ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/25aug327

Demystifying Clinical Trials in Oncology: A Foundational Guide for Students and Beginners with Emphasis on LMICs

Pournima Kale[1]; Praghnya Tejale[2]; Ashok Diwan[3]; Vijay Mahobia[4]; Nihal Padole[5]

[1,2,3,4]Department of Radiation Oncology, Government Medical College and Hospital, Nagpur, Maharashtra, India
[5]Department of Head and Neck Oncosurgery, National Cancer Institute, Nagpur, Maharashtra, India

Publication Date: 2025/08/16

Abstract: Clinical trials form the foundation of evidence-based medicine (EBM), especially in the field of oncology, where ongoing innovations in surgery, chemotherapy, radiotherapy, immunotherapy, and targeted agents are transforming patient outcomes. These trials not only evaluate the efficacy and safety of novel interventions but also serve as a critical tool to establish standard-of-care protocols. However, a major challenge remains: while the global cancer burden is rapidly increasing, the participation and representation of patients from low- and middle-income countries (LMICs) in clinical research remain disproportionately low.

This mismatch is concerning, as LMICs now account for more than 70% of global cancer deaths, yet contribute to less than 10% of oncology clinical trials. Contributing factors include limited infrastructure, inadequate funding, ethical and regulatory hurdles, low research literacy, and logistical challenges. Moreover, many international trials conducted in high-income countries often lack external validity for LMIC settings due to differences in patient demographics, comorbidities, treatment compliance, and access to care.

This paper offers a comprehensive, beginner-friendly overview of clinical trials, designed specifically for medical students, residents, and early researchers in oncology. It systematically explains essential trial concepts including phases (I–IV), trial design (randomization, blinding), sample size estimation, ethical considerations, analysis methods, and endpoint definitions (e.g., OS, PFS, QoL). Additionally, the paper highlights common biases in trial conduct and interpretation, and the importance of context-specific trials in ensuring equitable global oncology care.

By focusing on practical knowledge and conceptual clarity, this review aims to empower budding clinicians and researchers—especially from LMICs—to not only interpret existing literature critically but also to initiate, design, and contribute to clinical trials that are ethically sound and regionally relevant. Bridging this gap is essential for advancing oncology care in resource-constrained settings and ensuring that progress in cancer treatment benefits all populations equitably.

Keywords: *Clinical Trials, Lmics, Understanding Research Methodology, Oncology Trials.*

How to Cite: Pournima Kale; Praghnya Tejale; Ashok Diwan; Vijay Mahobia; Nihal Padole (2025), Demystifying Clinical Trials in Oncology: A Foundational Guide for Students and Beginners with Emphasis on LMICs. *International Journal of Innovative Science and Research Technology*, 10(8), 415-418. https://doi.org/10.38124/ijisrt/25aug327

I. INTRODUCTION

The global cancer burden is increasing at an alarming rate, with GLOBOCAN 2020 reporting over 19.3 million new cancer cases and 10 million cancer-related deaths annually [1]. Notably, over 70% of these cases are now seen in low- and middle-income countries (LMICs), where healthcare systems are often underfunded, fragmented, and unequipped to manage the complexity of cancer care [2]. Despite this disproportionate burden, the vast majority of clinical trials and evidence-based guidelines originate from high-income countries (HICs), where disease patterns, patient demographics, and healthcare resources differ markedly [3]. Applying this data uncritically in LMICs may result in inequitable or ineffective outcomes, especially due to regional differences in genetic background, co-morbidities,

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/25aug327

nutritional status, late-stage presentation, and treatment accessibility [4].

This profound disparity underscores the urgent need for region-specific research that reflects the real-world context of LMICs. It is therefore imperative for oncologists, residents, and medical students in LMICs to move beyond passive consumption of external guidelines and actively participate in local clinical trials**.** By doing so, they can help generate data that is relevant, ethically sound, and more applicable to their patient populations, ultimately fostering more equitable global oncology care [5].

.

II. UNDERSTANDING CLINICAL TRIALS: CORE CONCEPTS

A. What is Clinical Trial?

A clinical trial is a prospective study that evaluates the safety, efficacy, or diagnostic value of a medical intervention against a standard treatment, placebo, or no intervention [6]. These trials are conducted in a regulated, ethical manner under the supervision of a principal investigator and monitored by Institutional Review Boards (IRBs) to safeguard participant rights.

B. Importance in Oncology

In oncology, clinical trials validate new chemotherapeutic agents, radiation protocols, surgery combinations, immunotherapies, and supportive care strategies. The sensitive nature of cancer care demands rigorous evidence before adopting new modalities.

