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MSc in Clinical Drug Development

Exploring the Disparities in Awareness of Clinical Research and Trials: A Meta-Analysis Comparison Between Developed and Developing Nations

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ABSTRACT:

Background:

The pharmaceutical industry is a research-driven industry, accelerating the development of a wide range of life-saving drugs (Scherer, 2000), which consists of 3 phases with an average success rate of 64% from phase I to II, 32% from phase II to III, 60% reaching NDA for approval, and 83% are approved(Schuhmacher *et al.*, 2025). It is a complex, time-intensive, and financially demanding process. Therefore, it is crucial to ensure that the obtained medicine is made accessible to everyone, regardless of their region, socioeconomic status, or location, to bridge the gaps in access and awareness of clinical research and trials, particularly in the context of disparities between developed and developing nations.

Aim:

The study aims to compare and determine public perception of clinical trials across diverse socio-demographic populations in developed and developing nations. It will examine the key factors influencing awareness, trust, and participation in clinical trials. The study findings will guide building strategies to improve public education and engagement in clinical research globally.

Methods:

A systematic search of PubMed and Google Scholar was conducted for studies published between January 2015 and April 2025. Around 9,812 studies were identified using the *Publish or Perish* software, excluding duplicates and ensuring comprehensive coverage. The Titles and abstracts were further screened using ASReview, focused on general adult populations and outcomes related to awareness, knowledge, perception, or attitudes toward clinical trials. Studies were included if they were survey-based or observational and reported extractable quantitative data. A Meta-analysis was conducted using a random-effects model to account for heterogeneity across study populations and methodologies.

Results and Discussion/Findings:

This meta-analysis reveals significant global disparities in public awareness of clinical research. The overall pooled awareness proportion was approximately 57%, highlighting a substantial knowledge gap. Notably, awareness was significantly higher in developed countries (63.6%) compared to developing nations (47.9%), underscoring the influence of national infrastructure, health literacy, and public engagement. Meta-regression confirmed that country development status was the strongest predictor of awareness, accounting for nearly 30% of between-study variance, while demographic and study-level variables had a limited impact. These findings emphasize that disparities in clinical trial awareness are primarily systemic and structural, requiring context-sensitive, country-level interventions to promote equitable participation and improve global trial outcomes.

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To become independent, one needs to be dependent

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ABBREVIATIONS

CT	Clinical Trial
FDA	Food and Drug Administration
EMA	European Medicines Agency
RCTs	Randomized Controlled Trials
NGOs	Non-Governmental Organizations
HICs	High-Income Countries
LMICs	Low and Middle-Income Countries
GCP	Good Clinical Practice
DCTs	Decentralized Clinical Trials
TB-DM	Integrated Diabetes and Tuberculosis
HINTS	Health Information National Trends Survey
ADCS	Abu Dhabi Cohort Study
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
UK	United Kingdom
US	United Stated
REML	Restricted Maximum Likelihood
CTRI	Clinical Trials Registry of India

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CHAPTER 1: INTRODUCTION

1.1. Background:

Clinical research and trials are fundamental to advancing medical science and improving patient outcomes. However, the success rates of these trials and the awareness surrounding them vary significantly between developed and developing nations, leading to disparities in healthcare outcomes.

In developed countries, robust healthcare infrastructure, substantial funding, and established research frameworks facilitate the efficient conduct of clinical trials. This environment often results in higher success rates, ensuring that individuals in these regions benefit promptly from medical advancements. Conversely, in developing countries, limited resources, inadequate research infrastructure, and systemic challenges impede the initiation and completion of clinical trials(Dandekar *et al.*, 2016). These barriers contribute to lower success rates and delayed access to new treatments for individuals in these regions.

A systematic review by Khoja et al. identified several significant barriers to conducting clinical trials (CTs) in developing countries, including a lack of funding, insufficient research infrastructure, and regulatory challenges (Cochrane and Manville,2014). These obstacles hinder the ability to conduct trials that are essential for addressing the health needs of populations in these regions. Moreover, the ethical complexities of conducting research in developing countries, such as ensuring informed consent and addressing cultural sensitivities, further complicate the research process(Grover *et al.*, 2017a).

The disparity in clinical trial success rates between developed and developing nations has profound implications for global health equity. Individuals in developing countries often face higher disease burdens and limited access to healthcare, making the need for effective clinical trials even more critical(Mumtaz *et al.*, 2024). However, the challenges in conducting these trials mean that

potential treatments may not reach these populations promptly, exacerbating health inequities.

Addressing these disparities requires a concerted effort to enhance research capacity in developing countries. This includes investing in infrastructure, training researchers, and establishing ethical and regulatory frameworks that facilitate the conduct of clinical trials. Furthermore, fostering international collaborations can help bridge the gap, ensuring that clinical research is inclusive and benefits individuals globally.

In conclusion, the success rates of clinical trials are not merely statistical outcomes; they have real-world implications for individuals, particularly in developing countries. Understanding and addressing the disparities in clinical trial awareness and success rates is essential for promoting global health equity and ensuring that all individuals have access to the benefits of medical advancements.

1.1.1. Overview of Clinical Research:

Clinical research, the cornerstone of medical advancement, has evolved significantly over the centuries, transitioning from rudimentary observations to rigorously structured studies governed by ethical and scientific frameworks. The origins of clinical research trace back to ancient civilizations, with early documentation of trial-like methods appearing in ancient Egypt, Greece, and China. However, one of the earliest recognized examples of a clinical trial occurred in 1747, when Scottish physician James Lind conducted a controlled study aboard a naval ship to identify the effects of citrus fruits on scurvy, a foundational moment in evidence-based medicine(Lind, 1753).

The 20th century marked a transformative period for clinical research, particularly in developed nations, spurred by scientific innovation, growing pharmaceutical industries, and increasing emphasis on medical ethics. The Nuremberg Code (1947) and the Declaration of Helsinki (1964) established critical ethical principles following egregious abuses during World War II, shaping modern

standards for human subject research(Shuster, 1997; Holm, 2019). In the United States and Western Europe, this period saw the institutionalization of clinical trials through regulatory bodies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), which formalized approval processes and reinforced the necessity of randomized controlled trials (RCTs). These regions developed sophisticated infrastructures for clinical trials, including university research centers, specialized hospitals, and private sector partnerships, thereby cultivating widespread public awareness and engagement.

In contrast, the evolution of clinical research in developing nations followed a more fragmented and delayed trajectory, often influenced by colonial histories, economic constraints, and limited healthcare infrastructure(Hyder *et al.*, 2004). During the mid-20th century, clinical trials were sporadically introduced in parts of Asia, Africa, and Latin America, frequently driven by external researchers from developed countries rather than local initiatives. While international collaborations brought some advancements, they often lacked sufficient oversight or ethical consideration, sometimes leading to exploitation and mistrust within local populations(Lang and Siribaddana, 2012).

The past few decades have seen concerted efforts to bolster research capacity in these regions, largely supported by global health organizations, non-governmental organizations (NGOs), and regional policy reforms. For instance, the establishment of national regulatory bodies and regional ethics committees in countries like India, Brazil, and South Africa marked significant progress toward developing autonomous research ecosystems. However, these developments have not uniformly translated into public understanding or trust in clinical trials, which remains disproportionately low compared to developed nations(Commission on Health Research for Development, 1990). Linguistic, cultural, educational, and socio-economic factors contribute to persistent disparities in awareness and participation.

As globalization of healthcare continues, developing nations have become increasingly important sites for multinational clinical trials due to their diverse populations and lower operational costs. Yet, the historical imbalances and uneven development of clinical research infrastructures highlight the pressing need for equity in both awareness and access. The legacy of how clinical research has evolved across regions, shaped by scientific breakthroughs, ethical milestones, and socio-political dynamics, sets the stage for exploring the contemporary disparities in knowledge and perception(Glickman *et al.*, 2009).

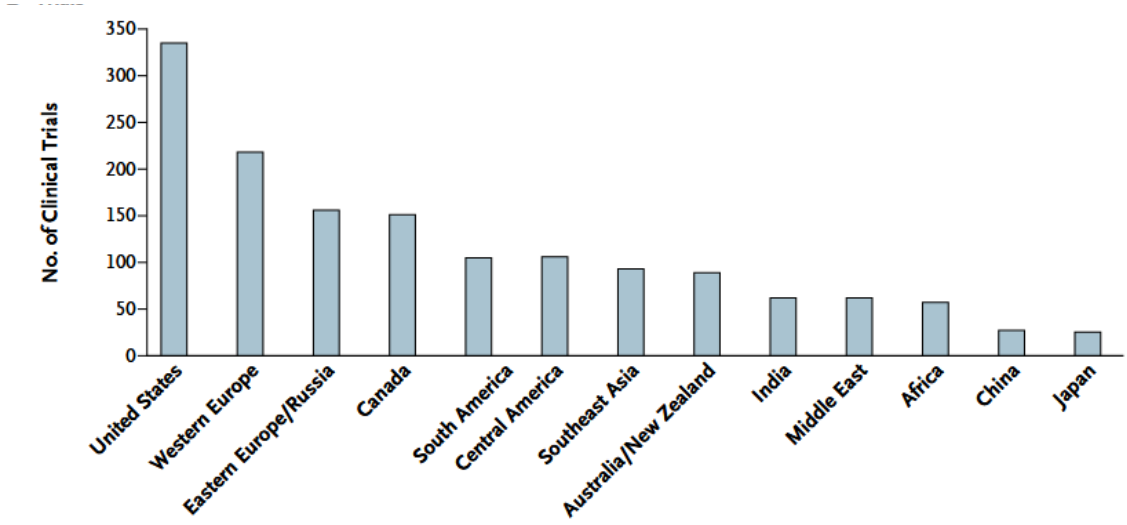

Figure 1: Difference in the number of trials conducted in various parts of the world as of 2007(Glickman et al., 2009)

Clinical research today serves as the backbone of evidence-based medicine, underpinning everything from next-generation anticancer therapies and mRNA vaccines to tailored diagnostics and population health interventions. Over recent years, the field has experienced a dramatic transformation driven by regulatory innovation, digital technology, and globalization(Glickman *et al.*, 2009).

In high-income countries (HICs), such as the United States, Europe, Japan, and parts of Asian nations, streamlined regulatory pathways, including adaptive trial designs and Emergency Use Authorizations, have accelerated drug development and deployment during the COVID-19 pandemic. Concurrently, the integration of

artificial intelligence and real-world data, coupled with decentralized trial models employing telehealth and wearable technology, has optimized patient recruitment, monitoring, and protocol management.

China now accounts for 29% of clinical trials worldwide, more than India (8%), and slightly less than the United States (~25%). India is increasing capacity through regulatory reforms and adopting study-advertising techniques similar to those in the UK and the US, driven by cost competitiveness and population diversity. While Australia's tax breaks and quick approvals have drawn trial sponsors from all around the world, South Korea is a leader in oncology trials. Nevertheless, despite reforms as CTR 536/2014, bureaucratic snags have caused Europe's share to decline from 22% to 12% between 2013 and 2023.

In low- and middle-income countries (LMICs), clinical research is a domain of both promise and recurring challenges. While LMICs see only 20% of global trial activity, they carry nearly 80% of the global disease burden. Barriers include chronic underfunding, regulatory delays, fragile ethics frameworks, personnel shortages, and underdeveloped infrastructure(Grover *et al.*, 2017b). Ethical dilemmas are prominent, including improper informed consent, placebo usage when effective treatments exist elsewhere, and passive exploitation of vulnerable populations raise serious concerns.

Nevertheless, emerging trends and regional initiatives are closing the gap. Technological tools such as mobile health, telemedicine, and electronic data capture are reducing logistical barriers and improving trial fidelity. Partnerships between North–South and South–South, facilitated through platforms like the EDCTP, are expanding clinical capacity in Africa and beyond. In Africa, institutions like H3D (University of Cape Town) are leading innovative malaria and tuberculosis trials, while global advocacy emphasizes Africa’s genetic diversity as vital for precision medicine (The Guardian, 2024). Reverse innovation from simple haemorrhage

devices to low-cost neonatal CPAP and oral rehydration therapy demonstrates how LMIC-derived solutions can influence HIC practice.

Frameworks for capacity-building and ethics are being reinforced. The goal of dual-review procedures, including local and sponsor IRBs, as well as guidelines like the Declaration of Helsinki and Belmont Report, is to improve participant protection. Good clinical practice (GCP), trial monitoring, workforce training, and infrastructure accreditation are the main focuses of capacity-building initiatives. To improve openness and encourage trial registration compliance, these initiatives are supplemented by policy-level campaigning for national registers (such as WHO ICTRP and India's CTRI)(Nundy and Gulhati, 2005).

In summary, clinical research now spans a dynamic global ecosystem: advanced economies deploy cutting-edge technologies and regulatory frameworks, emerging hubs leverage diversity and efficiency, and LMICs build essential infrastructure and ethics capacity to address local health priorities(Grover *et al.*, 2017b). The resulting heterogeneity in trial design, oversight, participant awareness, and outcomes underscores the importance of comparative meta-analyses.

In examining the differences in awareness of clinical research and trial accessibility between developed and developing nations, this dissertation seeks to elucidate the structural, cultural, and technological factors that can facilitate the harmonization of global best practices and ensure equitable access to the benefits of modern clinical research.

