# Oncology-specific Considerations in Conduct of Pragmatic Trials: Lessons Learnt From ClinicalTrials.gov Registry Audit

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## INTRODUCTION

- Pragmatic clinical trials in oncology assess real-world effectiveness, focusing on typical clinical settings and diverse patient populations.[1]
- Unlike traditional RCTs, pragmatic trials generate real-world data that reflect treatment performance in broader, more diverse populations.
- Integrating pragmatic elements in drug development can expedite novel therapies, ensuring findings are applicable to clinical practice and meet regulatory standards.[2]
- Limited literature on conducting oncology pragmatic trials creates challenges in developing robust methodologies for clinical decision-making.
- Systematic audits of registered oncology pragmatic trials can reveal methodological insights, best practices, and areas for improvement.

## OBJECTIVES

This registry audit aims to assess the methodological aspects of these trials to inform future real-world evidence (RWE) methodology guidance in oncology.

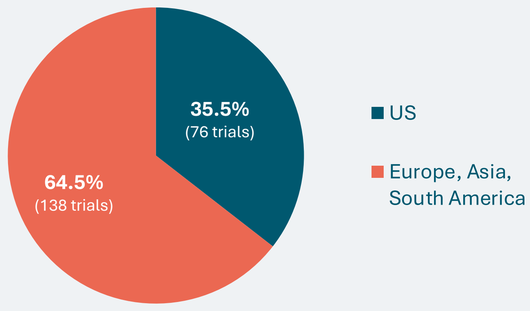
## METHODS

- **Data Source**: Analyzed trials data from ClinicalTrials.gov.
- **Search Terms**: Used the terms “Cancer” and “Pragmatic Trial” to identify relevant studies.
- **Data Extraction**: Generated an Excel spreadsheet with relevant trials, detailing study characteristics.
- **Analysis**: Conducted descriptive analysis on demographics, study design, primary and secondary outcomes, and geographical locations, etc.
- **Data Visualization**: Presented findings using tables, bar graphs, and pie charts.
- **Methodological Mapping**: Compared study designs against the European Medicines Agency (EMA)'s RWE draft reflection paper (2024) to identify inter-regional methodological differences.

## RESULTS

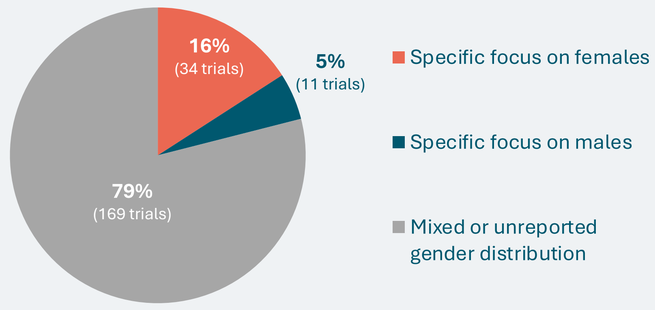
- **Total Trials Identified**: 214 pragmatic trials.
- **Geographical Distribution**:

### Geographical Distribution



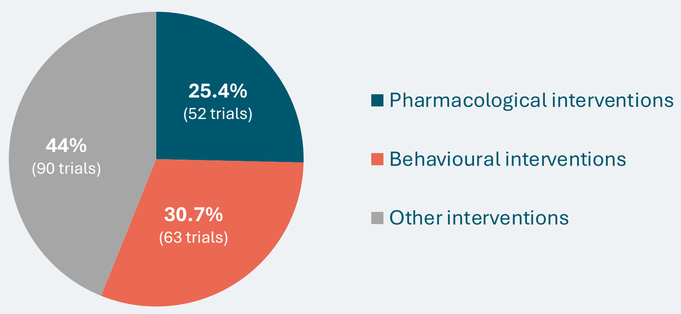

  - Other trials spanned Europe, Asia, and South America, though with fewer numbers, indicating regional gaps in conducting pragmatic trials.
- **Sample Size**:
  - Only 13 trials had a sample size greater than 5000, emphasizing the need for more large-scale pragmatic clinical trials to ensure robust generalizability.
- **Target Population**:
  - **Adults**: 192 of 214 trials (89.7%) targeted adult populations.
  - **Gender**: 34 trials (15.9%) had a specific focus on females, compared to only 11 trials (5.1%) for males, with the remainder involving mixed or unreported gender distribution.

