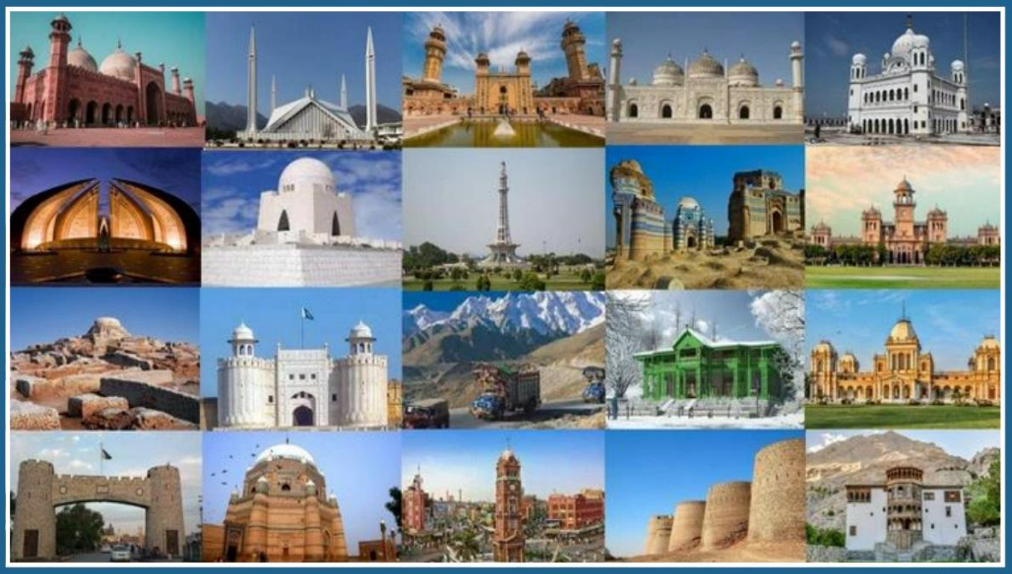

PAKISTAN CLINICAL RESEARCH LANDSCAPE

REPORT 2025

Supported by

APPNA MERIT, BMY HEALTH, ACRP AND
DRUG REGULATORY AUTHORITY OF PAKISTAN

ACRP Ambassador's Club

BMY Health

APPNA Association of Physicians of Pakistani Descent of North America

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Message From Representative

Dr. Baber Saeed Khan,
Founding President ACRP Ambassadors Club Pakistan

"Under the guidance and vision of pioneering researchers and institutions, the clinical trial landscape in Pakistan has begun its transformative journey. As key advocates for integrating clinical research frameworks, we have worked tirelessly to lay the foundation for a future where Pakistan becomes a regional hub for clinical trials. Through collaborations, capacity building, and commitment to excellence, we aim to elevate the quality and impact of clinical research in the country. This report reflects the collaborative efforts to enhance research infrastructure and ensure ethical, evidence-based practices that will benefit researchers and patients alike."

Dr. Bushra Anwar,
Director of BMY Health (Canada & Pakistan)

“The vibrant clinical research network in Pakistan has been a tremendous source of inspiration for our efforts towards launching the ACRP Ambassadors Club, and this report integrates data from clinical trial registries, APPNA webinars, and input from stakeholders in Pakistan. Promoting clinical research is one of the most significant initiatives in advancing healthcare. BMY Health (Pakistan and Canada) wishes to support this endeavor in Pakistan in every possible way.”

Dr. Syed Uzair ul Ghani,
Chairperson of APPNA MERIT RESEARCH Subcommittee

"The APPNA MERIT Subcommittee is honored to present this comprehensive report on clinical research webinars conducted over the past four years and the situation analyses of clinical research in Pakistan. This initiative reflects our unwavering commitment to advancing healthcare research and education in Pakistan and beyond. Together, we continue to build a future where collaborative knowledge drives impactful clinical outcomes."

Mr. Asim Rauf,
CEO, Drug Regulatory Authority of Pakistan (DRAP)

"Under the stewardship of key stakeholders, various clinical research activities have illuminated the path towards elevating Pakistan's standing in global clinical trials. At DRAP, we are committed to fostering an environment where regulatory excellence ensures ethical, efficient, and impactful research. This report reflects a collective effort to bridge gaps, streamline processes, and drive advancements that will benefit researchers and patients."

Acknowledgments

“We would like to sincerely thank our esteemed members from Pakistan and North America for their invaluable contributions in writing and reviewing the report. Your dedication and effort have been instrumental in bringing this work to fruition.

We would also like to express our deep appreciation to the distinguished speakers from Pakistan and the APPNA MERIT team for their unwavering support and insightful contributions to the webinars. Your collective efforts in sharing the rich knowledge of the Pakistani industry with the global community have made a lasting impact. Thank you all for your time, expertise, and commitment.”

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Abbreviations

Acronyms	Abbreviations
ACRP	Association of Clinical Research Professionals
ADR	Adverse Drug Reaction
AHRPP	Association for Accreditation of Human Research Protection Program
ARI	Acute Respiratory Infection
BE / BA studies	Bioequivalence/ Bioavailability studies
BMGF	Bill & Melinda Gates Foundation
CAD	Coronary Artery Disease
CAP	College of American Pathologists
CEC	Central Ethics Committee
CPP	Certificate of Pharmaceutical Product
CRA	Clinical Research Associate
CRO	Contract Research Organization
CSC	Clinical Study Committee
CT	Clinical Trials
CTA	Clinical Trial Agreement
CTMS	Clinical Trial Management System
CTU	Clinical Trials Unit
CVDs	Cardiovascular Diseases
DM	Diabetes Mellitus
DRAP	Drug Regulatory Authority of Pakistan
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
EMR	Electronic Medical Record
eTMF	electronic Trial Master File
FDA	Food and Drug Administration
GDPR	General Data Protection Regulation
GMC	General Medical Council
GMP	Good Manufacturing Practices
HEC	Higher Education Commission
HIPPA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
HRI	Health Research Institute
HTN	Hypertension
ICH-GCP	International Conference on Harmonization-Good Clinical Practice
ICTRP	International Clinical Trials Registry Platform
IHITC	Isolation Hospital and Infections Treatment Center
IP	Investigational Product

IPR	Intellectual Property Rights
IRB	Institutional Review Board
IRC	Institutional Review Committee
IRCT	Iranian Registry of Clinical Trials
ISO	International Organization for Standardization
IMPs	Investigational Medical Products
JCI	Joint Commission International
KPI	Key Performance Indicators
LBW	Low Birth Weight
LMICs	Low Middle-Income Countries
MNC	Multinational Companies
MOHME	Ministry of Health and Medical Education
NBC	National Bioethics Committee
NCDs	Non-Communicable Diseases
NIH	National Institutes of Health
PHRC	Pakistan Health Research Council
PI	Principal Investigator
PMDC	Pakistan Medical and Dental Council
PMRC	Pakistan Health Research Council
PSF	Pakistan Science Foundation
PV	Pharmacovigilance
RBM	Risk-Based Monitoring
R&D	Research and Development
SDV	Source Data Verification
TB	Tuberculosis

Executive Summary

The Islamic Republic of Pakistan was created on 14th August 1947 and after seventy-seven years, it is now a melting pot of more than 20 ethnicities, 60 languages, 4 religions and over 250 million people making it one of the most diverse and resilient countries on the planet.

In this report, our aim is to showcase Pakistan's clinical research potential, current standing and way forward for the clinical research industry. The information presented in this document has been collected through robust primary and secondary research, consultation with subject matter experts and key opinion leaders of the industry and by collaborating with public and private sector stakeholders such as NGOs, CROs, Academic and Medical Institutions and advocacy groups.

The readers will benefit from high level insights that will enable an accurate assessment of opportunities, various analyses, trends and challenges in the clinical trial market of Pakistan. This information will also include industry size, sources of funding, regulatory framework and timelines, clinical research capabilities of sites and CROs, quality standards and disease/epidemiological incidence and prevalence data.

After reading this document, we hope to convince the readers that Pakistan is also amongst prime locations for conduct of entire spectrum of clinical trials. This notion is reflected through harmonization of quality and integrity of clinical research at par with any other developed regions of the world. The regulatory, business and service level stakeholder.

1. Introduction

Clinical trials (CTs) are integral to evaluating preventive, diagnostic, and therapeutic interventions. These evaluations are required for regulatory approvals of new drugs and clinical practice guidelines [1].

Clinical research is essential for advancing medical knowledge, improving patient care, and shaping healthcare policies. As the global clinical trials market grows, South Asia, including Pakistan, is becoming an increasingly attractive destination for pharmaceutical and vaccine trials [2]. Although Pakistan's role in clinical research has been limited, recent industry shifts offer significant growth opportunities.

With a sizeable treatment-naive population, a high disease burden, and relatively flexible regulatory policies, Pakistan is well-positioned to attract international sponsors. However, to fully leverage this potential, it is crucial for both the government and private sector to foster an environment conducive to clinical trials [3].

This report analyzes Pakistan's current clinical trial landscape, examining key factors such as regulations, research infrastructure, trial affordability, human resources, and data availability. Drawing on insights from webinars organized by APPNA MERIT, this report highlights the opportunities and challenges in making Pakistan a competitive player in the global clinical trials market.

2. Trends in Clinical Trial Research

2.1 Global

Globally, the trend of Clinical Trials (CTs) is rising, as shown in the figure below.