1.1.2. Clinical trial awareness:

Clinical trial awareness varies significantly between regions, shaped by a complex interplay of socio-economic, educational, cultural, and systemic factors. In many developed countries, high public literacy, proactive healthcare policies, and media engagement foster relatively robust awareness of clinical research. For instance, a

survey in China found that around 61% of respondents demonstrated qualified awareness of drug clinical trials, with higher education and better urban infrastructure identified as strong predictors of this awareness(Wang *et al.*, 2024a). Yet, even in high-income settings, misconceptions persist, as in Australia, many parents lack understanding of randomisation and placebo use in paediatric trials. This shows that educational attainment alone does not guarantee sound comprehension of trial methodology.

In contrast, awareness in developing nations is often limited by low functional literacy, poor healthcare infrastructure, and cultural barriers(Wang *et al.*, 2024a). In West Africa, studies have revealed that up to 90% of participants misunderstand key trial concepts like withdrawal rights and side effects. Saudi Arabia's primary-care survey showed only 30% of patients were aware of clinical trials, with fear of risk cited by nearly 80% as a deterrent(Al-Dakhil *et al.*, 2016). Qualitative research in Ghana further highlights inadequate community engagement as a root cause of mistrust and poor trial participation(Appeaning *et al.*, 2022a).

Awareness is also shaped by cultural norms. Participation in trials may be encouraged or restricted in sub-Saharan Africa due to community decision-making, where family or clan elders have an impact on individual choices(Al-Dakhil *et al.*, 2016). Mistrust is increased by traditional vulnerability, which is characterized by poverty and ignorance. In certain places, historical wrongdoings, such as unethical medical experimentation, continue to have a lasting impact on public opinion. Ethical trial behavior frequently falls flat in the absence of culturally sensitive communication. Awareness gaps are exacerbated by systemic barriers. In many low- and middle-income nations, the ethical and regulatory framework may be sluggish or cumbersome, which could cause delays or reduce the visibility of trials(Al-Dakhil *et al.*, 2016).

Funding deficits, lack of trained personnel, and brain drain further weaken local trial ecosystems, making sustained community outreach and education challenging.

However, improved awareness can follow targeted interventions. In China, outreach campaigns combined with digital resources have uplifted public knowledge about decentralized clinical trials (DCTs), now understood by over 70% of the public, though only 16% have participated. In developed settings like the U.S. and Europe, trusted sources (e.g., primary care providers, patient advocates) significantly influence trial awareness; yet, many patients still rely more on online sources, underlining evolving communication pathways.

In summary, the awareness gap between developed and developing regions is fueled by disparities in education, infrastructure, culture, ethics, and communication strategies. Addressing these gaps requires multifaceted efforts such as simplifying consent materials, using audio-visual tools, engaging community leaders, reinforcing ethical oversight, and leveraging digital platforms (Kean, S., 2012). Visual tools such as infographics and community-focused campaigns are essential in bridging knowledge divides (Kean, S., 2012). Meta-analytic evidence indicates that such interventions are most effective when contextually tailored, culturally sensitive, and ethically stringent. Improving awareness is not just about boosting participation; it's about empowering individuals to make informed decisions and furthering equitable global clinical research.

1.1.3. Developed Vs Developing Countries:

In comparing clinical trial awareness and participation across developed and developing nations, the disparities are evident, shaped by divergent infrastructure, regulatory systems, and cultural contexts. Developed countries consistently dominate global clinical research. For instance, in 2022, Australia (population ~26 million) registered 2,284 clinical trials, while Cameroon, a nation of similar

population size, registered only 15 trials(Mbuagbaw *et al.*, 2011). This vast gap reflects broader trends, over 90% of trials are conducted in high-income nations, leaving low-income countries significantly underrepresented despite bearing a disproportionate disease burden.

West Africa's CAMPS study in Cameroon, which examined motivational SMS interventions to enhance HIV patients' adherence to anti-retroviral therapy, provides a compelling example.(Mbuagbaw *et al.*, 2011). Despite being the first technology-driven, investigator-led trial in the region, it faced multilingual consent challenges, ethical review adaptations, and concerns about confidential message delivery in stigmatized communities. Regulatory hurdles like translating consent documents into English and French, and ethical adjustments (e.g., handling data privacy), delayed initiation, and highlighting how bureaucratic processes impede trial awareness and execution.

By contrast, developed settings benefit from robust infrastructure. In Malawi, a Phase IIA trial of clofazimine for HIV-related diarrhoea overcame significant logistical and regulatory barriers by prioritizing operational planning, demonstrating that careful systems design can mitigate common barriers in the Global South. However, such successes remain exceptions rather than the norm across low-resource settings.

In South Asia, disparities take different forms. India, hosting approximately 27% of global TB patients, saw successful pilots integrating diabetes and tuberculosis (TB-DM) screening and treatment at a primary care level. Despite this integration, a 2022 stakeholder study in Kerala and Bihar revealed ongoing shortcomings in lab infrastructure, data systems, and training, a barrier to scaling community-based trial awareness. Notably, the prevalence of TB-DM comorbidity in India (20% of TB patients) further underscores the public health need for integrated, trial-informed interventions.

Historical case studies highlight persistent ethical and regulatory vulnerabilities. In 2006, the Aggrenox stroke prevention trial in Sevagram, India, demonstrated early promises of local research capacity but revealed deep ethical tensions, local doctors struggled to communicate trial risks, and financial incentives risked exploitation. These ethical concerns, coupled with poor informed consent, highlight how even seemingly well-intended trials can erode public trust, a core element of awareness and participation(Jawa *et al.*, 2023).

On the other hand, high-income countries maintain a relatively consistent level of trial engagement and transparency through mature infrastructure and regulatory oversight. Yet even they face challenges, for example, while digital innovation has fostered decentralized trials with convenience and flexibility, public misconceptions around randomisation and placebo methods remain, particularly among parents evaluating paediatric studies, a reminder that awareness is not guaranteed merely by infrastructure(Unger *et al.*, 2016).

These case studies illuminate a layered disparity where developed nations lead in trial volume, density, and public engagement, while many developing countries struggle with regulatory complexity, ethical oversight gaps, underdeveloped infrastructure, and low public trust(Unger *et al.*, 2016). To narrow the awareness divide, global trial frameworks must prioritize capacity-building (e.g., local lab accreditation, bilingual consent forms), strengthen ethical clarity, and integrate research into community-level care via pilot projects like CAMPS and TB-DM integration. Without such context-specific interventions, awareness will remain shallow, unequal, and insufficient, especially in regions where the disease burden is greatest.

1.1.4. Major factors influencing trial participation:

Clinical trial participation is influenced by a complex interplay of socio-economic, educational, cultural, and structural factors, which vary significantly between developed and developing nations.

One of the most pervasive barriers is socioeconomic status. In low-income settings, individuals often prioritize immediate needs such as food, housing, and employment over research participation(Molyneux, Peshu and Marsh, 2005). Trials may be viewed as burdensome due to lost income from travel or time off work, especially in regions lacking transport subsidies or compensation policies. Even in high-income countries, low-income and uninsured populations are often underrepresented due to logistical constraints and historical mistrust of the medical system(Molyneux, Peshu and Marsh, 2005).

Education is another powerful determinant. In both settings, individuals with lower literacy or health literacy levels struggle to comprehend complex clinical concepts like randomisation, placebo control, or long-term follow-up(Molyneux, Peshu and Marsh, 2005). This gap often leads to confusion, fear, or refusal to consent. In developing countries, limited formal education reduces the effectiveness of written informed consent processes, making verbal or visual communication tools crucial for comprehension(Shavers, Lynch and Burmeister, 2002). Conversely, in developed nations, while education levels are generally higher, a lack of specific clinical research knowledge still hinders understanding and informed decision-making.

Cultural beliefs and attitudes also significantly influence participation. In some communities, illness is seen through religious or traditional lenses, leading to reluctance in participating in biomedical research(Shavers, Lynch and Burmeister, 2002). For example, distrust in Western medicine or beliefs that clinical trials are exploitative or experimental are common in certain rural or indigenous

populations(Jawa *et al.*, 2023). Historical abuses, such as the Tuskegee Syphilis Study or unethical pharmaceutical trials in Africa and India, have further eroded trust and fuelled cultural stigma around trial participation. Even in developed countries, minority ethnic groups often cite cultural barriers, fear of discrimination, and language issues as key deterrents(Jawa *et al.*, 2023).

Structural factors, including the availability of healthcare infrastructure, trial sites, and trained staff, create a foundational disparity. Developing nations often lack research facilities, ethical review boards, or trained investigators, which limits public exposure to clinical trials altogether. In high-income countries, despite the availability of infrastructure, geographic disparities (e.g., rural vs. urban) can still restrict access to trials (Weigmann, 2015). Moreover, the lack of integration between primary care and research systems in both contexts can prevent trial opportunities from reaching eligible participants.

Ultimately, addressing these multifactorial influences requires tailored approaches that go beyond generic recruitment strategies, embedding trial education in community settings, training culturally competent staff, and reducing logistical barriers are essential to enhancing participation and equity in global clinical research.

Table 1: Comparison of various factors affecting trial participation between Developed and developing countries.

Factors	***Developing Nation***	***Developed Nation***
Socioeconomic status	Basic needs (Food, Shelter, Income) are prioritized over participation.	Underrepresentation of specific cohorts due to lower income/mistrust of healthcare systems.
Education & Health Literacy	Low literacy levels affect the understanding of trials/informed consent,	Limited understanding of trial-specific information.

	which often requires verbal or visual tools.	
Cultural beliefs & trusts	Traditional/religious beliefs may conflict with biomedical research.	Minority groups may fear discrimination or exploitation.
Infrastructural	Lack of trial sites, trained personnel, or ethics review boards. Trials are often inaccessible to the public.	Infrastructure exists, but rural/remote areas lack access. Poor integration with primary care.

1.2. Objectives:

The primary objective of this dissertation is to perform a comprehensive meta-analysis to evaluate and compare the awareness of clinical trials between developed and developing countries. The study further aims to:

1. Assess the factors influencing awareness of clinical trials across diverse regions worldwide, identifying socio-economic, cultural, educational, and structural determinants that contribute to variations in public knowledge and perception.
2. Analyze the difficulties in clinical trial success rates, including recruitment, retention, and completion, between developed and developing nations, to better understand how awareness levels impact trial outcomes.
3. Examine the significance of including diverse populations in clinical trials, emphasizing how broader demographic representation enhances the relevance and applicability of research findings globally.
4. Develop evidence-based recommendations to improve the conduct, outreach, and participation in clinical trials within developing countries by addressing the unique challenges and barriers they face.

By achieving these objectives, this dissertation seeks to provide valuable insights into global disparities in clinical trial awareness and contribute to strategies that promote equitable participation in clinical research worldwide.

1.3. Scope:

This dissertation conducts a global meta-analysis to explore disparities in awareness of clinical research and clinical trials between developed and developing countries. The study focuses exclusively on adult populations aged 18 and above, drawing on peer-reviewed studies published between 2015 and 2025. Using the World Bank's country classification system, the research compares populations from high-income (developed) and low- and middle-income (developing) nations. The central objective is to assess the general public's awareness, perceptions, and attitudes toward clinical trials and to understand how these factors influence willingness or likelihood to participate.

The scope includes examining how awareness levels vary across urban and rural settings within these country categories. Awareness is defined broadly to include recognition of what clinical trials are, their purpose, ethical aspects such as informed consent, perceived risks and benefits, and trust or skepticism toward the process. Perception refers to how individuals feel about clinical trials and the motivations or concerns they associate with participation. Attitude encompasses both behavioral intentions and predispositions toward being involved in research studies. Together, these components form the basis for understanding how public awareness influences trial participation across differing socioeconomic and geographic contexts.

While the primary focus remains on the general population, the study acknowledges that certain demographic and contextual variables, such as employment background, may influence awareness levels. If available data within included studies distinguishes between individuals with and without medical or

healthcare-related employment, such distinctions will be noted for contextual insight. However, employment background is not treated as a primary variable, and healthcare professionals or researchers are not studied as independent target groups. Their awareness is only considered when included in general population samples and when relevant to interpreting broader patterns.

In addition to excluding data on children and adolescents, this dissertation does not thoroughly analyze participation rates, clinical trial results, or regulatory contexts. In a similar vein, factors like media exposure, health literacy, and computer access are not examined directly, though they might be included when providing context. Methodological rigor is maintained by excluding non-peer-reviewed sources and grey literature.

This study provides a targeted and comparative understanding of public awareness differences by establishing these boundaries, which will aid future initiatives to enhance clinical research engagement globally through more focused education and communication tactics.

1.4. Significance:

Understanding and addressing disparities in public awareness of clinical research and trials is crucial for promoting global health equity and ensuring the ethical conduct of clinical studies. Clinical trials are the cornerstone of medical advancement, providing evidence for the safety and efficacy of new treatments, interventions, and preventive strategies. However, the benefits of these trials can only be fully realized when participation is representative of diverse populations across geographic, economic, and cultural boundaries. When awareness is significantly lower in developing nations or among marginalized groups, it undermines the inclusivity, generalizability, and fairness of medical research outcomes. This creates a persistent gap in the distribution of healthcare knowledge, innovation, and ultimately, access to life-saving therapies. Thus,

disparities in awareness are not merely academic concerns; they have tangible consequences for public health outcomes, policy development, and clinical trial validity.

