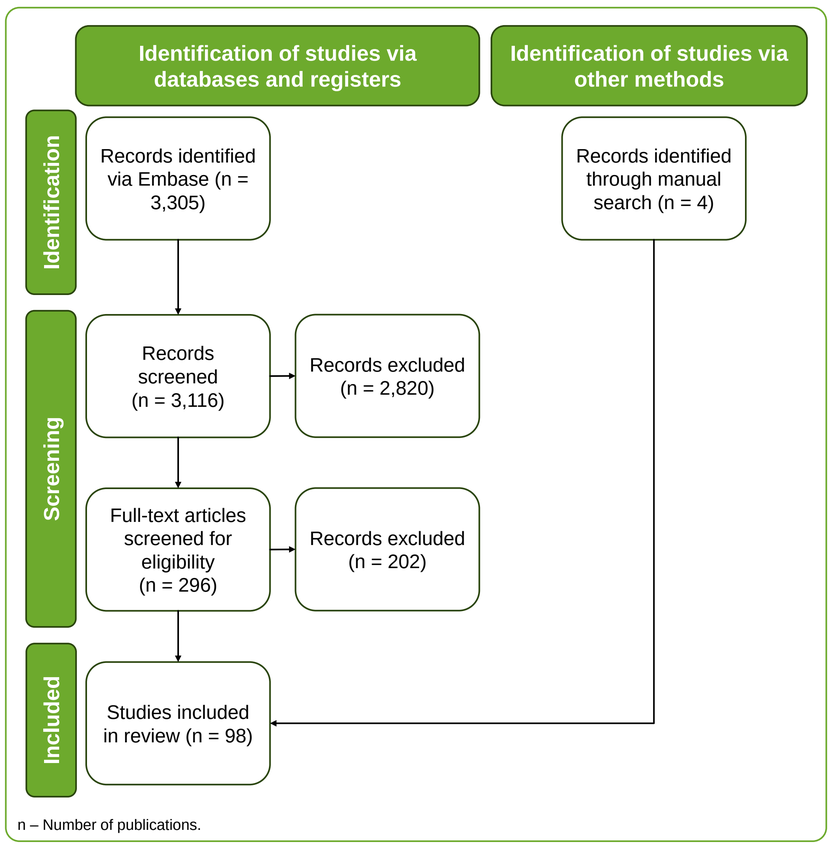
Study Selection

- A total of 3,309 abstracts were identified from the review including 3,305 records via Embase, and four additional records through hand searching (**Figure 1**). Following full-text screening, 98 records were included in the qualitative synthesis.

Study Characteristics

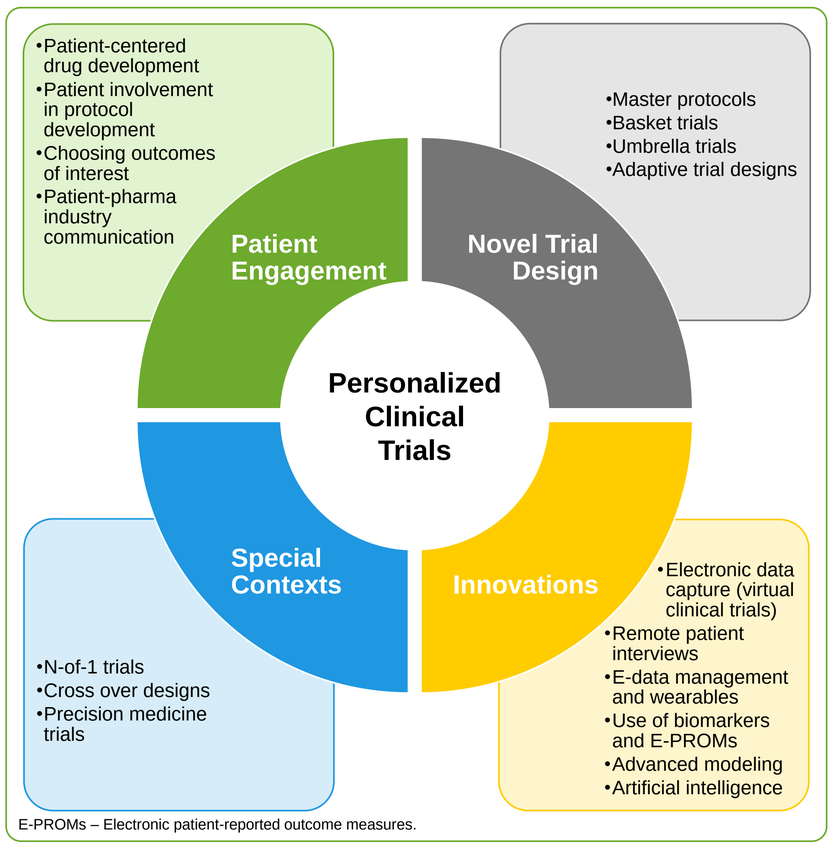
- The most common study design among the included studies was narrative reviews (n = 71).
- Other study designs included systematic reviews, case studies, surveys, cohort studies and clinical trials.