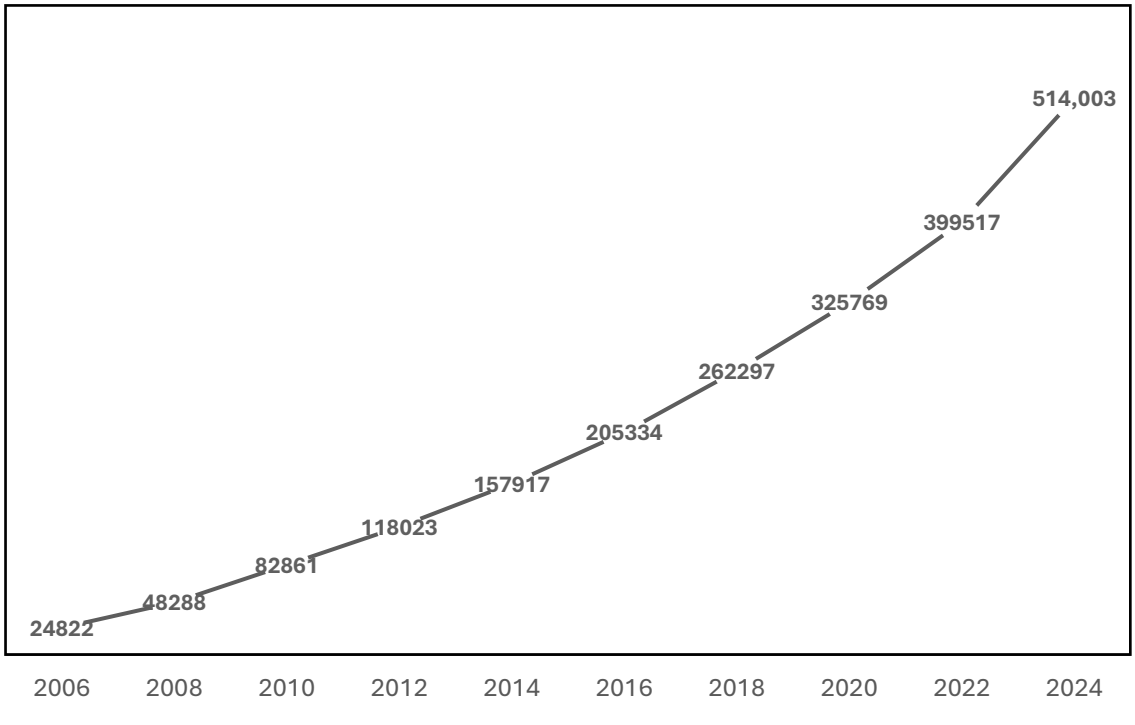


Figure 1: Number of registered studies over time

(The figure shows the total number of studies posted on ClinicalTrials.gov since 2006, based on the First Posted date[4])

The rise in this industry has been significant since COVID-19. The aggregate number of CT subjects exceeded 2 million for the first time in 2021, half for COVID-19.

The Clinical Research Organizations (CROs), which support these CT's execution in partnership with academia, clinical setups, and other research centers, are a big source of revenue. In 2010, this market generated around $24 billion globally, followed by a 50% growth due to a rise in the CTs market until 2015. Close to 2516 clinical trials were registered globally as of Nov 27, 2020, with 1278 actively recruiting participants. The global market for clinical trials, valued at USD 84.61 billion in 2024, is expected to experience significant growth, reaching USD 91.50 billion in 2025 and potentially hitting USD 146.60 billion by 2033, with a steady annual growth rate of 6.07% [5].

A comprehensive analysis of funding for COVID-19 research in the Asia-Pacific region was published by Global Research Collaboration for Infectious Disease Preparedness (GloPID-R) in BMJ Global Health in 2023. The aim of the study was to assess the funding landscape of COVID-19 research projects in Lower-Middle Income Countries (LMIC) and their alignment with the WHO research priorities. The

study showed that 117 funders invested at least $604 million in COVID-19 research, and nearly seventy percent of funding sources were based in China, India, and Australia alone. There is a need for enhanced and more equitable coordination among regional and global stakeholders [6].

With an exclusive focus on the Middle East, South Asia and African Regions, the market stands at about $3.8 billion in 2022 and is forecasted to stand at $5.2 billion by 2032. The region is expected to grow much faster than the rest of the world in the next ten years; this region will contribute the most to the favorable growth trends of the industry for the next decade [7].

i. Trends in Disease Coverage

Globally, Asia has the greatest proportion growth of early-stage Phase I trials, with the top therapeutic areas being Oncology, Infectious Disease and Central Nervous System [8]. The top four therapeutic areas — oncology, immunology, metabolic/endocrinology, and neurology — account for 79% of clinical trial starts and have seen less decline than other diseases. Clinical trial activity for rare diseases remains strong, decreasing slower than trials focused on larger patient populations. Rare disease research is mainly concentrated in oncology, while trials for more common conditions cover a wider array of diseases. New approaches in oncology, such as cell and gene therapies, antibody-drug conjugates (ADCs), and multi-specific antibodies, now represent 25% of all oncology trials [9] .

ii. Challenges Faced Globally

Recruitment issues in clinical trials in the US and Western Europe involve challenges in participant recruitment and retention, resulting in longer lead times. In the U.S., only 6% of patients participate in clinical trials, causing 87% of trials to fall behind schedule in recruitment and enrollment. Additionally, 86% of trials face delays, with 94% experiencing delays of over a month. Poor patient accrual is responsible for half of these delays, as it is critical for trial success. Since recruitment in developing countries like China and India is 5–10 times faster than in the U.S. or Europe, pharmaceutical companies are increasingly turning to these regions for quicker enrollment, taking advantage of large patient pools to accelerate trials [10].

2.2 Regional

Trends show that most research publications have come from North America, Western Europe, and China, making the impression that research output is maximal in big countries with large funds. In 2023, North America held a 50% share of the global market and is projected to maintain its dominance throughout the forecast period [11.] This may seem untrue looking at countries in the Middle East with low output despite big funds. As per unpublished data, Iran is publishing twice as much as Pakistan with a population as less as one third of Pakistan, Israel running >8000 trials in a small country with support from Diaspora and Pakistan despite being a highly populated country has run <2000 trials until 2020 [12].

According to clinicaltrials.gov, the numbers from ten countries belonging to the MENA and Southeast Asia region are as follows[4]

Table 1: Clinical Trials Market Size in MENA & Southeast Asia

Country	Total # of clinical trials	Clinical Trials Market Size ($)	CAGR (%)	source
China	40772	4.9 billion	7.4	Grand View Research
Egypt	12671	48.99 million	6.2	Grand View
Israel	9977	9.9 million	6.5	Grand View
India	5832	1.42 billion	8	Grand View
Pakistan	3822	150 million		Business Recorder
Saudi Arabia	1396	115.8 million	7.1	Grand View
Iran	1336	188.3 million	7.6	Grand View
Jordan	517	1.2 billion	6.1	Grand View
MENA UAE	483			
Qatar	221			

We retrieved data regarding population and number of trials in different regions of the world and analyzed for equity in the distribution of trials according to population size. An overview of trial distribution in different regions of the world is given below.

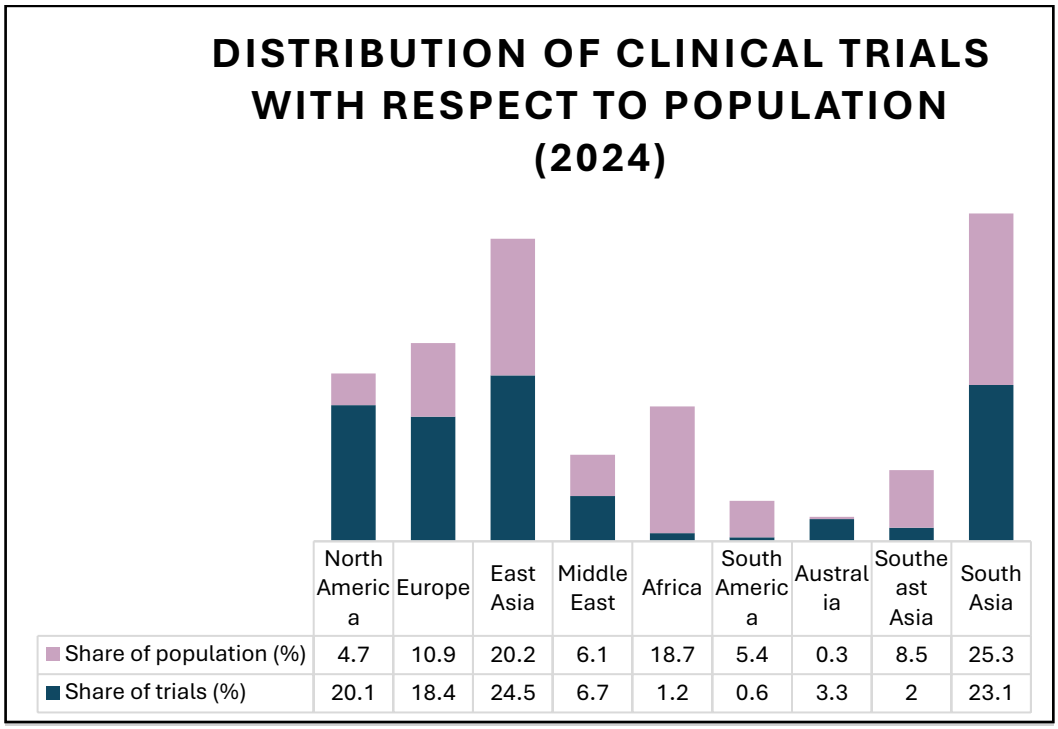


Figure 2: Clinical Trials coverage of world's population (Analyses of WHO ICTRP registered trials) [13,14]

In contrast to the CT distribution, disease distribution shows the opposite trend. Trends for some DALYs have been shown below.