The significance of this study lies in its effort to systematically evaluate and compare levels of awareness, perception, and attitude toward clinical research between populations in developed and developing countries. This study reveals areas where educational initiatives, public engagement tactics, or legislative reforms may be critically needed by highlighting the gaps and their breadth. Increased understanding promotes better decision-making, more ethical participant recruitment, and greater trust. People in less conscious areas could unintentionally take part in trials without completely comprehending their rights or the goal of the study, which raises significant ethical questions about autonomy and informed consent. In situations where healthcare literacy and research infrastructure may be lacking, addressing these differences is crucial to guaranteeing that clinical trials follow universal ethical norms.

Moreover, the findings of this dissertation have the potential to inform global health organizations, regulatory bodies, and research institutions in developing more inclusive and culturally sensitive approaches to clinical trial design and communication. In an era of international and multi-site trials, global disparities in awareness can hinder the scalability and success of clinical research efforts. If certain populations are systematically underinformed or excluded, it risks perpetuating existing health inequities and limits the broader applicability of medical research findings. As the world moves toward more collaborative approaches to tackling health challenges from pandemics to non-communicable diseases, ensuring equitable access to research knowledge and participation is both a scientific and moral imperative.

Ultimately, this study contributes to a deeper understanding of the social and structural barriers that influence clinical research participation on a global scale. It

underscores the need for tailored awareness campaigns, community engagement, and educational outreach in both developed and developing nations. By shedding light on these disparities, the research supports the development of more ethical, representative, and effective clinical trials that can serve all populations fairly and transparently.

CHAPTER 2: LITERATURE REVIEW

2.1. Introduction:

A vital component of medical research is clinical trials, facilitating the development and validation of new therapies, interventions, and preventive measures. However, sufficient participant enrollment and retention are just as important to the outcome of clinical studies as scientific accuracy. The general public's awareness and understanding of clinical trials are crucial in this regard. People are less inclined to engage if they are not sufficiently informed, which can cause recruiting difficulties that impede the advancement of research and limit the extent to which the results can be applied.

Globally, disparities exist in the level of public awareness and understanding of clinical trials, with significant variations noted between developed and developing countries. These disparities are shaped by a complex interplay of socio-economic, cultural, educational, and structural factors. Developed countries often have more robust healthcare infrastructures and public education campaigns that support higher levels of awareness, while developing countries face numerous barriers, including limited access to information, mistrust of medical research, and lower literacy rates.

The COVID-19 pandemic further highlighted the importance of public understanding of clinical research, as rapid vaccine development and emergency use authorizations brought clinical trials into the public spotlight worldwide. Yet, there remains limited understanding of how such global events affect awareness longitudinally.

This literature review synthesizes findings from 25 peer-reviewed studies included in a meta-analysis examining public awareness, knowledge, attitudes, and willingness to participate in clinical trials. The studies span both **developed** and **developing countries**, reflecting diverse social, cultural, and healthcare contexts. Collectively, they provide a nuanced understanding of how different populations perceive clinical research and the factors that influence their level of engagement.

2.2. Overview of Methods:

The meta-analysis comprised 25 studies, one of which used mixed-methods research, while the other investigations used a quantitative approach. Most of them used cross-sectional survey techniques, which allowed for quick insights into public perceptions and attitudes at moments in time. The surveys can effectively collect data from large, diverse groups, and so they were chosen as the predominant method.

Cross-Sectional Surveys:

The studies (Whiting *et al.*, 2024), (Figer *et al.*, 2021), (Chu *et al.*, 2015),(Schultz *et al.*, 2021),(Appeaning *et al.*, 2022b),(Cięszczyk *et al.*, 2024),(Wang *et al.*, 2024b) by authors from India, Ghana, the USA, and France relied on structured questionnaires either administered in person or through online platforms.

The data captured in the surveys are about public awareness of clinical research/trials, their willingness to take part in research, their perceptions and attitudes about risks and benefits of taking part in a trial, and the sources they used to gain knowledge about clinical trials.

Cross-sectional designs are useful for large-scale quantitative research, but they are constrained by their inability to demonstrate causality or track development over time.

Survey-Based:

US-based studies such as (Occa *et al.*, 2024),(Yadav *et al.*, 2022),(Langford, Orellana and Buderer, 2022),(Leiter *et al.*, 2015) employed national surveys such as the **Health Information National Trends Survey (HINTS)**. These studies made it possible to compare population-level patterns across survey cycles and demographic strata, including age, education level, and political affiliation, by providing solid, large-scale data.

The HINTS dataset employs a **probability-based sampling strategy**, ensuring national representativeness. It uses a **stratified, multi-stage sampling design**, typically involving the following elements:

- Random selection of addresses from the U.S. Postal Service delivery sequence file.
- One adult per household selected to complete the survey using a paper-based or web format.
- Oversampling of underrepresented groups in certain iterations to enhance subgroup analysis.

Core modules of the questionnaires were repeated to allow for longitudinal comparisons, and the questionnaires were standardized across cycles. Likert-type scales and closed-ended items are both used in the self-administered data-gathering process. The architecture enables complex sample analysis and weighting, which is essential for generating estimates that can be applied nationally.

These studies are characterized by:

- Large sample sizes (often exceeding 3,000 respondents per cycle).
- Use of standardized questions related to clinical trials, awareness, trust, and media exposure.
- Inclusion of comprehensive demographic and behavioural variables.

Although HINTS-based studies are constrained by their cross-sectional nature and self-reported data, they are regarded as methodologically robust due to the instrument's consistency and nationwide reach.

The other survey-based studies include (Nguyen *et al.*, 2023), (DasMahapatra *et al.*, 2017), (Al-Lawati *et al.*, 2018), (Choi *et al.*, 2016), (Raj *et al.*, 2024), (Adewale, Schoeman and Roussouw, 2015), (Al-Shami, Ahmed and Alzoubi, 2022), (Wienroth *et al.*, 2018), (Willison *et al.*, 2019), (Onyeaka *et al.*, 2023) from various countries, including both developed and developing nations.

Mixed-Methods Study design:

The study (Mowlabaccus and Jodheea-Jutton, 2020) employed a mixed-methods design to examine perceptions of clinical research in Mauritius. This approach combined both qualitative and quantitative methodologies in a two-phased structure:

Qualitative Phase:

This utilized open-ended narrative responses collected through online self-administered surveys. Participants were adults with internet access, and responses were analyzed using **thematic analysis** to identify common ideas and emergent themes(Mowlabaccus and Jodheea-Jutton, 2020). These themes informed the development of a structured questionnaire for the next phase.

Quantitative Phase:

Based on qualitative findings, a closed-ended survey was developed and distributed to a sample of 400 community members, recruited from public areas and institutions(Mowlabaccus and Jodheea-Jutton, 2020). The questionnaire included demographic information, Likert-scale items, and structured questions regarding familiarity with clinical trials. Data were analyzed using both descriptive and inferential statistics to identify associations between demographic variables and familiarity with clinical trials.

Focus group study design:

The study conducted in the United Arab Emirates (UAE)(Al-Shami, Ahmed and Alzoubi, 2022) adopted a qualitative **focus group methodology** to explore public perceptions and understanding of clinical research. This approach aimed to delve deeper into the nuances of awareness and attitudes, particularly among populations for whom the term "clinical research" may be unfamiliar or culturally contextualized.

A total of **six focus groups** were conducted as part of the **Abu Dhabi Cohort Study (ADCS)**. Participants included adult Emirati nationals recruited from various socio-demographic backgrounds, ensuring diversity in age, gender, education level, and occupation. The sessions were held in Arabic, facilitated by trained moderators using a semi-structured discussion guide developed around key themes: awareness of clinical research, trust in medical studies, motivations for participation, and barriers to involvement(Al-Shami, Ahmed and Alzoubi, 2022).

This qualitative design allowed for the capture of contextual factors influencing awareness, such as religious beliefs, cultural norms, and trust in institutions, which are often not focused on in survey-based approaches. The findings informed ongoing community engagement strategies for the ADCS and highlighted the importance of culturally sensitive communication in promoting clinical research participation in the Gulf region(Al-Shami, Ahmed and Alzoubi, 2022).

While focus group studies do not offer generalizable statistical data, they provide rich, in-depth insights that complement the quantitative findings of this meta-analysis. Their inclusion has strengthened the analysis by illuminating how awareness is shaped by local contexts and collective experiences.

Table 2: *Summary of various methods used to identify the awareness levels across studies.*

Study Design	***No. of studies***	***Countries***	***Strengths***	***Limitations***
Cross-sectional Survey-based	8	India, Ghana, USA, France, China, Poland	Easy to collect data, applicable to a wide and diverse population, and provides descriptive insights.	Cannot assess the influencing factors due to the constraints of the limited timepoints.
Survey-based (HINTS/Other surveys)	15	USA, Canada, India, Nigeria, Oman, Saudi Arabia, UK, Korea	Focus on specific cultural or healthcare systems, which allows for large samples and demographic comparisons.	Risk of bias from self-reported information, heterogeneity in quality, and sampling methods across the studies.
Mixed-Methods	1	Mauritius	Provides more context-specific insights.	Time-consuming and limitations of generalizability beyond the target region.
Focus groups	1	UAE	Captures cultural nuances, social	Limitations in interpretation and risk of bias

			dynamics, and lived experiences not measurable via surveys.	from the researchers during analysis, a small sample group, and cannot be generalized.

2.3. Disparities in clinical trial awareness and participation:

Clinical trial participation plays a vital part in advancing medical research and enhancing health outcomes. The trial participation requires awareness, which includes an understanding of the existence of clinical trials and their benefits/risks. The nation that provides the opportunity to conduct trials and raise awareness among the public will help its citizens lead a better future. A cohort that is left uninformed about the clinical research opportunities is unable to participate without any choices provided, resulting in exclusion and unfairness.

Disparities in clinical trial awareness and participation between rich and poor nations are widely established and becoming increasingly important in terms of global health equity. The existing research identifies the differences in their trial knowledge between developed and developing countries due to various factors, including demographic, educational, and economic factors.

This section combines information from various geographic and demographic contexts to help explain these inequalities and investigate their underlying causes.

Developed Countries – Awareness:

Developed countries have a higher baseline awareness of clinical trials due to established healthcare infrastructure, significant research activity, and substantial

public health campaigns. However, this awareness is not evenly distributed. Several studies from the United States, Europe, and East Asia have found persisting differences across racial, ethnic, age, and socioeconomic groups.

A cross-sectional study was done in an underprivileged community in Washington, DC (Whiting *et al.*, 2024). For example, there is a lack of clinical trial awareness among the population despite the presence of multiple academic research institutes nearby.

The findings were consistent with broader national statistics, which showed that racial minorities and low-income groups had much lower levels of awareness than their White, higher-income counterparts (Langford, Orellana and Buderer, 2022; Yadav *et al.*, 2022). Similarly, a study focusing on older adults aged 65 and above discovered that, while general awareness has risen over time, significant gaps in knowledge exist regarding trial purpose and participation logistics(Nguyen *et al.*, 2023).

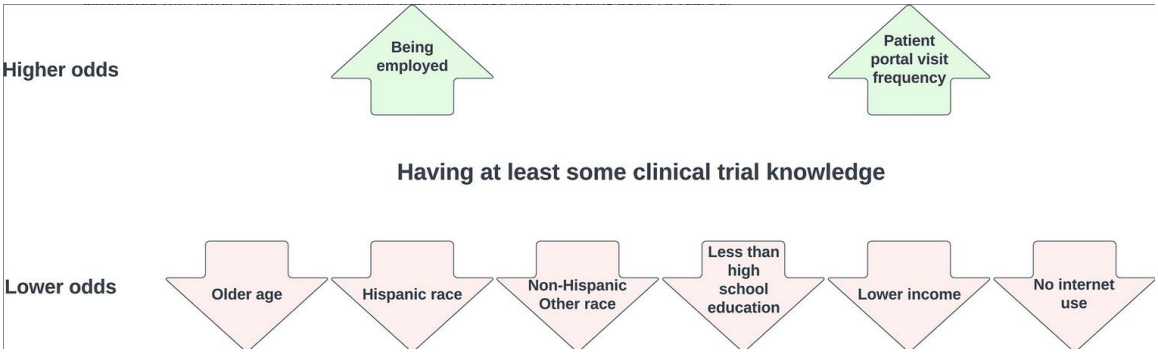

Figure 2: Factors associated with awareness level in a cohort living in a developed nation(Nguyen et al., 2023)

Furthermore, statistics from the Health Information National Trends Survey (Langford, Orellana and Buderer, 2022; Yadav *et al.*, 2022) indicates that education level is substantially correlated with clinical trial awareness. Those with higher educational attainment have a better comprehension and are more willing to seek information proactively. Digital media and online health resources are important information sources, but digital literacy gaps impede access for older persons and economically disadvantaged populations (Wienroth *et al.*, 2018).