Figure 1: PRISMA Flow Diagram



n – Number of publications.

Figure 2: Factors for Personalized Clinical Trials



E-PROMs – Electronic patient-reported outcome measures.

Factors for Personalized Clinical Trials

- A summary of the factors involved in personalized clinical trials is presented in **Figure 2**.
- **Patient Engagement and Trial Planning**
  - Clinical trials have been influenced by a social transformation in drug research, with a growing emphasis on patient-centered drug development.
  - Patients’ associations have also gained power in pushing their agenda and can work with the pharmaceutical industry, which aids in clinical trial conduct.[5-8]
- **Novel Trial Design**
  - **Master protocols** (including basket, umbrella trials, and platform trials) and adaptive trial designs are major innovations in clinical trial research. They offer flexibility and innovations such as using precision oncology to identify histology-agnostic trials (i.e., basket trials), to optimize conduct from centralized screening for multiple biomarker-enriched cohorts (i.e., umbrella trials), and to establish a common trial infrastructure (platform) to enable evaluation of multiple interventions (i.e., platform trials).
  - **Adaptive trial designs**, on the other hand, are useful to optimize clinical trials: optimal dose, optimal population, sample size; and to mitigate risks and costs of clinical development programs.
  - Sequential designs and other adaptive trial designs naturally fit into the Bayesian statistical paradigm that allows incorporation of accumulating trial data to enable important modifications to the trial designs.
  - Other designs include response adaptive randomization, adaptive enrichment designs, and seamless designs.
    - Cluster, factorial, and pragmatic designs may also be used in certain contexts.[20-22]
- **Innovations in Biotechnology and Information Technology**
  - The use of electronic data capture has transformed the way we interact with patients during clinical trials. Methods such as at-home patient interviews have led to decentralized and virtual clinical trials.[9,10]
  - E-data management increases efficiency for on-time decision making by means of linking to electronic patient-reported outcome measures and wearables. [11,12] The discovery of numerous biomarkers and genetic markers has had major consequences on the way trials are conducted.[13]
  - Advanced modeling has been developed along with access to big data, most of which are from machine learning systems. Models extensively use Bayesian approaches to include patient characteristics and assess causality at an individual level.[14-16]
  - An important use of modeling is for protocol development and trial planning. Artificial intelligence is present at all stages of drug development to a certain degree, guiding researchers and providing relevant information to make rapid decisions.[17-19]
- **Special Contexts**
  - Key innovations in special contexts included patient-centered clinical trials, rare disease clinical trials, n-of-1 clinical trials with cross-over design, and precision medicine trials.[23]

Conclusions

- Innovations in patient involvement in clinical trials, novel trial designs and using biotechnology and information technology are being utilized to achieve patient-centric trials.
- Taken together, these innovations increase the efficiency of clinical trials in identifying, selecting, and evaluating new drugs, as well as being more patient-centered.
- Future advancements in clinical trials in the context of drug development programs is anticipated to be driven by rapid progress in biotechnology and information technology, and more extensive use of real-world data for advanced modeling.
- Additionally, a necessary progressive social transformation to personalized medicine can further improve clinical trials.

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Authors report employment with Evidinno Outcomes Research Inc.

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