DALYs lost from all causes

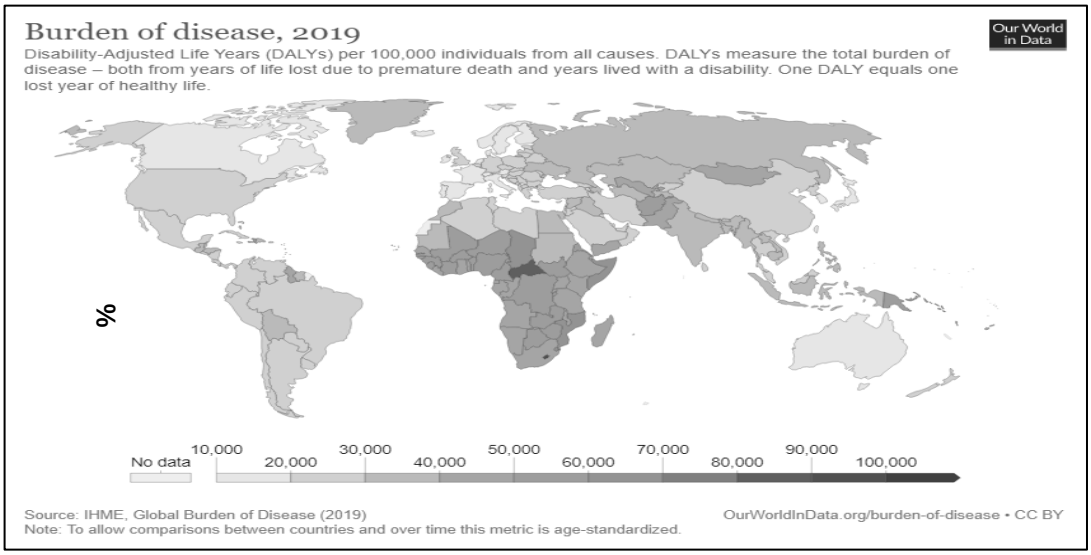


Figure 3: World map of DALYs distribution[13]

As evident above, despite the higher disease burden in developing countries, there is gross under-representation in global CTs.

“Diseases which are more common among deprived communities are being studied in healthier populations. This matters because findings from healthier populations may not be held in communities that face greater challenges to health and well-being. It is also unjust as publicly funded research should be accessible to all.” [12]

The reasons for the low representation of developing countries are lack of commercial viability and research capacity, regulatory and operational barriers, and lack of funding. [15]. There is a significant gap in the coverage of studies covering regions, ethnic groups, and communities according to their susceptibility to the disease under study.

The Asia Pacific region has witnessed steady growth in the number of clinical trials over the past five years, with the total increasing from 11,571 trials in 2019 to 14,346 trials in 2023 [2]. The clinical research market in South Asia is growing rapidly, fueled by increasing healthcare needs, a large and diverse population, and a growing emphasis on improving medical outcomes. However, the market faces challenges and opportunities for development [10].

Big Pharma from the US and Europe has historically carried out 70–80% of the trials; however, recently, the percentage of Asian sponsors, particularly those from China, has increased to about 20–30% of all trials[16].

In Table 2 below is an overview of the clinical research market in South Asia, highlighting key aspects such as market size, trends, opportunities, and challenges.

Table 2: A comparison of clinical research markets of South Asia

Country	No. of clinical research studies*	Opportunities for Research	Challenges
Afghanistan	26 *0.00067 studies/ 1000 population Population size 38, 928, 346	-High disease burden, -Government efforts to rebuild the healthcare system with foreign aid[1].	-Economic and socio-political instability -Limited amenities and infrastructure[4]
Bangladesh	502 0.003/ 1000 population Population size 164,689,383	-High disease burden, -International sponsors interested in trials -Strong local pharma industry	-High reliance on international CROs
India	4,941 0.0035 studies/1000 population Population size 1.42 billion	-Regulatory approvals in 6 to 8 weeks, -Duty exemption on import of IPs and research services. -Cost of trials 50-79% of that in Europe. -English speaking professionals, -750+ sites, with good facilities. -Measures to ensure participant safety e.g. unannounced audits, collation of Significant Adverse Events and their compensation forms, stringent review of informed consent drafts, and greater liability on sponsor and CRO.[1]	-Investigator shortage, -High annual turnover of staff (28-35%), -Variability in ethical practices, -Limited infrastructure for communication and drug / sample storage. -Most medical schools lack a course research training -History of violation of patient rights[4]

Bhutan	3 0.0039/ 1000 population Population size 771,608	-Efficient health system with access to basic public health services, -Rapidly expanding services	-Shortage of specialist doctors, -High clinical workload, -Limited funding, -Lack of collaborations
Sri Lanka	98 0.0046/ 1000 population Population size 21,413,249	-Favorable national policies, -Growing economy and rapid digitalization, -92.5% literacy rate, -Free standard of care, -NCD burden equals western countries, -Qualified medical practitioners and researchers -English proficiency -Robust regulatory framework and ethical reviewing process[1]	-Infectious disease burden[4]
Nepal	229 0.0078/ 1000 population Population size 29,136,808	-Researchers, experienced with WHO in Vi-DT typhoid conjugate vaccine (last major phase 3 trial)	-Lack of training -IRBs capacity building required, -Low resource settings[4]
Pakistan	2027 0.0092/ 1000 population Population size	-High disease burden -English proficient & qualified professionals -Well-equipped CTUs -Relaxed regulations and import rules for clinical research products	-Political instability -Uncertain time approvals -EMR lacking in many potential sites

	240.5 million		
Iran	1192 0.014/1000 population Population size 89.17 million	-Large pharmaceutical market, Government's strategy to achieve self-sufficiency in pharmaceutical industry, -Fast-growing population, -FIPPA protection to foreign investors, -Improved regulatory conditions, Modernization of the health care industry	-Uncertainty of changes in laws and regulations, and protection of patent (Simone Colonnello, 2016)

i. Regional Best Practices

Iran:

Iran has made significant strides in health research and clinical trial governance over the past two decades. In 2008, the IRCT was established as the only Persian English primary registry under the WHO ICTRP. Created by the MOHME and the Iran University of Medical Sciences (IUMS), the IRCT aims to educate the public about ongoing trials and implement the International Committee of Medical Journal Editors (ICMJE) mandate requiring trial registration before participant enrollment.

- Development of Iranian Osteoporosis Research Network (IORN) and Iranian National Diabetes Research Network (INDRN) in 2002.
- National Ethical guidelines for biomedical research drafted in 2006
- The Iranian Registry of Clinical Trials (IRCT) was set up in collaboration with the WHO Registry Network under the Ministry of Health and Medical Education (MOHME) in 2008.
- Implementing the International Committee of Medical Journal Editors (ICMJE) mandate requiring trial registration before participant enrolment.
- National Scientific Plan for Health introduced in 2009
- Ethics Committees constituted in all medical universities by 2011
- Student Research Committees instituted in universities.
- Cochrane Iran Associate Center launched at the National Institute for Medical Research Development (NIMAD) in 2017
    - Producing Evidence: Organizing 37 training sessions across 64 medical campuses and offering grants for high-impact research publications
    - Making Evidence Accessible: Translating over 2,500 Cochrane abstracts into Persian and integrating Persian as a language on Cochrane.org.
    - Advocating for Evidence: Promoting systematic reviews through the Iranian Systematic Review Network (ISYREN) and engaging local communities via media and social platforms.
    - Building Sustainability: Encouraging medical schools to form systematic review networks, with Shahid Beheshti and IUMS taking the lead.

India:

- Rocky road of India’s Regulatory history.
    - Drugs and Cosmetics Act of 1940, followed by Drugs and Cosmetic Rules of 1945
    - CDSCO and MoHFW are the relevant regulatory authorities.
    - Guidelines and requirements for clinical trials issued in Schedule Y in 1988

  - Ethical Guidelines for Biomedical Research on Human Subjects released in 2000
  - 2 studies on cervical cancer led to the deaths of more than 250 subjects
  - The US Office for Human Research Protection (OHRP) investigation found irregularities in the consenting process
  - Local NGO Swasthya Adhikar Manch filed a PIL in the Supreme Court in 2012, and Women's health activists filed 2nd PIL in the Supreme Court in 2013
  - MoHFW mandated EC accreditation by the National Accreditation Board for Hospitals and Healthcare Providers (NABH), which started in 2018.

- The stringent regulations and proposed bills since 2013 have hindered meaningful clinical trials of new therapeutic agents. As the President of the Indian Society for Clinical Research stated in a 2016 article, these "hasty regulatory reforms have posed a challenge to conducting clinical [research] in the country".
- Regulatory reforms after 2013 and the introduction of New Drugs and Clinical Trial Rules of 2019 have partially streamlined the approval processes
- Number of Phase-II and Phase-III trials grew by 15-18 percent between 2017-2023
- Adopting and integrating new technology such as artificial intelligence, machine learning, and blockchain is fueling an exponential increase in the demand for clinical trials by positively impacting data collection, trial completion, regulatory approvals, etc.
- Digitalization has further streamlined clinical trial processes, improved accessibility and reduced costs.
- Pharmacovigilance Program of India (PvPI) was established in 2010 and is an integral part of the Central Drugs Standard Control Organization (CDSCO)
- More than ten modifications were made to the Drugs and Cosmetics Act of 1940 to simplify the process, reduce bureaucracy, and improve transparency, according to Badhri Srinivasan.
- New legislation being drafted in 2023 creating a separate vertical for medical devices
- Private sector hospitals with seventy percent of patients' populations are expanding networks and diversifying to improve the decentralization of clinical trials. *References for above details*[17,18]

Malaysia:

Established in 2012 by the Ministry of Health Malaysia, Clinical Research Malaysia (CRM) is a globally trusted Research Management Organization member of the International Clinical Trial Center Network (ICN). With support from the Ministry of

Health CRM, it offers services tailored to the needs of sponsors from the pharmaceutical, biotech, and medical device industries and CROs. Their services include feasibility studies, investigator selection, placement and development of study coordinators, trial budget management, CTA reviews, and updates on local laws, guidelines, and regulations. CRM also focuses on raising awareness about CTs through marketing and promotional efforts.

In 2024, CRM and AstraZeneca were given the UK-Malaysia Partnership of the Year Award hosted by the British Malaysian Chamber of Commerce (BMCC). The collaboration resulted in a marked increase in CTs in 2023, the launch of a First-in-Human (FIH) study, and a significant contribution to Malaysia's Gross National Income (GNI).