Healthcare professionals continue to be important communicators, but studies have found variations in provider-initiated trial conversations, which are frequently influenced by unconscious biases and time constraints (DasMahapatra *et al.*, 2017). Countries such as South Korea and France provide parallel evidence. A statewide survey in Korea (Chu *et al.*, 2015) found significant heterogeneity in awareness based on age, education, and urban-rural residency.

In France, the COVID-19 pandemic increased public awareness of clinical research, although mistrust and misunderstanding remained, particularly among lower socioeconomic groups (Schultz *et al.*, 2021). Collectively, these findings demonstrate that awareness differences in industrialized nations are complex, reflecting overlapping socioeconomic variables rather than simply access to information.

Developing Countries – Awareness:

In developing countries, awareness is comparatively low and far more heterogeneous than in developed countries. The studies from various developing nations conclude that public knowledge of clinical research is limited and often impaired by misconceptions.

In India, a survey of non-science background college students found significant confusion about clinical trial concepts, with many participants connecting trials with unrestrained experimentation or mistaking them for ordinary healthcare (Raj *et al.*, 2024). A community-level study conducted in Mumbai showed that the awareness levels dropped based on the socioeconomic status of the sample from upper to lower (Figure 3) and based on the literacy levels (Figure 4)(Figer *et al.*, 2021).

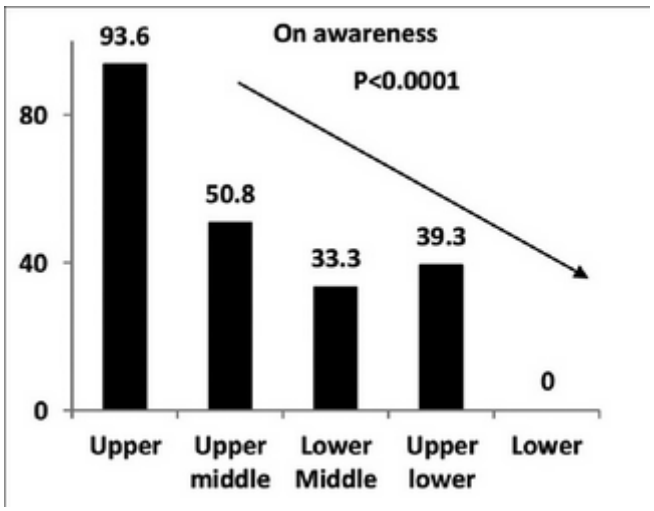

Figure 3: Awareness levels associated with socioeconomic status(Figer et al., 2021)

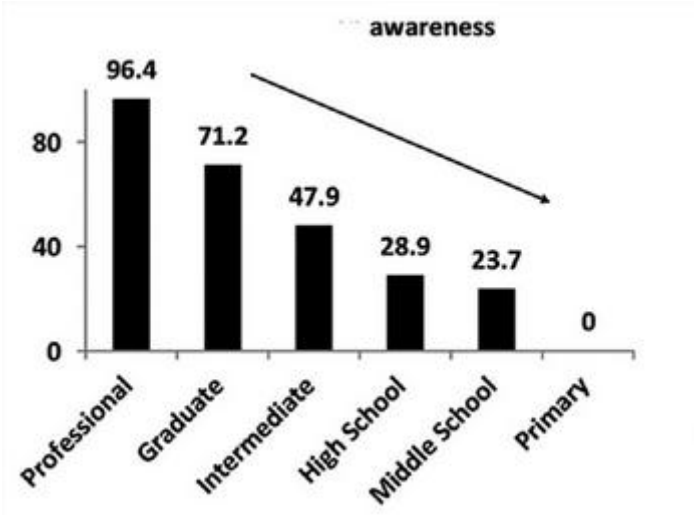

Figure 4: Awareness levels associated with literacy status(Figer et al., 2021)

Similarly, Nigerian populations and Ghanaian communities have limited exposure to clinical trial information, which is typically exacerbated by cultural myths that cast clinical research in doubt or fear(Adewale, Schoeman and Roussouw, 2015; Appeaning *et al.*, 2022b). A history of unethical medical practices intensified these perceptions, limiting transparency in health communication.

Saudi and Omani studies show a gradual improvement in knowledge, driven by government health measures, although considerable gaps remained, particularly

among rural and less educated populations(Al-Dakhil *et al.*, 2016; Al-Rawashdeh *et al.*, 2019).

The barriers to low awareness in LMICs include insufficient media coverage, limited engagement of healthcare providers in research promotion, and language. Furthermore, trust deficits, molded by sociopolitical history and the low-quality healthcare system, lead to a reluctance to participate in clinical trials, even when awareness exists (Mowlabaccus and Jodheea-Jutton, 2020).

Influencing factors:

Multiple factors influence the awareness levels across both developed and developing nations.

1. Literacy Levels:
   A higher level of education enhances the ability of an individual to understand CT concepts and seek more information. The studies conducted in the US(Langford, Orellana and Buderer, 2022), India(Raj *et al.*, 2024), and Poland(Cięszczyk *et al.*, 2024) confirm this, evidently.

2. Healthcare provider communication:
   Healthcare professionals are often considered to be sources of health information. However, inconsistent communication, provider biases, and a lack of training hinder their ability to serve as effective advocates for clinical trial awareness. Underserved groups frequently report having fewer clinical trial discussions with their doctors(DasMahapatra *et al.*, 2017; Whiting *et al.*, 2024).

3. Technology:
   The proliferation of digital health information has increased awareness in developed countries, but digital divides exclude older, poorer, and rural populations. In developing countries, limited internet penetration and less targeted media campaigns reduce the impact(Wienroth *et al.*, 2018; Wang *et al.*, 2024b).

4. Cultural beliefs and trust:

   A deep-seated distrust of medical research, sometimes rooted in historical abuses or cultural misunderstandings, reduces awareness and the desire to engage (Adewale, Schoeman,.

5. Public engagement:

   Transparent, ethical research oversight and community engagement strategies build public confidence and awareness(El Obaid *et al.*, 2016).

Participation rates and barriers:

Awareness plays a vital role in recruiting volunteers; however, not sufficient for participation. Many informed individuals do not take part in the trial due to various barriers.

Despite reasonable levels of awareness, research in industrialized nations shows that racial minorities, elderly persons, and low-income groups continue to be underrepresented in trials(Yadav *et al.*, 2022; Onyeaka *et al.*, 2023; Whiting *et al.*, 2024). Participation hurdles include mistrust, fear of adverse effects, logistical challenges, a lack of trial invites from researchers, and perceived costs, including time, travel(DasMahapatra *et al.*, 2017; Langford, Orellana and Buderer, 2022). Provider gatekeeping remains a serious concern, as clinicians may selectively offer trial opportunities to patients depending on their perceived interest or compliance potential.

Developing countries may face more fundamental challenges. Systemic limitations include restricted trial availability, insufficient healthcare infrastructure, and logistical and budgetary constraints (Adewale, Schoeman and Roussouw, 2015; Al-Rawashdeh *et al.*, 2019; Appeaning *et al.*, 2022b). Even motivated persons confront barriers to trial access due to low-quality services, insufficient transportation, and a lack of nearby research sites.

Impact of COVID-19:

The COVID-19 pandemic has been a double-edged sword in this context. It brought clinical research into the spotlight worldwide, raising widespread understanding and enthusiasm for trials, particularly vaccination studies (Schultz *et al.*, 2021; Langford, Orellana and Buderer, 2022). Public campaigns and media coverage increased understanding in many industrialized countries, but also revealed the persistence of mistrust and disinformation, particularly among minority populations(Yadav *et al.*, 2022).

In LMICs, pandemic-related interruptions hampered trial implementation and community outreach, aggravating knowledge gaps (Mowlabaccus and Jodheea-Jutton, 2020; Al-Shami, Ahmed and Alzoubi, 2022). However, the increased focus on clinical research during the pandemic may present a unique chance to raise awareness in the future, assuming lessons on culturally appropriate communication and equity are integrated.

Summary:

Globally, clinical trial awareness continues to be a significant barrier to trial participation. While knowledge is generally higher in industrialized nations, there are still enduring differences among populations, which are a reflection of intersecting socioeconomic variables, including education, income, and race. Developing nations experience more severe awareness gaps, which are influenced by historical, cultural, and infrastructure issues. Improving education and health literacy, empowering healthcare professionals as communicators, utilizing media and technology inclusively, and fostering trust via openness and community involvement are all important components of addressing these inequities. In order to eliminate participation barriers and pave the way for more inclusive clinical research, awareness must be raised fairly.

2.4. Health equity and access to clinical trials:

Inclusion in clinical trials requires awareness; however, accessibility is equally important for engaging a diverse population in research. This includes

accessibility to trial sites, infrastructure, research information presented in lay terms or their native language, i.e, simple to understand, and acceptability regardless of participants' backgrounds.

Health equity in clinical research allows minimisation of these barriers so that wider populations can participate and benefit from advances in medicine. This section explores how access varies across developed and developing nations, examines underlying systemic and structural barriers, and considers the profound implications for equitable health outcomes.

Access in Developed Countries:

Developed countries benefit from sophisticated research infrastructures, with numerous trials conducted in academic research centers and well-resourced hospitals. However, disparities in access persist, disproportionately excluding certain demographic groups.

Geographic Distribution and Urban-Rural Disposition:

Clinical trials tend to cluster in metropolitan hubs, academic medical centers, and large hospitals(Yadav *et al.*, 2022; Whiting *et al.*, 2024). This urban concentration creates geographic barriers for rural residents, who may face long travel times, higher costs, and difficulty coordinating participation with work and family responsibilities. Even within urban areas, underserved neighbourhoods often lack local research sites, exacerbating inequity.

Economic Barriers:

Low-income individuals experience significant indirect costs associated with trial participation, including transportation, childcare, and lost wages(Whiting *et al.*, 2024)(Figure 5). These financial burdens discourage enrollment, even when direct medical costs are covered by the trial sponsor. Additionally, individuals without health insurance or with unstable employment are less likely to be invited or feel empowered to participate(Onyeaka *et al.*, 2023).

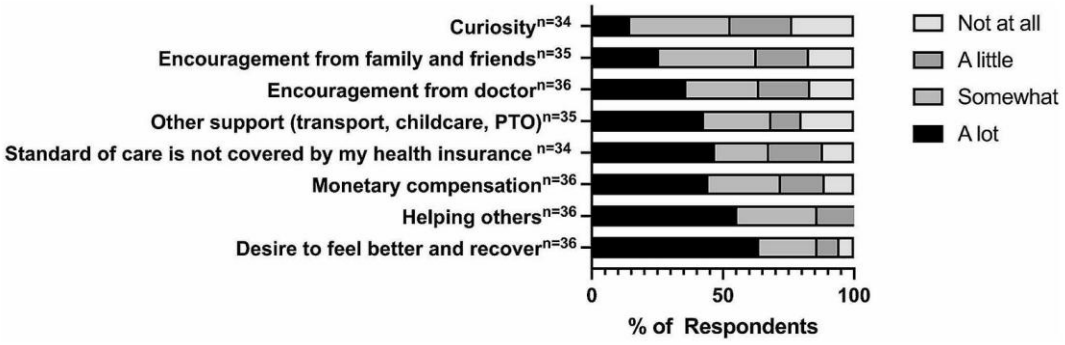

Figure 5: *Frequency of factors influencing the clinical trial participation(Whiting* et al.*, 2024)*

Impact of Healthcare Providers:

Providers play a critical role in patient recruitment but may unintentionally limit access through biased assumptions about patients' willingness or ability to participate. The studies (DasMahapatra *et al.*, 2017; Willison *et al.*, 2019) show that minority and lower socioeconomic patients receive fewer invitations to enroll, reflecting systemic biases and time pressures in clinical settings.

Impact of Digital Advancements:

The rise of online recruitment platforms has expanded trial visibility for digitally connected populations. However, this model marginalizes older adults, low-income individuals, and others lacking digital access or literacy, reinforcing disparities.

Trust and Cultural Sensitivity:

Historical medical abuses, such as the Tuskegee Syphilis Study in the US, have fostered mistrust in clinical research among racial minorities(Amanda Leiter *et al.*, 2015). Even with trial availability and invitations(Eggly *et al.*, 2015), these communities may hesitate to participate without culturally sensitive engagement and transparent communication(Hong, Alishahi Tabriz and Turner, 2021).

Altogether, it is important to overcome these barriers to ensure equitable access with various strategies.

Access in Developing Countries:

The LMICs face multiple challenges in accessing trials, which include,

Structural Barriers and geographical distribution:

Many LMICs have few dedicated research centers, limited trial site capacity, and a shortage of trained personnel(Seruga *et al.*, 2014; Grover *et al.*, 2017c). This restricts the number of available clinical trials and their geographic spread(Khoja, Kazim and Ali, 2019). Urban centers often dominate research activity, leaving rural populations excluded.

As in developed countries, clinical research is concentrated in tertiary hospitals located in the capital or major cities. For rural residents, especially in regions like Ghana (Appeaning *et al.*, 2022b) and Nigeria (Adewale, Schoeman and Roussouw, 2015), this means long travel distances, poor transportation infrastructure, and high costs to reach trial sites.

Economic Barriers:

The LMICs hold the financial burden as a major concern from setting up the trial, logistics, and compensating ancillary expenses, including travel costs. Most of the respondents from Mauritius are expecting to be paid for taking part in the trial(Mowlabaccus and Jodheea-Jutton, 2020).