III. TYPES AND DESIGNS OF CLINICAL TRIALS

The Table 1 outlines the five major types of clinical trials conducted in oncology. Prevention trials focus on avoiding cancer development, while screening trials aim to detect cancer early. Diagnostic trials assess new tools for accurate diagnosis, and treatment trials evaluate novel therapeutic approaches including drugs and radiation. Supportive care trials seek to enhance patient comfort and manage side effects during or after cancer treatment.

Table 1 Types of Clinical Trials

Type	Description
Prevention Trials	Study agents that prevent cancer development
Screening Trials	Determine early detection methods
Diagnostic Trials	Validate novel diagnostic tests
Treatment Trials	Test new drugs, RT protocols, surgery techniques
Supportive Care	Improve quality of life and manage symptoms

➢ *Observational vs Interventional Designs*

- *Observational:* No intervention; includes descriptive and analytical studies
- *Interventional:* Includes randomized or non-randomized allocation of treatment

IV. PHASES OF CLINICAL TRIALS IN ONCOLOGY

There are four phases of clinical trials in oncology, each with distinct objectives and participant sizes. (Table 2)

➢ Phase I trials assess safety, tolerable dosage ranges, and pharmacokinetics in a small group (typically 20–100 participants).
➢ Phase II trials evaluate the efficacy and monitor side effects in a slightly larger cohort.
➢ Phase III trials compare the new intervention with standard treatment in a large population to confirm effectiveness.
➢ Phase IV trials are conducted after regulatory approval to monitor long-term safety and real-world effectiveness in the general population

Table 2 Phases of Clinical Trials

Phase	Objective	Participants
I	Safety, dose, pharmacokinetics	20–100 healthy/affected
II	Efficacy and side effects	100–300 patients
III	Confirm effectiveness vs standard	300–3000+ patients
IV	Post-marketing surveillance	Large population

➢ In Radiation Oncology**,** most trials begin at Phase II/III due to established safety profiles of techniques like IMRT, SBRT, etc.

V. KEY ELEMENTS IN CLINICAL TRIAL DESIGN

A. *The PICO Framework*:

A Foundation for Evidence-Based Clinical Trials

The PICO framework is a structured approach used to formulate clear, focused, and answerable clinical research questions. It ensures that all critical elements are considered during the conceptualization of a trial and guides literature search, study design, and data interpretation.

P – Population - The group of patients or population under investigation, defined by disease, stage, age, or other relevant characteristics.

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/25aug327

I – Intervention - The treatment, procedure, diagnostic test, or exposure that is being evaluated**.**

C – Comparator - The control or comparison group, which may receive a placebo, standard treatment, or no intervention.

O – Outcome - The specific measurable effect of the intervention, such as symptom improvement, tumor response, survival, or quality of life.

B. Sample Size Estimation

Accurate sample size reduces errors:

- Type I Error (α): False positive (≤ 5%)
- Type II Error (β): False negative (≤ 20%)
- Power ≥ 80%
- Calculated based on anticipated effect size, dropout rates, and variability.
- Example: For conducting a Phase III trial comparing: Concurrent chemoradiotherapy (CRT) vs radiotherapy alone in locally advanced cervical cancer
- Objective: To detect a 10% improvement in 3-year disease-free survival (from 50% to 60%)
- Parameters:

- α = 0.05 (95% confidence)
- Power = 80% (β = 0.2)
- Effect size = 10% difference
- Dropout rate = 10%

- Result: Using sample size calculation

- Required sample = 350 patients per arm
- Total = 700 patients + 10% for dropouts = 770 patients

This ensures your trial can detect the expected benefit with confidence, while accounting for real-world losses.

VI. RANDOMIZATION AND BLINDING

- *Simple Randomization:* Coin toss method
- *Block Randomization:* Maintains balance between groups
- *Stratified Randomization:* Ensures balance for prognostic factors

A. Types of Blinding:

- *Single-blind:* Participant unaware
- *Double-blind***:** Participant + Investigator unaware
- *Triple-blind:* Participant + Investigator + data analyst unaware

Randomization eliminates selection bias, while blinding reduces performance and measurement biases.

VII. ETHICAL CONSIDERATIONS

A. Informed Consent

Important aspects include:

- Purpose, risks, and benefits
- Alternative treatments
- Right to withdraw
- Confidentiality
- Compensation for harm

B. Institutional Review Board (IRB)

Every study must receive ethics approval. This is crucial in LMICs where vulnerable populations must be protected from exploitation.