CRM's operational milestone includes a 94% average recruitment rate in studies managed in 2023. Additionally, CRM ensures an efficient CTA review process, maintaining a 14-day timeline. The organization is ISO-certified, achieving ISO 9001:2015 for Quality Management Systems (QMS) in 2019 and ISO 37001:2016 for Anti-Bribery Management Systems (ABMS) in 2021. CRM launched the Phase I Clinical Trial Guidelines in 2017 to establish and expand early-phase research. Additionally, there is a growing emphasis on innovative fields like genomics, regenerative medicine, and personalized medicine.

Malaysia has a perfect record; no FDA Form 483 or similar warning letters have been issued. There are 250 approved clinical trial sites in Malaysia as of 2023, all of which follow protocols that meet ICH GCP standards[4].

Philippines:

The Philippines has established itself as a competitive hub for clinical trials, offering a streamlined regulatory framework that aligns with international standards. The country's regulatory processes are efficient and compliant, with review timelines averaging 2–4 months for local ethics committee approval, 2–3 months for Philippine FDA approval, and 4–5 months from submission to site initiation. This efficiency is complemented by the country's ability to achieve rapid participant enrollment, as demonstrated by a COVID-19 vaccine trial enrolling 9,000 participants in just two months and a schizophrenia study recruiting 1,000 participants in one month.

The cost-effectiveness of trials in the Philippines is another key advantage, with expenses approximately 60% lower than in the US and 20–30% lower than in Western Europe. The average per-patient cost for a Phase III trial ranges from $1,800 to $2,500, making the Philippines an attractive destination for sponsors seeking affordability without compromising quality. The country's high standards in clinical trial conduct have been consistently validated by international regulatory authorities, including the US FDA, Japanese PMDA, and Chinese regulators, with no warning letters issued during inspections.

To further enhance its clinical trial landscape, the Philippines is advancing regulatory initiatives such as the pending Clinical Trial Innovation Act. This legislation aims to incentivize sponsors and CROs through tax benefits, streamline approval processes

for innovative medicines and introduce managed entry agreements to the Philippine National Drug Formulary. Additionally, the recently implemented Regulatory

Reliance Guideline (2023) has significantly reduced clinical trial approval timelines to just 20 working days for eligible studies.

2.3 Local

The academia in Pakistan has been actively involved in CTs in the country. The first trial dates to 1992. First Contract Research Organizations was established in 2005. Partnerships with International CROs were started to promote businesses. Trade and Development Authority Pakistan (TDAP) highlighted the potential of Pakistan's clinical research industry in 2008, inviting international sponsors. Lead sponsors were industry (23%), NIH USA (1%), multiple sponsors, and others. 71.5% of observational trials have been conducted in the last decade between 2010 and 20191. Until February 2019, 508 CTs were recorded in ClinicalTrials.gov, rising to 1846 after the COVID-19 pandemic. During COVID-19, collaborations were open in a virtual environment. Fast-track approvals were started for vaccines and ventilators. Pakistan takes 6 -7 years in drug trials, starting from preclinical through phase IV of CTs. In COVID-19, phases 1 and 2 were carried out together, and then phases 3 and 4 compressing time from 6 years to 18 months for Emergency Use Authorization[19].

3. Clinical Trials in Pakistan

3.1 History

Pakistan ranks fifth among the most populated countries in the world. With great genetic diversity, the Pakistani population presents as a minority ethnic group with unique lifestyle, socioeconomic, cultural, and environmental factors for the clinical trials. Also, Pakistan holds a larger patient pool with a high burden of communicable diseases, and it is recognized as an attractive country for clinical research.

As Pakistan became independent in 1947, the government established medical colleges and research institutes nationwide. During this era, Aga Khan University was a notable institution established in 1983, significantly advancing medical education and research. During the 1970s and 1980s, governmental bodies and private organizations intensified their focus on healthcare and research. As a result, multiple medical colleges and universities have been established, creating expanded avenues for clinical research. Despite this progress, clinical research remained relatively limited compared to developed countries.

During the early 2000s, Pakistan experienced a surge in international collaborations with organizations and universities from developed countries. These partnerships enhanced research facilities, increased funding, and access to specialized expertise. Consequently, clinical research in Pakistan started gaining global recognition. In 2005, there were more Phase IV trials. Pakistan Association of Pharmaceutical Physicians (PAPP) was active mostly with multinational companies. Trial registration was not mandatory and local trial data was not captured entirely.

From 2005 onwards, research cooperative groups were formed. The First Contract Research Organization by the name of Metrics Research, was established in 2005, and now there are 26 licensed CROs in Pakistan, according to DRAP. Partnerships with International CROs were started to promote businesses. Trade and Development Authority Pakistan (TDAP) highlighted the potential of Pakistan’s clinical research industry in 2008, inviting international sponsors.i

During COVID-19, collaborations were easy and open in the virtual environment. International community was more open with Pakistan for having high recruiting sites. Shifa International Hospital reported that COVID19 boosted patient enrolment and randomization from 1500 in 2019 to 7000 in 2022. Fast-track approvals were started for vaccines, COVID drugs, and various exploratory interventions for the diagnosis and management of COVID-19. Conventionally, Pakistan takes 6 -7 years in the drug development process, starting from preclinical through phase IV of CTs. During the COVID-19 pandemic, several aspects of phase 1 and phase 2 trials overlapped and/or conducted simultaneously along with expediting phase 3. This significantly shortened the timeline for the path to Emergency Use Authorization and achieved the goal of herd immunity against the novel virus.

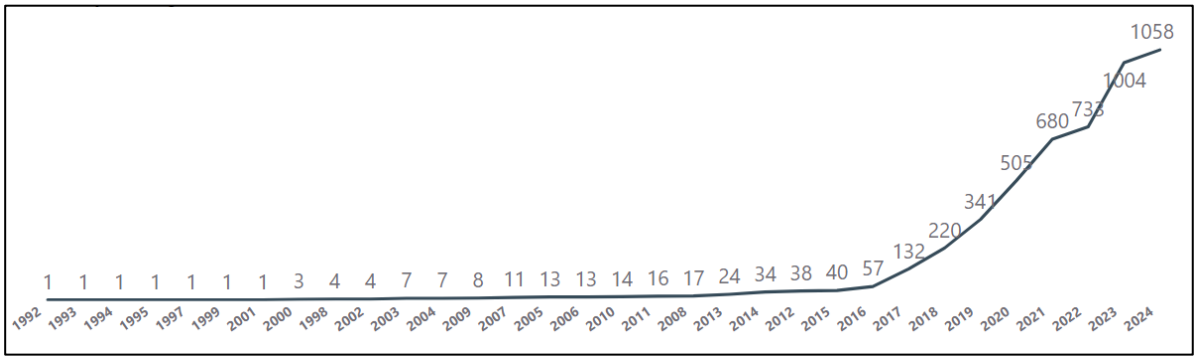


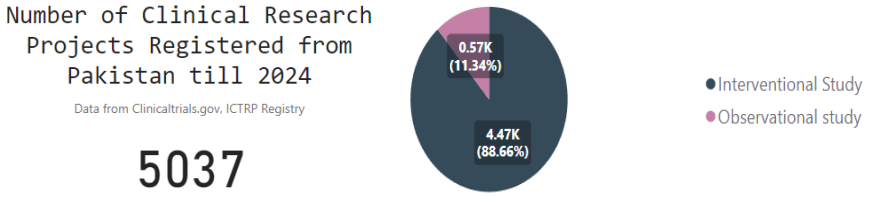
Figure 4: No. of CR projects (Interventional & Observational) registered in WHO ICTRP and Clinicaltrials.gov from Pakistan, with unique IDs.

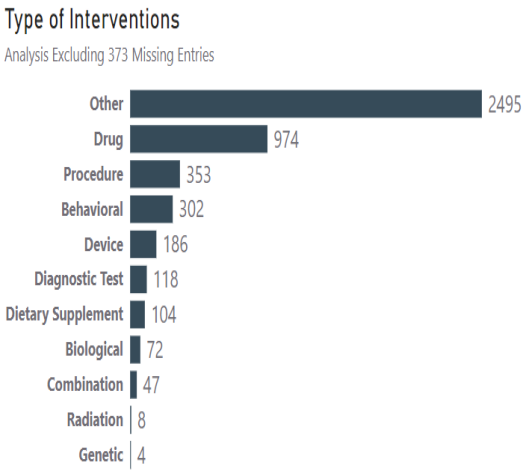
3.2 Overview of Clinical Research Trends in Pakistan

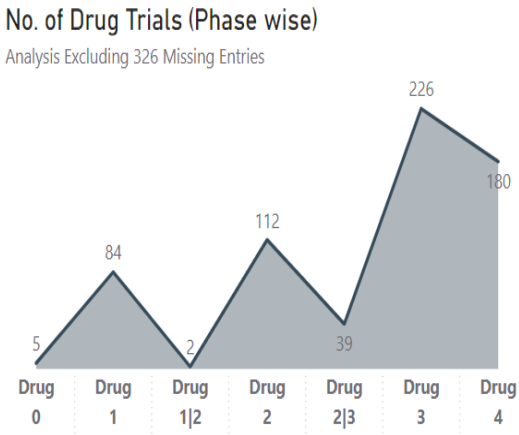
An Overview of Pakistan Clinical Research (Analyses on Data Retrieved from WHO ICTRP, Clinicaltrials.gov) is presented below:

i. <u>Total Number of Clinical Research Projects Registered till 2024:</u>

A total of 5037 projects were registered in the two selected registries as of 28th Dec. 2024 (date of data retrieval). Projects with a unique Trial ID were included in the analyses. Among these, most were interventional. 974 of these were drug interventions, mostly evaluated as Phase 3 and 4 trials. Recruitment status was complete for most of the projects as per their last updated status in the registry.