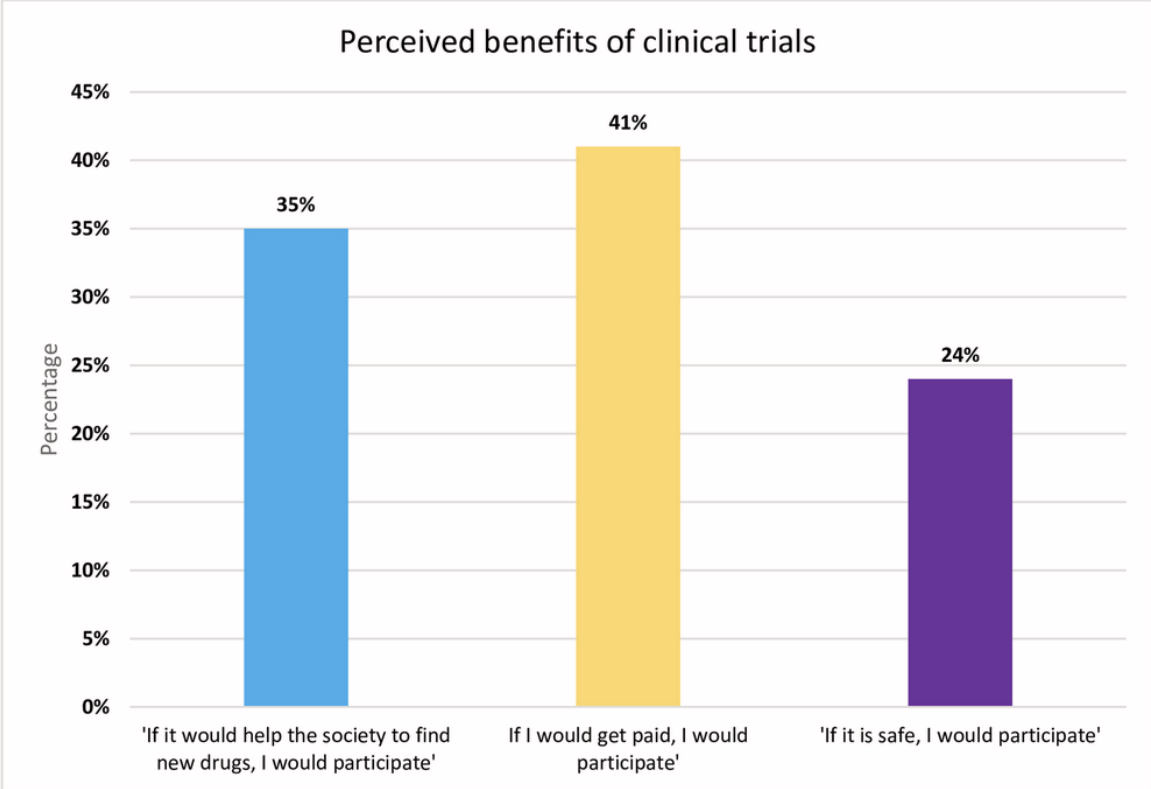

Figure 6: *Perceived benefits of trial participation (Mowlabaccus and Jodheea-Jutton, 2020)*

Regulatory and Ethical Oversight Gaps:

Many LMICs have evolving or weak regulatory frameworks for clinical research, which can delay trial approvals, limit trial diversity, and reduce public confidence. Inadequate ethical oversight raises concerns about participant protection and transparency(El Obaid *et al.*, 2016).

A study conducted in Nigeria, where an unregistered drug was tested in a vulnerable population like children and infants, led by a leading company, Pfizer, raises safety concerns(Devasenapathy, Singh and Prabhakaran, 2009).

Health System Capacity and Integration:

In several LMICs, healthcare systems lack integration with research activities. Frontline healthcare workers may be unaware of ongoing trials or lack training to

inform patients, reducing trial visibility and access(Al-Shami, Ahmed and Alzoubi, 2022).

Cultural and Social Factors:

Community mistrust and misconceptions about research, combined with low health literacy, discourage participation even when trials exist(Adewale, Schoeman and Roussouw, 2015; Mowlabaccus and Jodheea-Jutton, 2020). Social stigma and misinformation further complicate engagement.

Implications for health equity:

The disparities in access to clinical trials have profound consequences for health equity at multiple levels.

- Clinical trials often provide access to cutting-edge therapies not otherwise available. When marginalized populations are excluded, they lose potential health benefits, perpetuating existing health disparities.
- Trials that disproportionately enroll privileged populations produce evidence less applicable to diverse real-world patients. This can lead to ineffective or harmful treatments in underrepresented groups, further exacerbating inequity.
- Equitable inclusion in clinical trials is a cornerstone of research ethics. Exclusion violates principles of justice and fairness, undermining public trust and the legitimacy of research enterprises.

Strategies to Improve Access:

Addressing disparities in clinical trial access requires concerted, multi-level efforts:

- **Community Engagement and Participatory Research:** Involving community stakeholders in trial design and implementation enhances cultural relevance and trust. Studies from Washington, DC (Whiting *et al.*, 2024) and the UK (Wienroth *et al.*, 2018) emphasize the success of community advisory boards and focus groups.

- **Decentralized and Mobile Trials:** Innovative trial models that bring research to communities via mobile units, satellite clinics, or telemedicine can reduce geographic and logistical barriers.
- **Financial and Logistical Support:** Providing transportation stipends, childcare, flexible scheduling, and compensation addresses economic barriers that disproportionately affect marginalized populations.

- **Healthcare Provider Training:** Educating providers about equitable recruitment practices, cultural sensitivity, and trial referral improves access and patient trust.

- **Infrastructure and Capacity Building in LMICs:** Investing in research infrastructure, ethical oversight, and workforce training expands trial availability and quality.

- **Policy and Regulatory Harmonization:** Streamlined and transparent regulatory frameworks facilitate ethical and timely trial conduct across diverse settings, fostering inclusion.

COVID-19's influence on access:

The COVID-19 pandemic accelerated the adoption of digital tools in clinical research, including remote consent, telehealth monitoring, and decentralized trial models (Schultz *et al.*, 2021). These innovations hold promise to reduce traditional access barriers. However, they risk exacerbating inequities for those lacking digital access or literacy.

Moreover, the pandemic diverted healthcare resources and delayed trial initiation in many LMICs, further limiting access. Yet, the global spotlight on research ethics and inclusivity during COVID-19 presents an opportunity to redesign trial access models with equity at their core.

Summary:

The access to clinical trials is unevenly distributed globally, shaped by complex social, economic, and systemic factors. Developed countries face barriers rooted in geographic, socioeconomic, and cultural dimensions, while developing countries confront more fundamental infrastructural and regulatory challenges. These disparities compromise health equity, limiting who benefits from research advances and perpetuating health inequalities.

Transformative strategies that prioritize community engagement, infrastructural investment, provider training, and policy reform are essential to ensure clinical trials become truly inclusive. The COVID-19 pandemic offered learnings and innovations that accelerate these efforts if equity remains central.

2.5. Ethical disparities – HICs Vs LMICs:

Ethical oversight and trial transparency are foundational pillars of clinical research integrity. While international ethical frameworks such as the Declaration of Helsinki and the Belmont Report offer universal guidance, their implementation varies significantly between high-income countries (HICs) and low- and middle-income countries (LMICs). These differences have direct implications for public trust, participant safety, and clinical trial awareness.

In HICs, ethical review processes are typically overseen by well-established Institutional Review Boards (IRBs) or Research Ethics Committees (RECs) embedded within research institutions. These bodies are supported by regulatory authorities such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA), which mandate rigorous standards for informed consent, risk assessment, and data transparency (Schultz *et al.*, 2021). Additionally, trial registration through publicly accessible databases such as ClinicalTrials.gov or the EU Clinical Trials Register is routinely enforced, enabling stakeholders and the public to track research activities and outcomes (Wienroth *et al.*, 2018).

By contrast, ethical review mechanisms in many LMICs remain underdeveloped. National or regional ethics committees often operate with limited funding, inconsistent training, and unclear jurisdictional authority (Grover et al., 2017b; Khoja, Kazim and Ali, 2019). In some contexts, these boards rely heavily on the ethical clearance of international sponsors, which may not fully consider local cultural norms, community dynamics, or language barriers (Lang and Siribaddana, 2012). As a result, informed consent processes may be inadequately explained or poorly understood by participants, compromising the ethical principle of autonomy (Appeaning et al., 2022b; Mowlabaccus and Jodheea-Jutton, 2020). Studies have highlighted frequent challenges in translating consent forms into local languages and explaining complex research concepts to participants with limited health literacy (Figer et al., 2021; Al-Dakhil et al., 2016).

Transparency is another key point of divergence. While HICs have embraced clinical trial registries and mandatory results reporting, many LMICs lack national registries or do not enforce trial registration consistently (Nundy and Gulhati, 2005). The World Health Organization's ICTRP and platforms like India's Clinical Trials Registry (CTRI) aim to address these gaps, but coverage and compliance remain variable (Grover et al., 2017b). Furthermore, trial results conducted in LMICs are often not disseminated back to participating communities, contributing to mistrust and perceptions of exploitation, particularly in regions with historical precedents of unethical research (Devasenapathy, Singh and Prabhakaran, 2009; Jawa et al., 2023).

These disparities in ethical infrastructure and transparency not only affect participant protection but also undermine the credibility and inclusivity of global research. Strengthening ethics oversight in LMICs requires capacity-building investments, standardized training for ethics committee members, and the development of enforceable national policies aligned with international standards (Seruga et al., 2014; El Obaid et al., 2016). The implementation of dual ethical review processes, one from the sponsor institution and one from a local,

independent ethics body, can help balance scientific rigor with local sensitivity (Al-Shami, Ahmed and Alzoubi, 2022).

Finally, enhancing transparency through mandatory trial registration, results dissemination, and community feedback mechanisms is essential. This not only increases public trust but may also improve awareness and willingness to participate in future research efforts (Mowlabaccus and Jodheea-Jutton, 2020; Whiting et al., 2024). It is critical to address these ethical and procedural asymmetries to foster equity, trust, and sustainability in global clinical research.

2.6. Gaps in the literature:

Despite a growing body of work on clinical trial awareness, several critical gaps persist:

1. Lack of longitudinal studies:
   The vast majority of existing research utilizes cross-sectional survey designs, offering only a snapshot of awareness at a single point in time. Consequently, there is limited understanding of how awareness of clinical trials evolves over time. Notably, there are no robust longitudinal studies that compare awareness levels before and after significant global events, such as the COVID-19 pandemic, which has profoundly impacted public health perceptions worldwide.

2. Absence of intervention-based research:
   There are very few studies that evaluated the effectiveness of specific interventions aimed at increasing awareness, such as educational programs, media campaigns, or policy changes. This limits the ability to recommend evidence-based solutions.

3. Underrepresentation of rural and marginalized populations:

The majority of research, whether conducted in developed or developing nations, was primarily focused on urban areas, ignoring sizable portions of the population that would be more vulnerable to poor awareness.

4. Lack of assessing language barriers:
   The challenge of comprehending translations and misunderstandings brought on by the back-and-forth interchange of information in different languages is not examined.

5. Inconsistencies in outcome definitions:
   The lack of standardized metrics for awareness and knowledge hinders meta-analytical synthesis and cross-study comparisons. There is a difference in how awareness is measured between developed and developing countries. In many developing nations, studies often focus on whether the public has heard of the term "clinical trial". In contrast, research in developed countries tends to assess the depth and extent of public knowledge regarding clinical research processes and ethics. These national differences in comprehension and measurement approaches complicate direct comparisons across studies.

2.7. Rationale for Meta-analysis:

The primary rationale for conducting this meta-analysis stems from the considerable variability observed across existing studies in terms of outcomes assessed, methodologies used to evaluate awareness, and sample sizes. These differences hinder direct comparisons and limit the generalizability of individual findings.

By employing a meta-analytic approach, this study systematically synthesizes and compares awareness levels of clinical trials between developed and developing countries. This method enables the estimation of a pooled effect size that provides a more precise and comprehensive measure of awareness across diverse settings.

Additionally, the meta-analysis facilitates exploration and identifies the potential moderators and variables. The pattern identification is crucial for designing future research and targeted interventions, ultimately leading to more robust and actionable evidence.

2.8. Conclusion:

The literature demonstrates clear disparities in awareness of clinical research between developed and developing countries. While structural advantages in developed nations support higher awareness, marginalized subgroups still face barriers. In developing countries, systemic and cultural challenges play a larger role in limiting public understanding of clinical trials. However, the current body of research is constrained by methodological inconsistencies, a lack of longitudinal data, and limited intervention testing. This underscores the need for a meta-analytic approach to provide more definitive conclusions and guide evidence-based awareness strategies across diverse settings.

CHAPTER 3: METHODOLOGY

3.1. Selection:

3.1.1 Sources:

This study employed a systematic and structured approach to identify relevant peer-reviewed literature for inclusion in the meta-analysis. The primary databases used were **Google Scholar** and **PubMed**, chosen for their comprehensive coverage of biomedical, social science, and public health research. Initial searches were conducted using Publish or Perish, which facilitated efficient extraction of citation data from Google Scholar. These results were imported into **ASReview**, an open-source machine learning tool used to prioritize and semi-automatically screen studies based on relevance to the research question. Following this, selected studies were organized and managed using Zotero for reference tracking, de-duplication, and citation management.