### Gender




  - **Inclusion of Age Groups**: Only 13 trials (6.1%) included participants across all age groups, highlighting an opportunity to include more diverse age demographics in future trials.
- **Trial Phases and Design**:
  - **Late-Phase Trials**: 56 (26.2%) trials were in late phases (Phase III/IV), making them more common than early-phase (Phase I/II) trials, which constituted just 10 (4.7%) of the total.
- **Study Types**:
  - 193 trials (90.2%) employed interventional designs.
  - Single-arm studies: 23 (10.7%)
  - Non-randomized studies: 15 (7.0%)
- **Types of Interventions**:
  - Out of the 205 studies, with ‘Interventions’ data available,
    - Pharmacological interventions: 52 trials (25.4%)
    - Behavioural interventions: 63 trials (30.7%)
    - Other interventions (including MedTech, surgical, and health system interventions): 90 trials (43.9%)

### Types of Interventions




- **Primary Outcomes**:
  - Overall survival was a primary outcome in 9 trials (4.2%).
  - Progression-free survival was a primary outcome in 8 trials (3.7%).
    - This signals an opportunity to further refine outcomes in line with RWE frameworks to better capture long-term patient outcomes and quality of life.
- **Methodology Mapping:**
  - Comparison of the trial methodologies against EMA’s 2024 RWE draft reflection paper revealed a lack of detailed reporting on key methodological elements, including bias correction techniques, contributing to minimal new insights. This gap underscores the need for more standardized reporting guidelines.

## DISCUSSION

- Pragmatic trials are critical to generating real-world evidence (RWE) in oncology, bridging controlled clinical settings with everyday practice.
- The audit highlights geographical gaps, with 35.5% of trials based in the US and fewer in Europe, Asia, and South America.
- Only 13 trials had sample sizes >5000, indicating the need for larger studies to improve generalizability.
- Limited inclusion of age groups (6.1%) and gender-specific trials shows opportunities to enhance demographic diversity in future studies.
- Late-phase trials (26.2%) dominate over early-phase trials (4.7%), reflecting a focus on interventions nearing clinical application.
- Few trials focus on key outcomes like overall survival (4.2%) and progression-free survival (3.7%), suggesting the need for outcome refinement aligned with RWE frameworks.
- Gaps in methodological reporting, such as bias correction, highlight the need for standardized guidelines to improve trial quality.

## CONCLUSION AND RECOMMENDATIONS

- **Identified Gaps**: The audit of oncology pragmatic trials highlights issues such as limited geographical diversity, small sample sizes, and inadequate representation of diverse demographics.
- **Methodological Shortcomings**: Trials face challenges like poor bias correction and a lack of focus on patient-centric outcomes, which affect the quality of RWE.
- **Need for Guidelines**: Clearer guidelines and enhanced reporting are essential for improving RWE applicability in oncology.
- **Broaden Scope and Size**: Increase trials in underrepresented regions and prioritize larger sample sizes to enhance generalizability.
- **Focus on Diversity and Outcomes**: Ensure diverse demographics are included and align outcomes with long-term survival and quality of life to reflect real-world oncology care effectively.

## STRENGTHS AND LIMITATIONS

- **Strengths**: Comprehensive analysis of pragmatic trials in oncology, identifying key trends in design and outcomes.
- **Limitations**: Incomplete or inconsistent data on ClinicalTrials.gov limits the audit’s conclusions, underscoring the need for improved trial reporting and data quality.

## REFERENCES

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