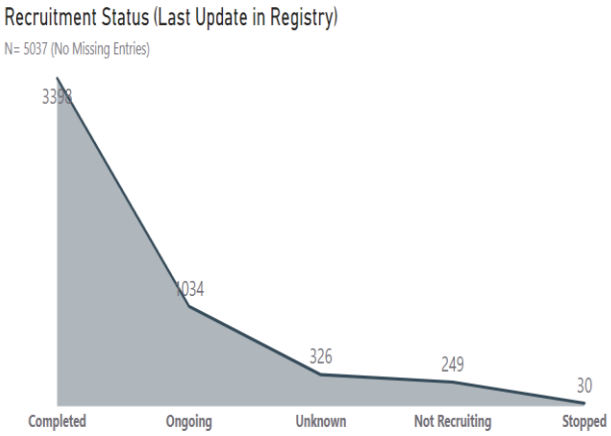


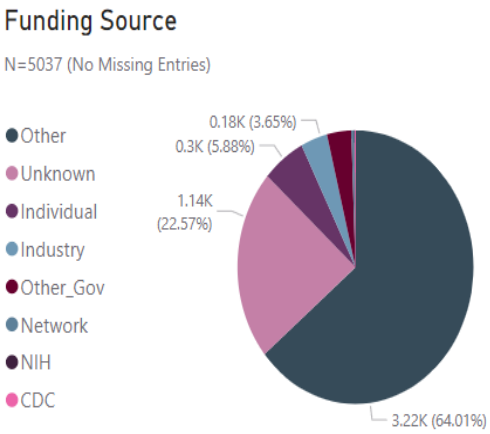




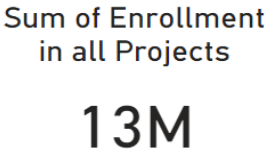
ii. Recruitment and Enrollment Status:

A total of 13 million patients/ healthy individuals have participated in clinical research in Pakistan throughout the years, most of them belonging to all ages and both gender groups. Maternal and child health projects saw the highest number of enrolled people. Though neurological and musculoskeletal projects were studied the most the enrollment among these patients was lower than all other categories.

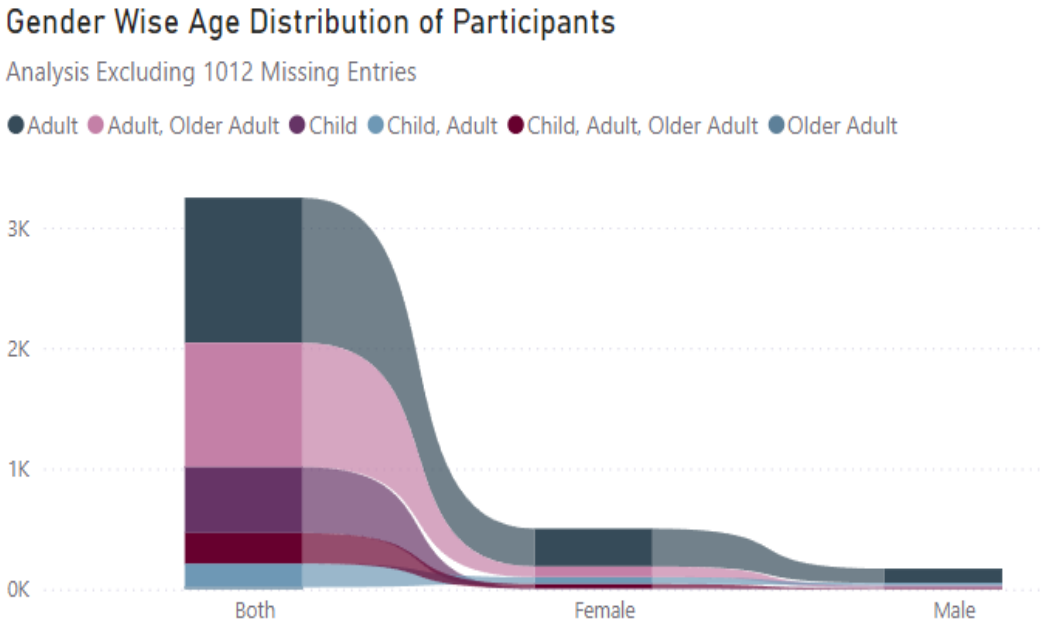




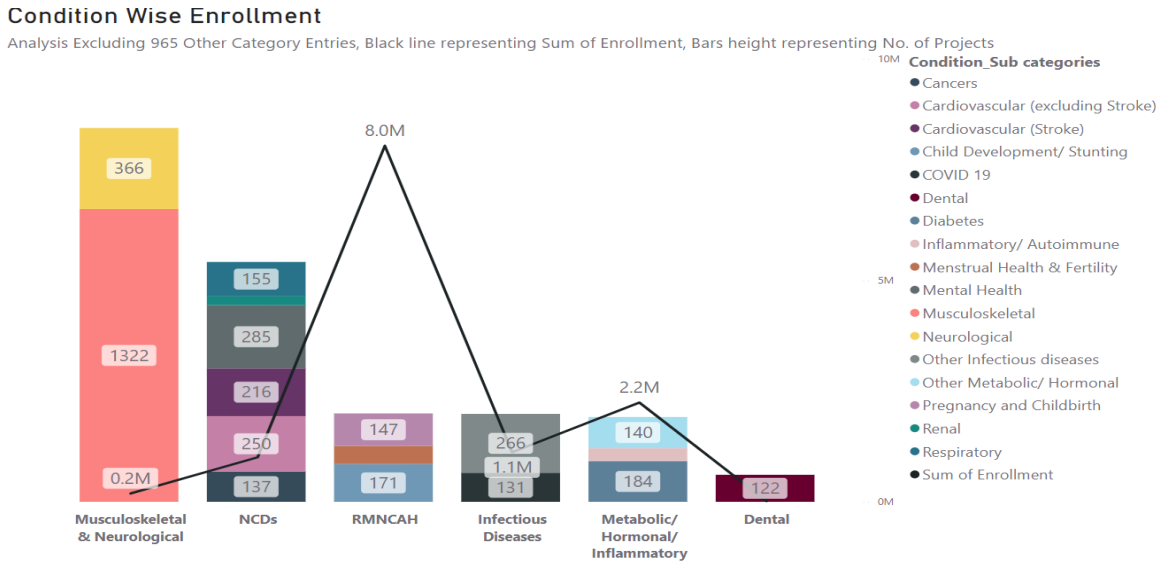
Enrollment Trends



iii. Gender Wise Age Distribution of Participant

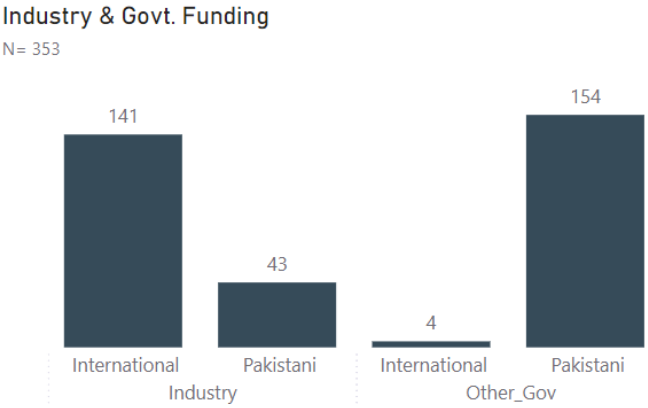


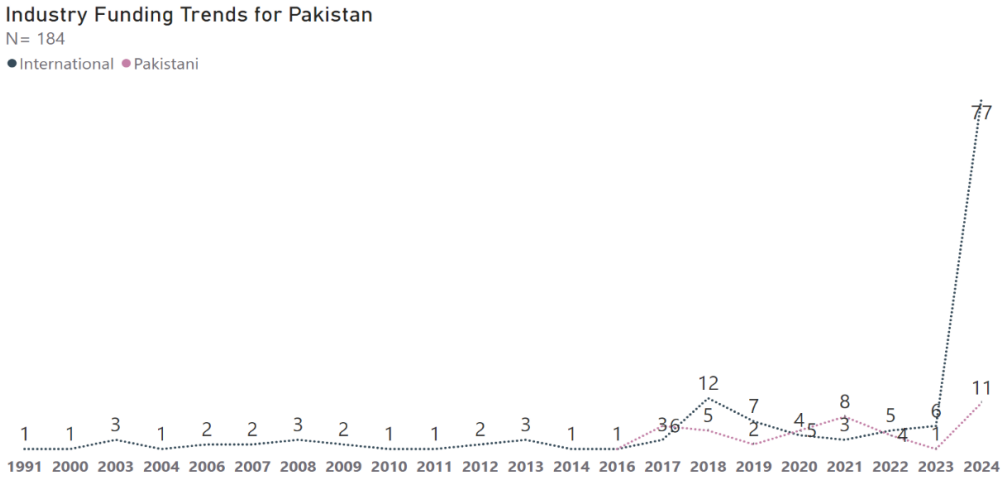
iv. Condition wise Enrollment



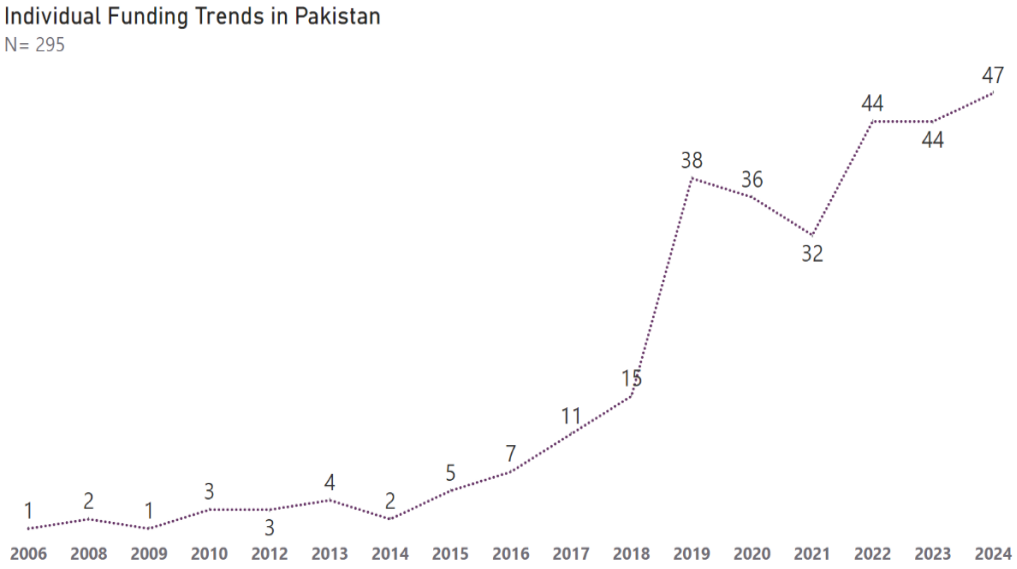
v. Funding Trends

This figure shows that most of the funding has been coming from the international community and the Pakistani government or other organizations.