The meta-analysis followed the **PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)** guidelines to ensure methodological transparency, consistency, and reproducibility throughout the selection process. A clearly defined set of inclusion and exclusion criteria was applied during screening. Inclusion criteria required that studies be original research employing cross-sectional, survey-based, or cohort designs that assess awareness, knowledge, perception, or attitudes related to clinical research or clinical trials. Only studies involving adults aged 18 and above, published between January 2015 and April 2025, and conducted in developed or developing countries as classified by the World Bank or United Nations, were considered. Studies were included if they were published in English or accompanied by reliable English translations and reported sufficient quantitative data (e.g., proportions, means, standard deviations, or odds ratios) for extraction and comparative analysis.

Exclusion criteria were strictly applied to ensure the relevance and quality of data. These included the elimination of case reports, editorials, review articles, and randomized controlled trials unless such studies explicitly measured awareness-related outcomes. Studies that were qualitative-only were excluded from the meta-analysis but retained separately for contextual interpretation where relevant. Research focused exclusively on pediatric populations or those conducted in ambiguous or unspecified geographic locations was excluded. Additionally, studies lacking adequate statistical data or reporting solely on participation or recruitment without measuring awareness, perception, or attitude were not included.

This rigorous sourcing strategy ensures that the final body of literature included in the meta-analysis reflects high methodological standards, thematic relevance, and international diversity. Full details of the search terms, screening process, and study selection are documented in the **PRISMA flow diagram** and accompanying appendices.

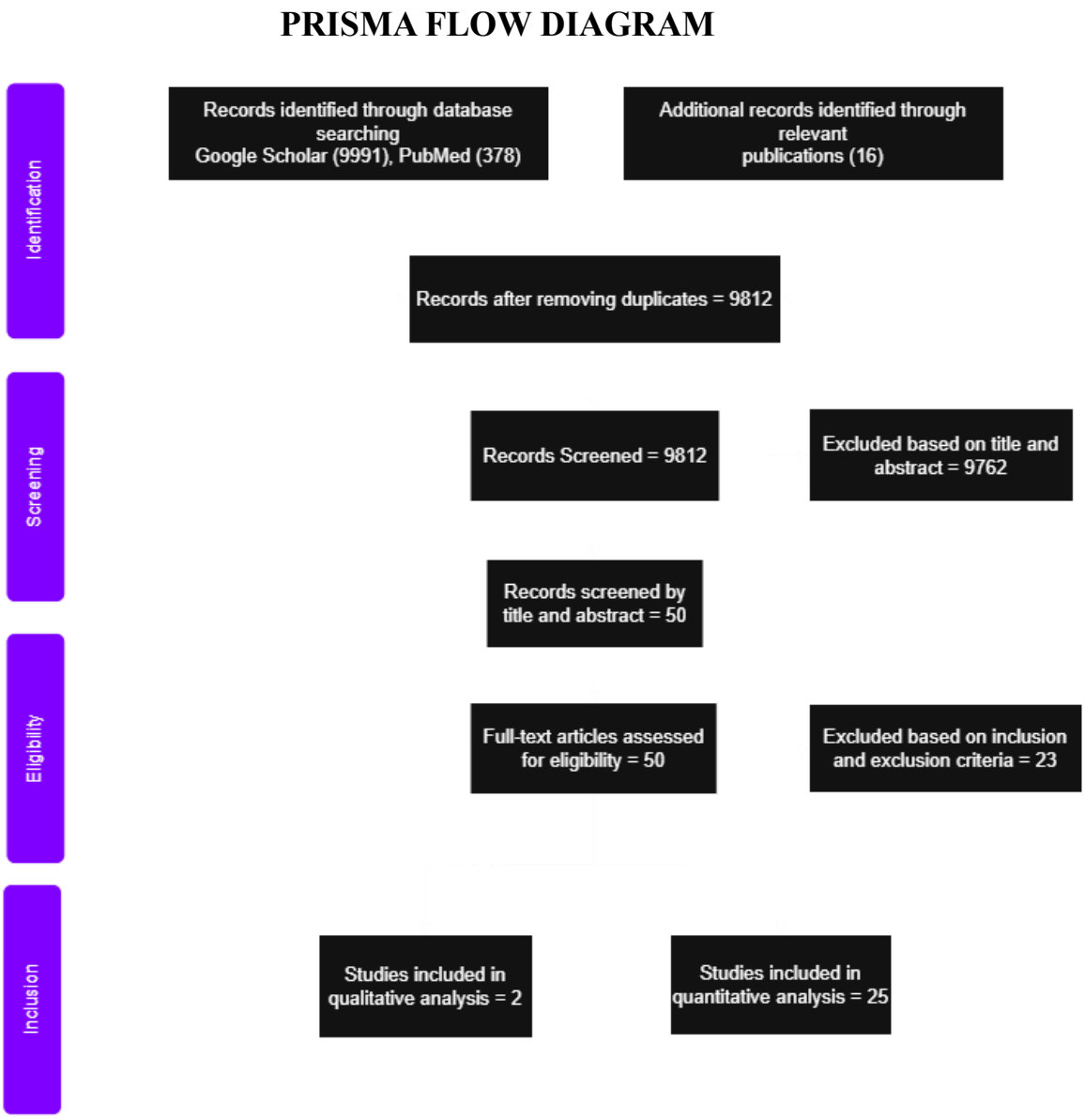

Figure 7: PRISMA Flow Diagram (drawn using draw.io)

3.1.2 Inclusion and exclusion criteria:

To ensure that this meta-analysis includes only high-quality and relevant studies, a clear set of **inclusion and exclusion criteria** was established and applied consistently throughout the selection process.

Inclusion Criteria:

Studies were included if they met the following conditions:

- ***Study Design:*** The research had to use a cross-sectional, survey-based, or cohort design to explore public awareness, knowledge, perception, or attitudes toward clinical research or clinical trials.
- ***Population:*** Only studies involving adults aged 18 years and above were considered.
- ***Geographic Focus:*** The study must have been conducted in a country classified as either developed or developing, according to the World Bank or United Nations.
- ***Publication Timeframe:*** Eligible studies were published between January 2015 and April 2025.
- ***Language:*** Only studies published in English or available with a reliable English translation were included.
- ***Outcomes Measured:*** The study needed to report quantitative data (e.g., Percentage awareness) related to awareness, knowledge, perception, or attitudes toward clinical research, sufficient for extraction and comparative analysis.

Exclusion Criteria:

Studies were excluded if they met any of the following conditions:

- ***Study Type:*** Editorials, opinion pieces, case reports, review articles, or randomized controlled trials not specifically assessing awareness were excluded. Qualitative-only studies were also excluded from the meta-analysis, although they may be reviewed separately for context.
- ***Population:*** Studies focused only on children or adolescents (under 18) were excluded unless data on adults were reported separately.
- ***Geographic Clarity:*** Studies conducted in unspecified or unclear geographic locations were excluded.
- ***Publication Date:*** Articles published before 2015 were excluded to maintain relevance to current research environments.

- ***Language:*** Studies published in non-English languages without accessible English translations were excluded.
- ***Data Quality:*** Any study lacking clear statistical or outcome data relevant to awareness or perception was excluded. Similarly, studies measuring only participation or recruitment rates, without linking them to awareness or attitude, were omitted.

These criteria were designed to focus the analysis on studies that best reflect the current global landscape of public understanding of clinical trials, allowing for a meaningful comparison between developed and developing countries.

Table 3: *Inclusion and exclusion criteria for meta-analysis.*

Criteria	***Inclusion***	***Exclusion***
Study Design	Cross-sectional, survey-based, mixed-methods, or cohort studies.	Case reports, editorials, reviews, RCTs (unless measuring awareness), qualitative-only studies.
Population	Adults (18+).	Pediatric populations.
Geographic Focus	Countries classified as developed or developing by the World Bank or UN classification.	Country not specified or unclear.
Timeframe	Published between January 2015 to April 2025.	Published before 2015.
Language	English or an available translation in English.	Non-English, without translation.
Outcomes measured	Awareness, Knowledge of clinical trials/research	Attitude towards participation, Participation rate, or

		recruitment, with no focus on awareness of clinical trials/research.
Data Availability	Full-text availability with raw data for extraction (eg, Percentage awareness, mean age, etc.)	Free access to full-text if not available, insufficient raw data.

3.2. Data interpretation methods:

To ensure rigorous and replicable synthesis of findings, this study employed a **meta-analytic approach using a random-effects model** to interpret data across diverse study populations and settings quantitatively. The random-effects model was chosen over a fixed-effects model due to the expected heterogeneity in study characteristics, such as geographic location (developed vs. developing countries), population demographics, and research design. This model assumes that the true effect size may vary from one study to another and accounts for both within-study and between-study variance, making it particularly appropriate for cross-national comparisons where contextual and cultural factors likely influence outcomes.

All statistical analyses were conducted using the **R programming language**, utilizing the meta, metafor, and metadat packages. The primary outcome, **awareness of clinical research or trials,** was operationalized as a proportion, calculated from reported percentages or raw data. To stabilize variances, a **logit transformation (PLOGIT)** was applied during meta-analysis, improving the accuracy and comparability of proportions across studies with varying sample sizes and baseline awareness levels.

Pooled estimates were generated using the **metaprop()** function, and results were visualized through **forest plots** to display individual and combined proportions with

95% confidence intervals. To assess the risk of publication bias, **funnel plots** were also produced. Heterogeneity was quantified using the **I^2 statistic** and **Cochran's Q test**, with I^2 values over 50% indicating moderate to high heterogeneity and justifying further exploration.

To examine potential sources of variation in awareness levels, a **meta-regression** was conducted. In this model, **country type (developed vs. developing)** was included as a moderator to test its influence on awareness outcomes. This allowed the analysis to go beyond pooled estimates and investigate whether country-type classification contributed significantly to disparities in clinical trial awareness. Although additional variables such as year of publication, mean age, gender composition, and setting (urban/rural) were considered, only those consistently available across studies were included in the final model.

By applying a systematic and transparent method of data aggregation through meta-analysis, this approach ensures that findings are not only statistically robust but also generalizable across varied national contexts. The use of open-source tools like R further strengthens the **replicability** of the study, allowing future researchers to validate or expand upon the results using similar datasets and scripts. Complete details of the coding process, functions used, and model specifications are available in the appendix for full transparency.

CHAPTER 4: DATA ANALYSIS AND RESULTS

4.1. Quantitative data analysis:

A comprehensive meta-analysis conducted to explore the disparities in awareness of clinical research and trials between developed and developing countries has resulted in significant outcomes. This analysis utilized robust data from 25 studies, comprising 35,749 participants and 22,332 reported awareness events. A random-effects meta-analytic approach was used due to high expected heterogeneity in study contexts, populations, and methodologies.

Descriptive Overview:

Out of 25 studies included, **14** were conducted in developed countries and **11** in developing countries. The average proportion of participants aware of clinical trials was found to be **56.9%** across all studies, with a 95% Confidence Interval (CI): 48.7% to 64.8%. A substantial variation was observed across studies in sample size, setting (urban vs. rural), gender distribution, and year of publication.

A forest plot was generated using R-Studio (Figure 8), illustrating point estimates and confidence intervals for each study included in the analysis.

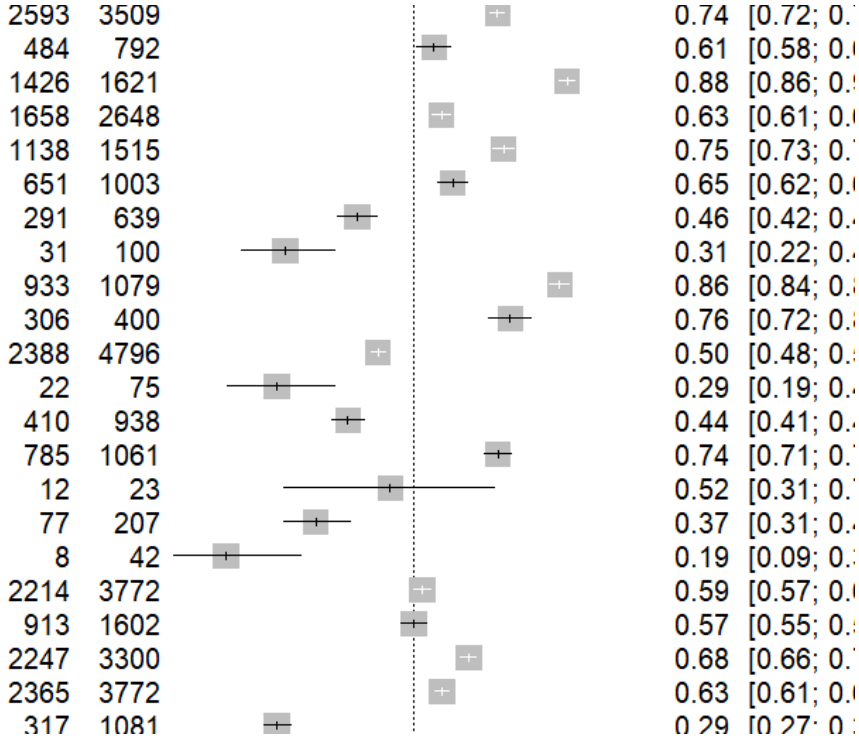

*Figure 8***:** *Forest-Plot of conducted meta-analysis (Excluding subgroup analysis) (generated using R-Studio).*

Overall Meta-Analysis Results:

A random-effects model was implemented due to expected heterogeneity among studies. The pooled awareness proportion was 0.569 (95% CI: 0.487–0.648). This indicates that only around 57% of participants from all the studies were aware of

CT opportunities. As expected, substantial heterogeneity was found and confirmed from the summary results of the analysis.