VIII. BIAS AND STATISTICAL ANALYSIS IN TRIALS

A. Common Biases:

- *Selection Bias:*

This occurs when participants selected for the trial are not truly representative of the general population or are not equally distributed between comparison groups.

- *Performance Bias*:

This arises when differences in care apart from the intervention affect outcomes. It happens when participants or caregivers know which group is receiving which treatment.

- *Attrition Bi*as:

This occurs when there are uneven dropout rates between groups, and those who drop out are systematically different from those who complete the trial

- *Reporting Bias*:

This bias arises when positive, favourable results are selectively reported, while negative, or non-significant findings are omitted

- *Confounding Bias:*

Occurs when a third variable (confounder**)** is associated with both the intervention and the outcome, thus distorting the true effect of the intervention.

B. Analysis Methods

- *Intention-to-treat (ITT)**:*** Preserves randomization integrity
- *Per-Protocol Analysis**:*** Only includes adherent subjects

IX. END POINTS IN CANCER TRIALS

These endpoints help evaluate treatment effectiveness and patient impact in cancer trials. (Table 3)

A. Overall Survival (OS):

Time from trial enrolment (randomization) until death from any cause. It is the gold standard endpoint in oncology.

B. Progression-Free Survival (PFS):

Duration during which a patient lives with cancer without disease worsening. Useful when OS takes too long to measure.

C. Disease-Free Survival (DFS):

Time from treatment completion to any recurrence (local or distant) or death. Often used after curative treatment.

ISSN No: -2456-2165 https://doi.org/10.38124/ijisrt/25aug327

D. Local Disease-Free Survival (LDFS):

Time until local tumor recurrence or death**.** Common in trials focused on local therapies like radiation.

E. Quality of Life (QoL):

Assesses patient well-being, symptoms, and daily functioning using validated questionnaires (e.g., EORTC QLQ-C30).

Table 3 End Points in Cancer Trials

Endpoint	Definition
Overall Survival (OS)	Time from randomization to death
Progression-Free Survival (PFS)	Time without disease progression
Disease-Free Survival (DFS)	Time without recurrence or metastasis
Local Disease-Free Survival (LDFS)	Time without local recurrence
Quality of Life (QoL)	Measured via standardized tools (e.g., EORTC QLQ-C30)

X. CHALLENGES IN CLINICAL TRIALS

Table 4 Challenges in Clinical Trials

Challenge	Explanation
Limited funding	Lack of national trial grants
Inadequate infrastructure	Poor lab, data storage, monitoring systems
Ethical hurdles	Less active IRBs, vulnerable populations
High dropout rates	Travel costs, social stigma, economic factors
Late-stage presentation	Reduced eligibility due to advanced disease
Low research literacy	Among both patients and junior doctors

Despite these challenges, LMICs offer untapped potential due to high disease burden and diverse patien populations[7]

XI. CONCLUSION

Understanding clinical trials is no longer optional — it is essential for every budding oncologist. Especially in LMICs, where the burden is highest, we must build robust, ethical, and relevant research ecosystems. With proper education and support, medical students and young researchers can become the innovators who bridge this evidence gap and contribute meaningfully to global oncology.

REFERENCES

[1]. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide. *CA Cancer J Clin*. 2021;71(3):209–249. https://doi.org/10.3322/caac.21660

[2]. Atun R, Jaffray DA, Barton MB, et al. Expanding global access to radiotherapy. *Lancet Oncol*. 2015;16(10):1153–1186. https://doi.org/10.1016/S1470-2045(15)00222-3

[3]. Unger JM, Cook E, Tai E, et al. The role of clinical trial participation in cancer research: Barriers, evidence, and strategies. *Am Soc Clin Oncol Educ Book*. 2016; 35:185–198. https://doi.org/10.14694/EDBK_159121

[4]. Sathian B, et al. Relevance of Clinical Trials in LMICs: The Missing Middle. *J Clin Diagn Res*. 2021;15(3):BE01–BE05. https://doi.org/10.7860/JCDR/2021/46426.14757

[5]. Subramaniam S, Aaltonen K, Kengne AP, et al. Building research capacity in LMICs for equitable cancer care: Challenges and solutions. *Lancet Glob Health*. 2023;11(5): e695–e703. https://doi.org/10.1016/S2214-109X(23)00100-6

[6]. Friedman LM, Furberg CD, DeMets DL. *Fundamentals of Clinical Trials.* Springer; 2010.

[7]. Sathian B, et al. Relevance of clinical trials in LMICs: The missing middle. *Journal of Clinical and Diagnostic Research.* 2021;15(3):BE01–BE05.