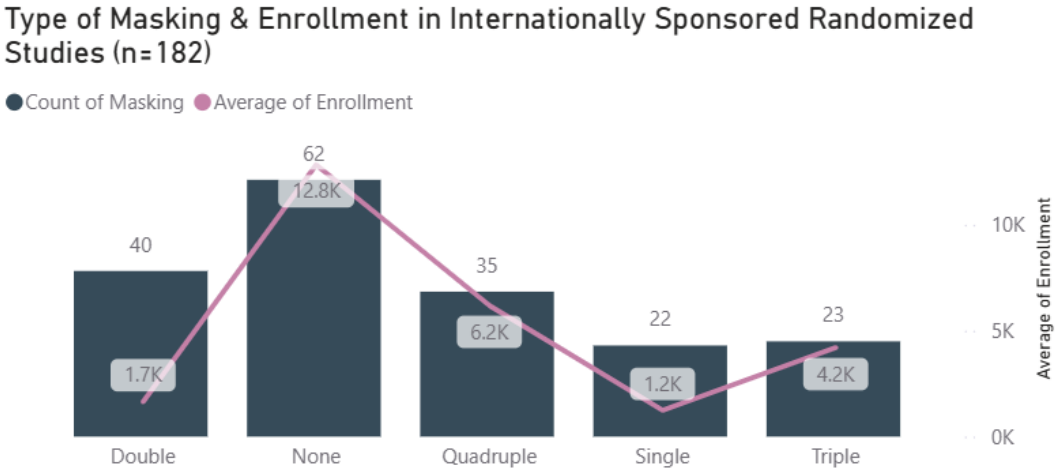


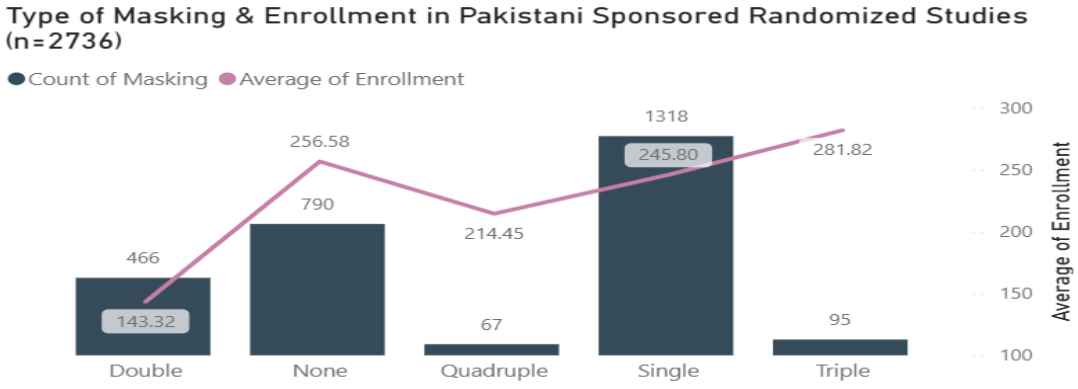
This Figure shows a positive attitude of industry towards funding in Pakistan in recent years

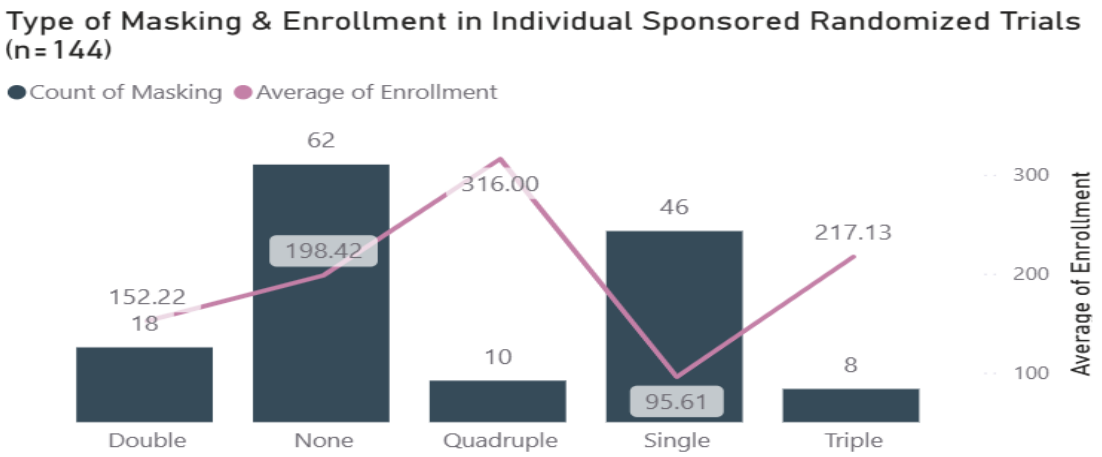


The rise in individual funding indicates an improving culture of clinical research.

vi. Quality of Trials in Funded Projects







3.3 Summarized Report of Bibliometric analyses of publications of last 5 years in PubMed using Bibliometric package of R:

Authors:

Prof. Dr Ayesha Humayun (ORCID 0000-0001-7992-8765), Dr. Muhammad Abdullah (ORCID 0000-0001-9121-2217).

Summarized Report:

The bibliometric package of R is used to search PubMed using the keyword RCT with Pakistan in all fields, and it came out to be 1589 published trials. Amongst them, 1140 were registered in the last 10 years, while 767 were registered in the last 5 years. The data shows the pattern of trials in the figures shared below.

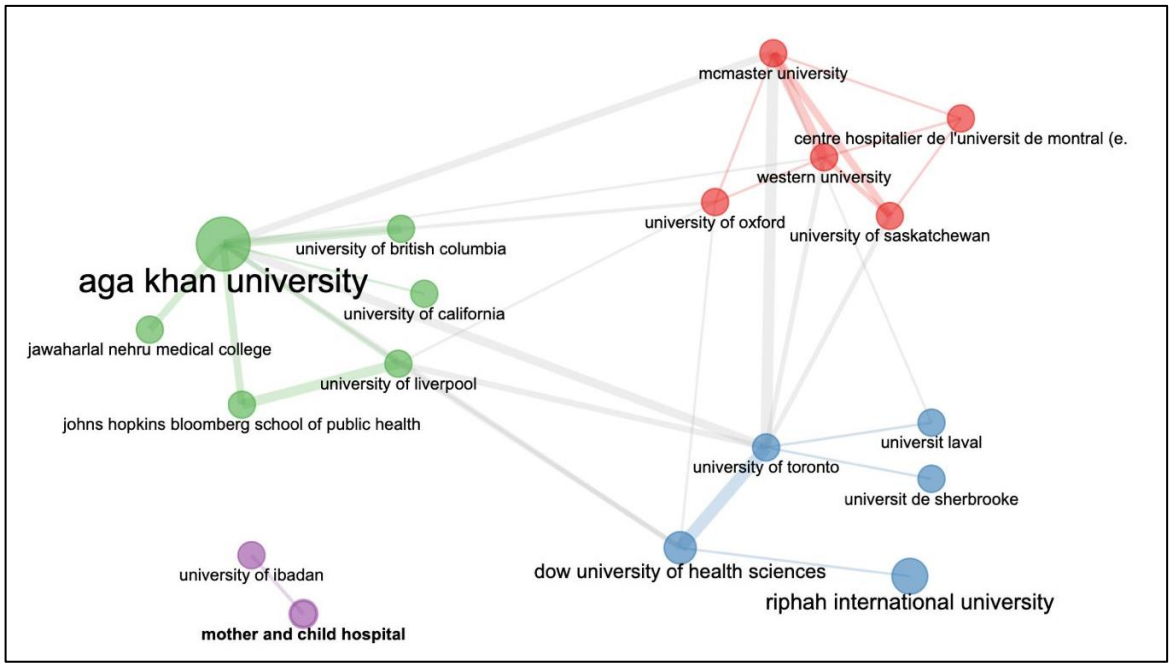


Figure 5: Collaboration between institutes

(The size of the node and the width of the line connecting shows higher number of documents produced and collaboration done)