$\tau^2 = 0.6887$, $I^2 = 98.9\%$, and **Q (Wald) = 2207.36, p < 0.001**

This shows that almost all variation was due to the original differences across studies rather than by chance. Due to high heterogeneity (**$I^2 = 98.9\%$**), subgroup analyses and meta-regression were conducted to explore potential moderators of awareness.

Subgroup Analysis by Country Type:

A subgroup analysis was conducted to identify the disparity based on the type of country where trials were conducted. This was done by grouping the studies based on country, and the following results were obtained:

Table 4: *Results from subgroup analysis based on the type of country*

Country Type	*Studies*	*Proportion*	*95% CI*	*I^2*
Developed	14	63.6	[52.2%; 73.7%]	98.6%
Developing	11	47.9	[39.5%; 56.5%]	98.1%

Q = 4.63, df = 1, **p = 0.0315**

A forest plot was generated using R-Studio (Figure 9), illustrating the pooled estimates for grouped studies of developed and developing nations. With p = 0.0315, thus accounting for a statistically significant outcome when $p < 0.05$.

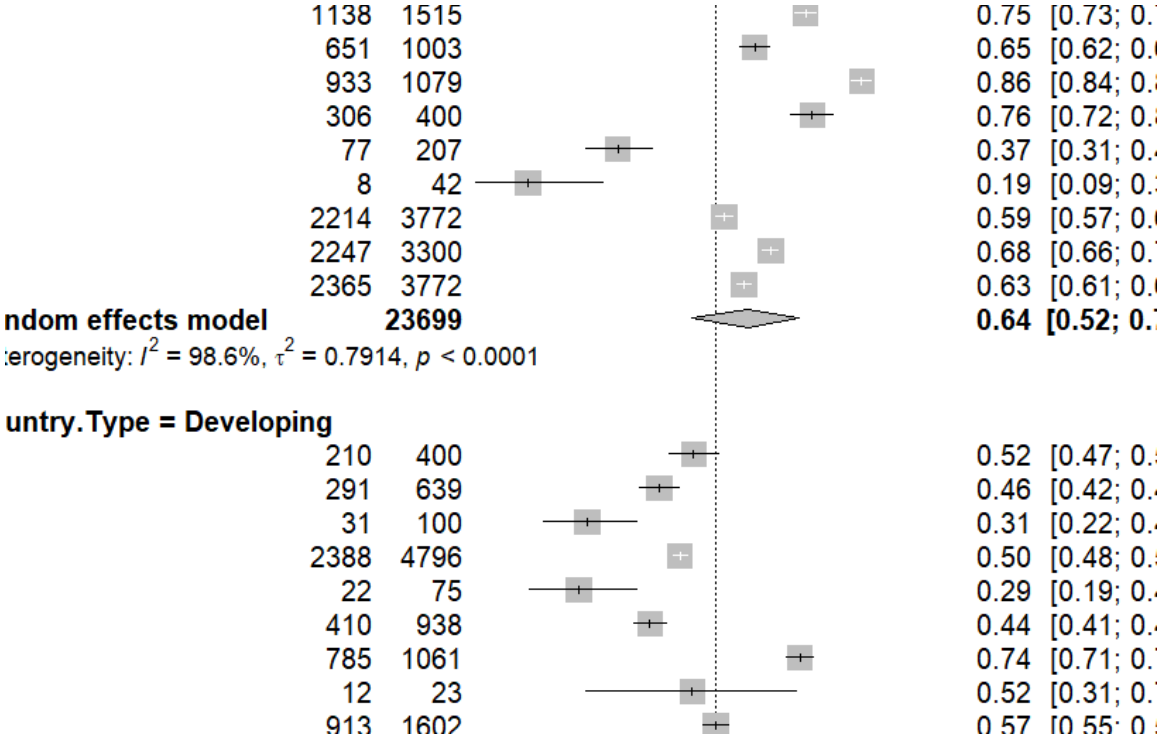

Figure 9: *Forest-Plot of the conducted meta-analysis, including subgroup analysis based on country type (generated using R-Studio).*

This can be interpreted as evidence that participants in developed countries are more aware of clinical research than those in developing countries. The statistically significant difference hereby suggests that the country's development status is an important factor in CT awareness.

Meta-Regression Analysis:

A meta-regression was conducted using five moderators:

1. Country Type (Developed vs. Developing)
2. Published Year
3. Mean Age
4. Female Percent
5. Setting (Urban vs. Rural)

These moderators were chosen for investigation based on assumptions and consistent data availability for meta-regression analysis. It included 22 studies out

of 25 for meta-regression, due to a lack of data in the remaining 3 studies, and utilized the Restricted Maximum Likelihood (REML) method.

Tau² = 0.4620, I² = 99.2% (High heterogeneity)

R² = 29.99% ~30% of between-study variance

p = 0.0216 (p<0.05)

Table 5: Results from meta-regression analysis depicting the impact of various moderators.

Moderators	*Estimates*	*p-value*	*Interpretation*
Country Type (Developing)	-1.10	0.027	Significantly lower awareness than the other country type (Developed).
Published Year	-0.025	0.611	Not Significant
Mean Age	-0.0077	0.774	Not Significant
Female Percent	-0.0192	0.295	Not Significant
Urban/Rural (Urban)	-0.688	0.178	Not Significant

A meta-regression plot was generated using R-Studio (Figure 10), which illustrates that country type is the only significant factor among the 5 moderators taken into account.

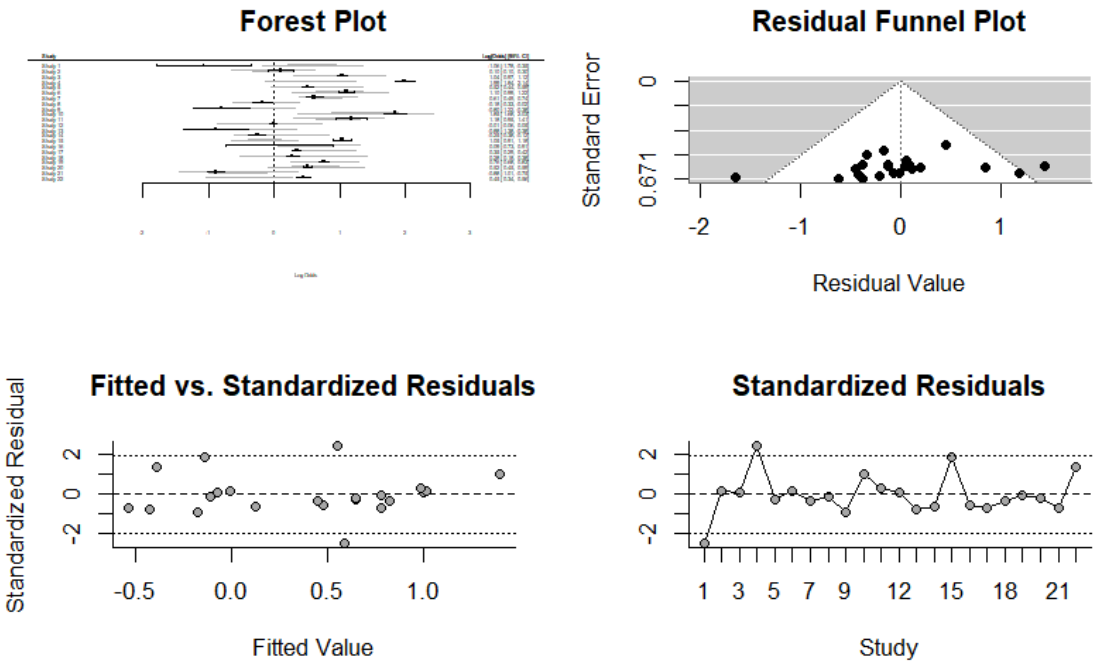

Figure 10: *Meta-regression plot (generated using R-Studio).*

Analysis of publication bias:

The risk of publication bias was analysed using a funnel plot for the studies included in the meta-analysis.

A funnel plot generated using R-Studio, indicating slight asymmetry with more studies on the left side of the plot. This implies the potential existence of heterogeneity, small-study effects, or publication bias.

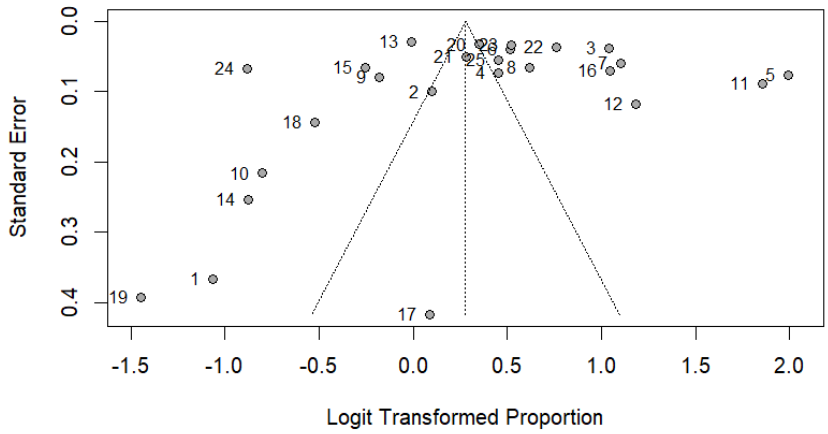

Figure 11: *Funnel plot (generated using R-Studio).*

Summary:

- The country type is the only significant factor influencing awareness.
- Even after adjusting for publication year, age, gender, and setting, participants in developing countries had significantly lower awareness.
- This confirms findings from the subgroup analysis and suggests that structural, health system, or educational differences at the country level are influential.
- Other moderators did not significantly explain variability, indicating that individual study-level demographic factors may be less important than national-level factors.

5.1. Key Findings:

In order to provide context and interpretation for the global differences in clinical research awareness, the quantitative findings of the meta-analysis are taken from the broader research objectives and discussed in this section. Each conclusion is backed up by statistical data and connected to possible socioeconomic, cultural, and structural elements that may have influenced the trends that were seen, which will be discussed later.

1. Global Awareness of Clinical Research is Limited

The pooled global awareness proportion was approximately **57%**, indicating that nearly half of the participants lacked knowledge of clinical trials.

2. Significant Awareness Gap Between Developed and Developing Countries

Awareness in developed countries was **63.6%**, compared to **47.9%** in developing countries, a statistically and practically significant difference.

3. Country Development Status is the Strongest Predictor

Meta-regression showed that development status alone explained **nearly 30%** of between-study variance, outperforming all other variables.

4. Participant Demographics and Study Characteristics Had Minimal Impact

Variables such as mean age, gender distribution, urban/rural setting, and year of publication were not statistically significant predictors of awareness.

5. High Heterogeneity Reflects Study Context Diversity

I^2 values exceeded 98%, suggesting substantial variability across study populations, health systems, and research environments.

6. Publication Bias

Regardless of the type of country, the majority of the studies were conducted in urban areas. Additionally, the funnel plot was used to confirm a slight bias based on the distribution of studies.

CHAPTER 5: DISCUSSION

5.1. Interpretation of results:

This section interprets the findings, links them to the research objectives and literature, and discusses their broader implications.

The primary finding, that only **57%** of people globally are aware of clinical trials, signals a major obstacle to equitable participation in medical research. This aligns with previous literature emphasizing limited public engagement, particularly in low-resource settings (Mowlabaccus and Jodheea-Jutton, 2020; Al-Shami, Ahmed and Alzoubi, 2022). Such low awareness can compromise informed consent, hinder recruitment, and exacerbate disparities in who benefits from medical innovation.

The 16% gap in awareness between developed and developing countries confirms that awareness is not evenly distributed and is likely driven by systemic factors. Higher awareness in developed nations may be attributed to:

- ✓ Stronger health communication infrastructure
- ✓ Greater transparency and normalization of clinical research
- ✓ More robust educational and regulatory systems
- ✓ Higher and easier accessibility

This supports Objective 1 of the study and emphasizes the need for structural interventions rather than individual-level fixes. There is a need to understand the level of awareness in rural areas of both developed and developing countries, as most of the studies are based on the city side of the nations.

The development status has explained nearly 30% of between-study variance, reinforcing the notion that clinical trial awareness is largely shaped by national-level systems, not just demographics or recruitment strategies. This suggests that building awareness requires country-specific investments in research infrastructure, education, and policy, aligning with Objective 4 of the dissertation.