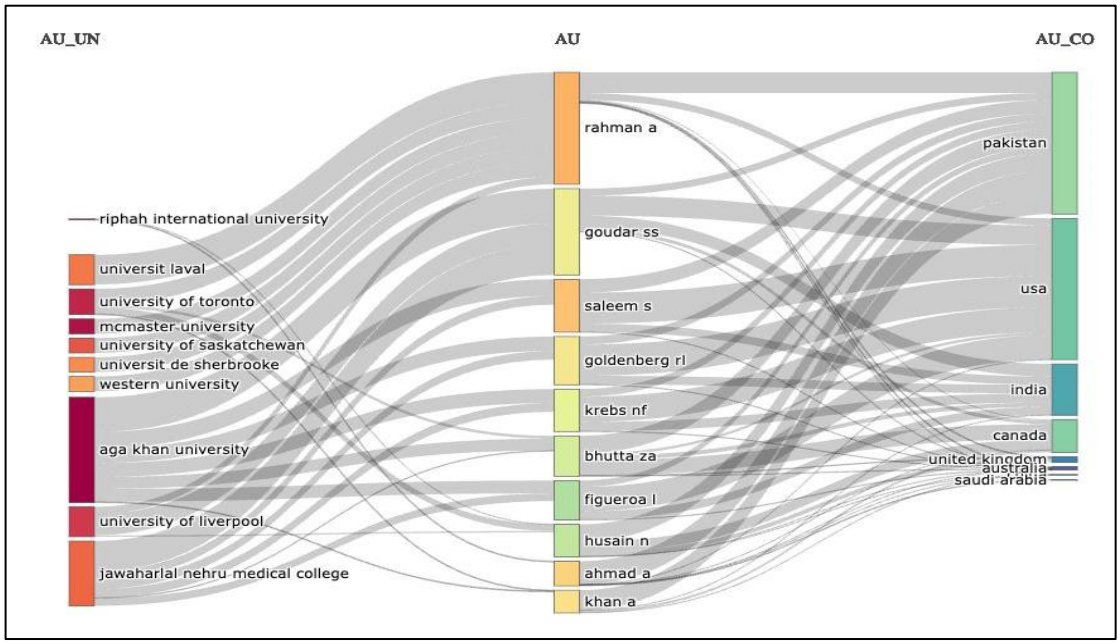


Figure 6:Three field plot for first author affiliation on left, first author name in middle, and corresponding author country on right: last 5 years 2019-2024