The lack of predictive power from variables such as age, gender, and study setting challenges assumptions often made in clinical research about who needs to be “targeted” for awareness. Instead, it highlights the importance of systemic and environmental influences. In addition, this finding suggests exploring the influence of other variables such as literacy level, socio-economic status, or language. The translation is one of the

unspoken barriers that doesn't allow a non-native speaker to be aware of CT opportunities.

While high I^2 values reduce statistical certainty, they point to the rich diversity of global health systems and public attitudes toward research. Rather than being a limitation, this underscores the need for tailored, context-sensitive awareness campaigns, not one-size-fits-all approaches. This directly supports Objective 4: developing recommendations rooted in local realities.

These findings highlight the urgent need for policy reforms, especially in low- and middle-income countries (LMICs), to close the awareness gap and promote equitable research participation. They also underscore the ethical imperative of ensuring that populations with the highest disease burdens are adequately informed and represented in clinical trials. Global trial sponsors and institutions must prioritize community engagement, health literacy, and research visibility in LMIC settings.

5.2. Limitations:

This dissertation offers important insights, there are quite a few limitations that must be acknowledged:

High Heterogeneity Across Studies

The meta-analysis revealed substantial statistical heterogeneity ($I^2 > 98\%$), reflecting variation in study design, geographic region, sample size, and measurement tools. Although a random-effects model was used to mitigate this, it limits the precision and generalizability of pooled estimates. To reduce this, a more robust method should be adopted for analysis that focuses on an outcome defined same way or data collected using the same method across studies.

Lack of Detailed Socioeconomic Data

Many included studies did not report granular socioeconomic variables such as education level, income, or healthcare access. These are likely to be important mediators of awareness and should be more consistently included in future research.

Language and Regional Bias

This review included only English-language publications, which may have excluded relevant data from regions such as Latin America, Francophone Africa, and Southeast Asia. This limitation may have introduced selection bias.

Cross-Sectional Design of Most Studies

The majority of included studies employed cross-sectional survey methods, capturing awareness at a single point in time. Longitudinal data are needed to evaluate how awareness evolves, particularly following public health interventions.

Exclusion of Qualitative and Contextual Factors

This meta-analysis focused on quantitative awareness measures. However, awareness is shaped by deeper factors such as cultural attitudes, ethical concerns, and trust in medical systems. These important dimensions were beyond the scope of this review.

Directions for Future Research

To address the above limitations and build on this study's contributions, future research should:

- Conduct longitudinal studies to track changes in awareness over time and in response to interventions.
- Explore qualitative dimensions of awareness, such as trust, misinformation, and ethical perceptions, through interviews and focus groups.
- Design and evaluate evidence-based interventions aimed at increasing awareness, particularly in LMIC settings.
- Include region-specific and non-English-language studies to improve representativeness and reduce language bias.
- Investigate the link between awareness and actual trial participation or outcomes (e.g., recruitment and retention rates).

5.3. Recommendations:

Based on the findings of this meta-analysis, the following recommendations are proposed to address global disparities in awareness of clinical research, with a particular focus on low- and middle-income countries (LMICs):

1. Governments and health authorities should invest in large-scale, culturally relevant public education campaigns to improve clinical research literacy(Grover *et al.*, 2017a). These efforts should leverage local languages, mass media, schools, and community engagement to build foundational awareness.

2. Awareness initiatives should be embedded within national health systems. Clinical research education can be incorporated into patient-provider interactions, routine public health messaging, and community outreach led by health workers.

3. Awareness improves when clinical research is visible and accessible. Expanding research infrastructure in LMICs through local trial centers, academic partnerships, and funding incentives can increase public exposure to clinical trials and normalize participation(Appeaning *et al.*, 2022a).

4. To overcome skepticism and cultural resistance, it is vital to collaborate with trusted community figures. Religious leaders, tribal elders, and civic organizations can act as mediators to promote clinical research in a culturally sensitive manner.

5. Sponsors, funders, and international regulatory bodies should require context-sensitive engagement strategies as part of ethical trial conduct. Awareness should be recognized as a prerequisite for ethical recruitment and representation, not an optional consideration(Glickman *et al.*, 2009).

6. Digital technologies such as mobile health applications, SMS reminders, and targeted social media campaigns can support scalable and cost-effective awareness efforts. These tools must be adapted to local literacy, language, and technological access(Nguyen *et al.*, 2023).

CHAPTER 6: CONCLUSION

This dissertation explored global disparities in awareness of clinical research and trials through a comprehensive meta-analysis comparing developed and developing nations. The analysis revealed that public awareness of clinical trials remains suboptimal worldwide, with pronounced differences based on country development status. These findings have important implications for the ethical conduct, design, and inclusiveness of clinical research on a global scale.

The meta-analysis estimated a global pooled awareness of 57%, indicating that nearly half of the population studied is unaware of clinical trials. More notably, a significant awareness gap was found between developed (63.6%) and developing countries (47.9%), underscoring the influence of structural and systemic disparities. Meta-regression confirmed that development status was the most powerful predictor of awareness, explaining nearly 30% of between-study variation, even after adjusting for demographic and contextual factors.

Contrary to expectations, individual-level variables such as mean age, gender distribution, urban/rural setting, and publication year were not statistically significant predictors of awareness. These findings challenge conventional assumptions and shift attention toward the institutional, infrastructural, and socio-economic conditions that shape public understanding of and engagement with research.

The high heterogeneity across studies ($I^2 > 98\%$) reflects the diverse research and healthcare environments globally, reinforcing the need for localized strategies to improve trial awareness. These strategies must be responsive to the unique cultural, political, and educational contexts in which they are implemented.

This study contributes a quantitative synthesis of global awareness disparities, bridging a gap in the existing literature. It not only highlights how much awareness varies but also offers insights into why these differences exist, shifting the narrative from individual responsibility to systemic accountability. The findings serve as a trigger to action for global research stakeholders to ensure that awareness, and therefore access to clinical research, is more equitably distributed.

For clinical trials to be inclusive, ethical, and representative, awareness must be treated as a foundational element, not a peripheral concern. As the global health landscape continues to evolve, particularly concerning increasing cross-border trials and emerging health threats, building public trust and understanding of research becomes ever more urgent. This dissertation offers evidence that meaningful change must begin not just with communities, but with the systems that shape their opportunities to engage.

APPENDICES:

Appendix A: Search Strategy

A comprehensive literature search was conducted using two primary databases: **PubMed** and **Google Scholar**, covering the publication period from **January 1, 2015, to April 15, 2025**. The search aimed to identify peer-reviewed, original studies that investigated **awareness, knowledge, perception, or attitudes toward clinical research and clinical trials** in both **developed and developing countries**. Only articles published in **English** were included.

PubMed Search:

The PubMed search was constructed using a combination of Medical Subject Headings (MeSH) and title/abstract keyword terms. The Boolean operators AND and OR were used to combine concepts relevant to awareness-related outcomes, clinical research context, study design, and country focus. The following search string was applied:

(("awareness"[Title/Abstract] OR "knowledge"[Title/Abstract] OR "perception"[Title/Abstract] OR "attitude"[Title/Abstract]) AND ("clinical trial"[Title/Abstract] OR "clinical research"[Title/Abstract]) AND ("survey"[Title/Abstract] OR "cross-sectional"[Title/Abstract] OR "cohort"[Title/Abstract]) AND ("developing countries"[MeSH Terms] OR "developed countries"[MeSH Terms] OR "India"[Title/Abstract] OR "Nigeria"[Title/Abstract] OR "Kenya"[Title/Abstract] OR "Bangladesh"[Title/Abstract] OR "Pakistan"[Title/Abstract] OR "Uganda"[Title/Abstract] OR "Ethiopia"[Title/Abstract] OR "Ghana"[Title/Abstract] OR "United States"[Title/Abstract] OR "UK"[Title/Abstract] OR "Canada"[Title/Abstract] OR "Germany"[Title/Abstract] OR "France"[Title/Abstract] OR "Australia"[Title/Abstract] OR "Japan"[Title/Abstract])) AND ("2015/01/01"[Date - Publication] : "2025/12/31"[Date - Publication]) AND English[lang]

This search yielded a total of **378 results**, which were exported for screening and selection.

Google Scholar Search:

The Google Scholar search used simplified keyword combinations due to platform limitations, focusing on the same conceptual domains. The following search string was applied:

("awareness" OR "knowledge" OR "perception" OR "attitude") AND ("clinical trial" OR "clinical research") AND ("survey" OR "cross-sectional" OR "cohort") AND ("India" OR "Nigeria" OR "Kenya" OR "Bangladesh" OR "Pakistan" OR "Uganda" OR "Ethiopia" OR "Ghana" OR "United States" OR "UK" OR "Canada" OR "Germany" OR "France" OR "Australia" OR "Japan")

The date range filter was applied to restrict the results to studies published between **2015 and 2025**. This search returned approximately **18,600 results**. After applying relevance screening using **ASReview**, a total of **9,991 relevant citations** were extracted, which were then merged with the PubMed results (378) for a combined initial pool of **10,369 records** (including duplicates).

Deduplication and Final Yield:

Using **Zotero's duplicate merge function**, duplicates were removed, reducing the dataset to **9,812 unique records**. After title and abstract screening, full-text review, and application of inclusion/exclusion criteria, **50 studies** were ultimately selected for inclusion in the analysis.

Geographic Distribution Overview:

To ensure geographic representation:

- **Developing countries** (e.g., India, Nigeria, Kenya, Bangladesh): Studies were tracked across five time intervals, 2015–2016, 2017–2018, 2019–2020, 2021–2022, and 2023–2025, with over **1,000 potential studies** identified initially for each interval.

- **Developed countries** (e.g., United States, UK, Canada, Australia): A smaller number of eligible studies were retrieved using the same search strategy, ensuring balanced representation in the final synthesis.

Further details, including the full list of included studies and PRISMA flow diagram, are available in the appendices.

Appendix B: Meta-analysis Inclusion/Exclusion Evaluation Data

Evaluation.xlsx

Appendix C: Meta-analysis Data

Study ID	% Awareness	Country-Type	Sample Size	Published Year	Urban-Rural	Mean Age	Female Percent
1	25.7	Developed	39	2024	Urban	39.5	62.2
2	52.5	Developing	400	2021	Urban	34.74	41.75
3	73.9	Developed	3509	2015	Urban	44.52	50.5
4	61.1	Developed	792	2023	Urban	73.75	
5	88	Developed	1621	2017	Urban	55	67
6	62.6	Developed	2648	2022	Urban	56.5	54.8
7	75.1	Developed	1515	2015	Urban	42.76	50.3
8	64.9	Developed	1003	2021	Urban	45.3	51.4
9	45.54	Developing	639	2022	Urban	29.03	48.04
10	31.3	Developing	100	2018	Urban	36	54
11	86.5	Developed	1079	2024	Rural	44.96	52.6
12	76.5	Developed	400	2016	Urban	41.5	51
13	49.8	Developing	4796	2024	Urban	19.69	47.1
14	29.3	Developing	75	2015	Urban	36.5	70.7
15	43.7	Developing	938	2019	Urban	32.46	38.4
16	74	Developing	1061	2022	Urban	27.7	50.2
17	52.2	Developing	23	2020	Rural	39.9	50.6
18	37	Developed	207	2018			
19	20	Developed	42	2016			
20	58.7	Developed	3772	2022	Urban	48.33	51.2
21	57	Developing	1602	2019	Rural	47.7	50

22	68.1	Developed	3300	2023	Urban	48.4	50.1
23	62.7	Developed	3772	2024	Urban	54.83	53.1
24	29.3	Developing	1081	2016	Urban	33.2	76.5
25	61.1	Developing	1380	2024	Urban	30.5	59.3

Appendix D: R-Script for meta-analysis

```r
#load meta-analysis package
library(metafor)
library(metadat)
library(meta)

#Read data
Data<- read.csv("D:/QMUL/Clinical drug development/Dissertation/Meta-analysis Data.csv")

#Calculate awareness proportion
Data$Proportion<-Data$X..Awareness/100

#Calculate number aware
Data$num_aware<-round(Data$Proportion * Data$Sample.Size)

#Perform Meta-analysis
meta_analysis <- metaprop(
  event = num_aware,
  n = Sample.Size,
  studlab = Study.ID,
  data = Data,
  sm = "PLOGIT",              # logit transformation (good for proportions)
  method.tau = "ML",      # GLMM requires Maximum Likelihood
  common = FALSE,
  random = TRUE,
  #subgroup = Country.Type     #Perform sub-group analysis
)
```

```r


#Plot forest
forest(meta_analysis)

#Plot funnel
funnel(meta_analysis, backtransf = TRUE, studlab = TRUE)

#Print
print(meta_analysis)

#Perform meta-regression
#meta_reg_data_filtered<- subset(Data, !is.na(Mean.Age) & !is.na(Published.Year) & !is.na(Female.P

meta_reg_data <- escalc(
  measure = "PLO",                # Proportion logit
  xi = num_aware,
  ni = Sample.Size,
  data = Data #meta_reg_data_filtered
)


meta_reg <- rma(yi, vi, mods = ~ Country.Type, data = meta_reg_data, method = "REML")
#meta_reg <- rma(yi, vi, mods = ~ Published.Year+Country.Type+Mean.Age+Female.Percent+Urban.Rural,

summary(meta_reg)

plot(meta_reg)
```

References:

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