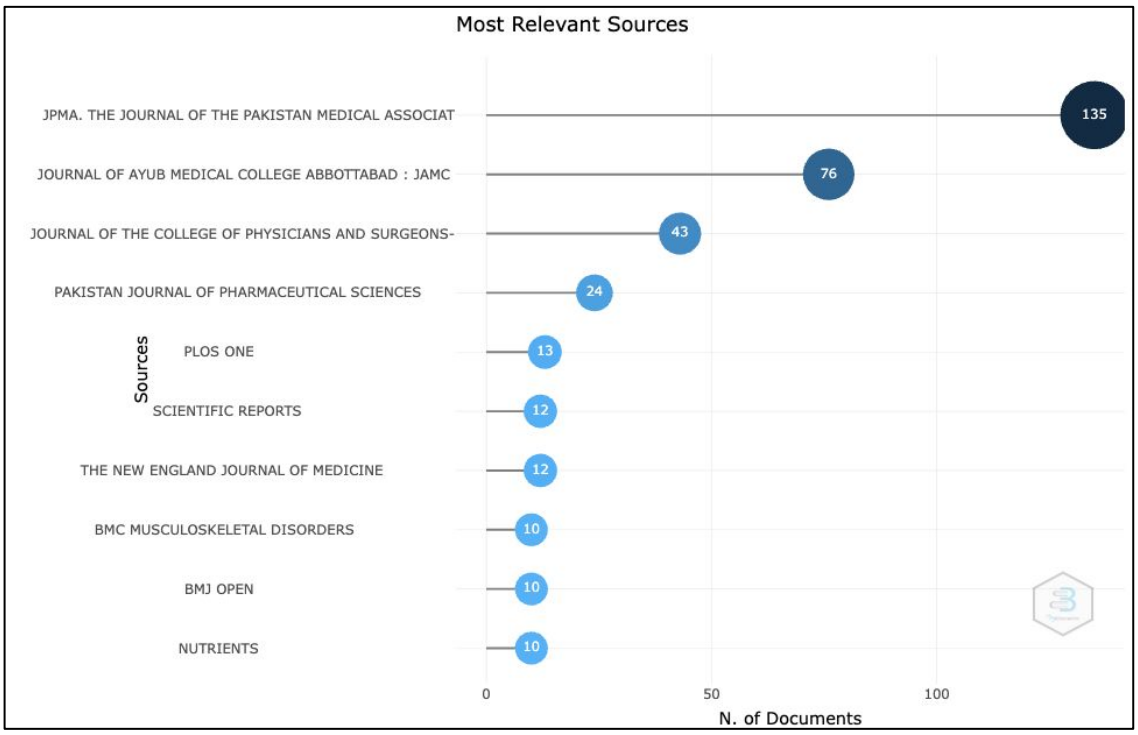


Figure 7: Top 10 sources of publication in the last 5 years

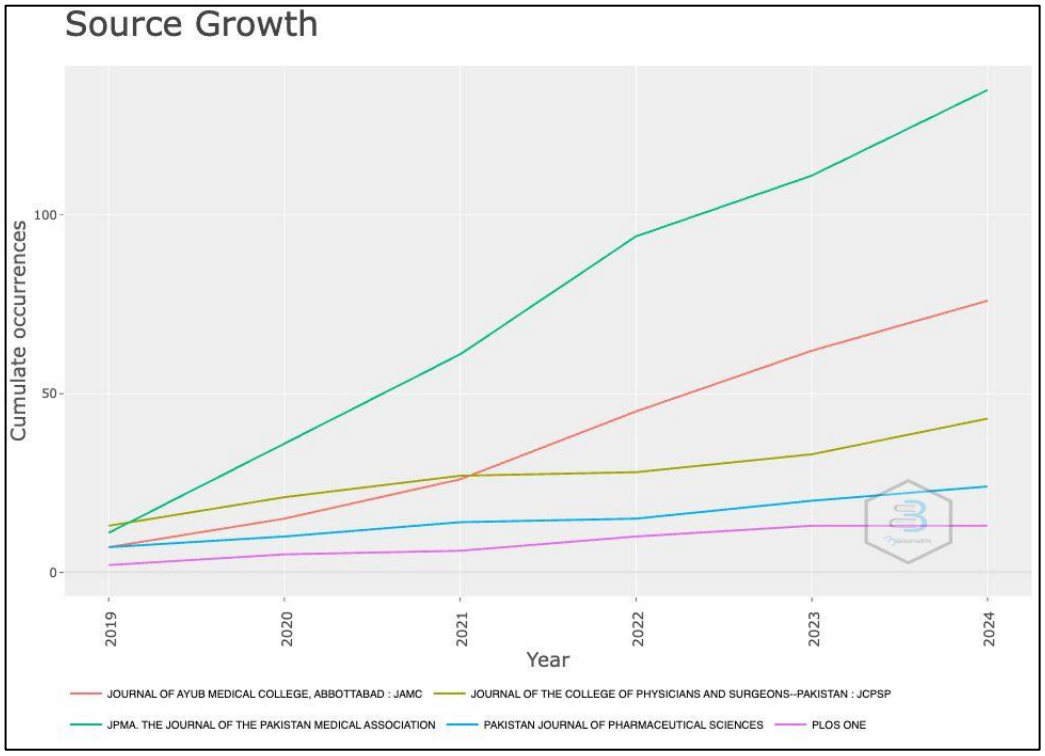


Figure 8: Growth of cumulative sources in the last 5 years

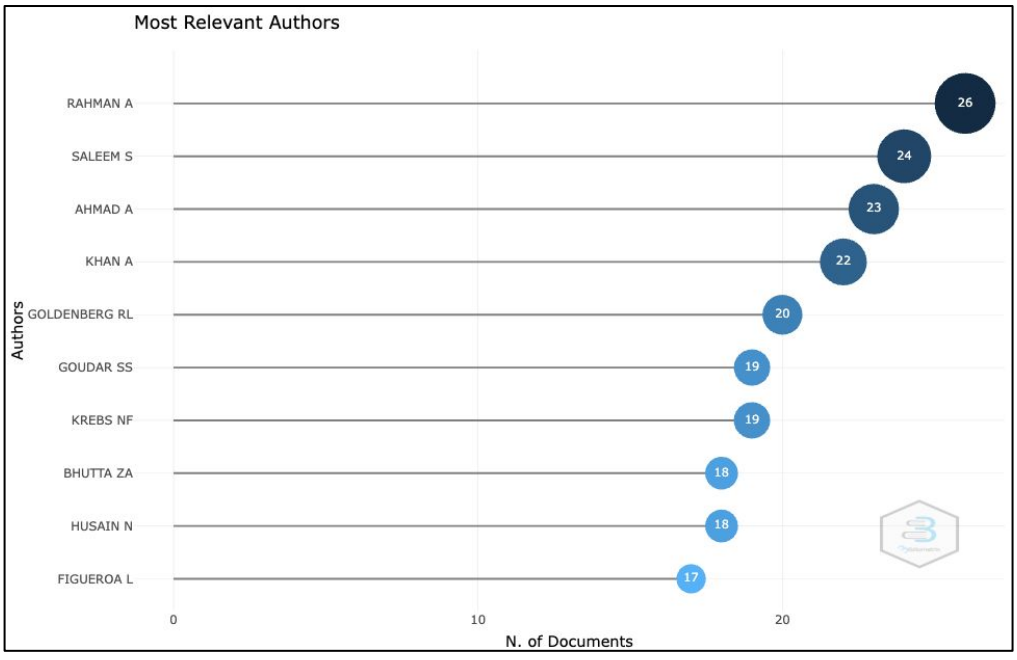


Figure 9: Top 10 most published first authors in last 5 years

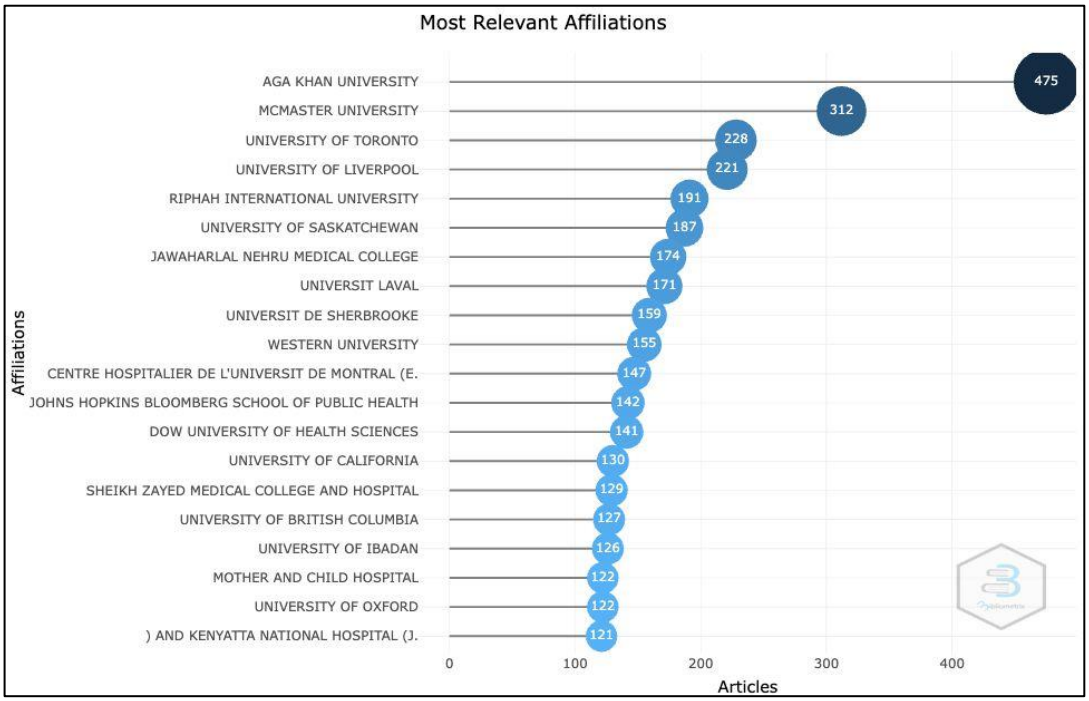


Figure 10:Top 20 affiliation (first author), in last 5 years

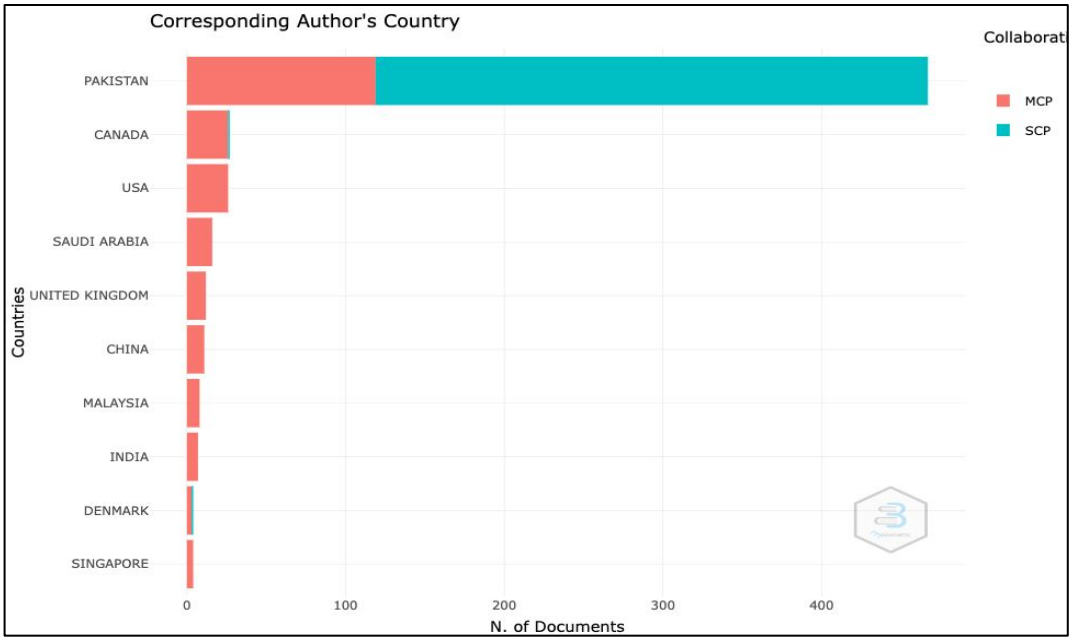


Figure 11: Top 10 corresponding authors' countries in the last 5 years

(Blue is a country publication, all authors from one country, while red is multi-country publication)

4. Strengths

4.1 Participant Access

Large population: We are the 5th most populous country, with a high population growth rate[13] . With literacy rates of 62.3% our population is literate and eligible to be considered for trials.[4] We have a treatment naïve population owing to several social, economic, demographic, and cultural factors. Firstly, most of the country's population, about 65%, is young, under the age of 30, and relatively healthy. Secondly, Pakistan has an out-of-pocket public healthcare expenditure system that only registers healthcare utilization at a time of acute need, such as emergencies. There are no public or private sector-mandated health screening and testing policies in place, which also limits epidemiological surveillance. Lack of awareness about one's health condition and non-compliance with prescribed treatments are other significant reasons for financial unaffordability.

Genetically diverse population: The guidelines we import to apply in Pakistan are not studied on our population, leading to a generalizability crisis. Some of the genetic differences are mentioned below.

- Pakistan has >50 million diabetics, about 25% of the **adult** population is either pre-diabetic or diabetic. There is a huge genetic predisposition to insulin resistance in the Pakistani population, which translates into diabetes, dyslipidemia, hypertension, and obesity later.
- We have a higher risk of CVDs; our HDL particles are smaller and less protective for CAD.
- Genetic diseases are prevalent in Pakistan due to the high rate of consanguineous marriages (>50%), which increases the expression of autosomal recessive disorders [20]. It is estimated, in Pakistan, that Poverty, malnutrition, birth trauma, and consanguinity were common causes of infant mortality and mental retardation in Lahore, Pakistan [21].

4.2 Burden of Diseases

Pakistan has a double burden of diseases with communicable and NCDs. It is endemic for Hepatitis B and C, has the fifth highest rate of TB in the world, and is at high risk for malaria, HIV, and vaccine-preventable diseases. Pakistan is one of the two countries with endemic wild poliovirus type I and is also lagging in achieving targets of COVID-19 vaccination. High rates of smoking, hypertension, cardiopulmonary diseases, cancers including lymphoma and leukemia, along with factors such as poverty, low literacy, gender discrimination, treatment gaps, limited resources, and health access disparities between regions present a risk to mental health as well[1,22].

Pakistanis are still dying from preventable diseases, neonatal diarrheas, respiratory infections, TB, XDR TB, COPD, diabetes, chronic liver disease due to hepatitis B, C and fatty liver disease, to name a few. 50% childbearing women are anemic, while 50% of school age children are overweight or obese according to studies. World population is aging, and Pakistan is the youngest nation in world with 32.8 million children <5 years, 50 million childbearing women, and have highest fertility rate in

the world >750 children born every hour. Worldwide 15% babies have LBW, in South Asia it is 26.4%, while in Rawalpindi Pakistan it was estimated to be 27.4%, which is a risk factor for NCDs later in life. According to a 2016 study, the age adjusted, weighted prevalence of hypertension was 46.2%. but only <7% of HTN are being managed, which is lowest in the world[4]. The recent floods have pushed us further back in the spectrum of diseases, with high rates of infections, vector borne diseases, poverty leading to further disease complications and mental health issues[16].

Incidence of cancer in Pakistan is 730,956/ annum. The population of Pakistan has been reported to have the highest rate of breast cancer of any Asian population (excluding Jews in Israel) and one of the highest rates of ovarian cancer worldwide[23]. Recessively inherited genes may contribute to breast and ovarian cancer risk in Pakistan[10].

The below figure shows the burden of Infectious and non-communicable diseases in Pakistan.

Infectious Disease	2022
Malaria	5,050,565
Diarrhea	1,753,452
TB	608,000
Typhoid	365,248
Hepatitis	234,107
Dengue	77,879
HIV	27,652
Leishmania	27,272
Measles	22,725
Mumps	19,816
Rubella	8,413
Influenza	3,248
Pneumonia	2,317
Respiratory syncytial virus (RSV)	1,723
Diphtheria	1,106
Varicella zoster virus (VZV)	614
Haemophilus Influenza	318
Pertussis	107
Epstein bar virus (EBV)	47
Polio	22

Figure 12: Incidence of Top 20 infectious Diseases in Pakistan 2022[24]

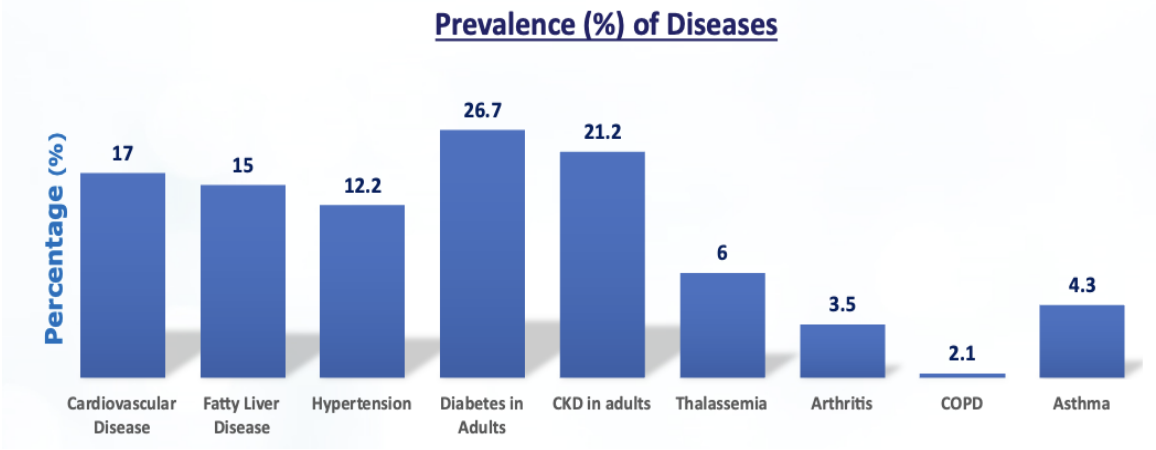
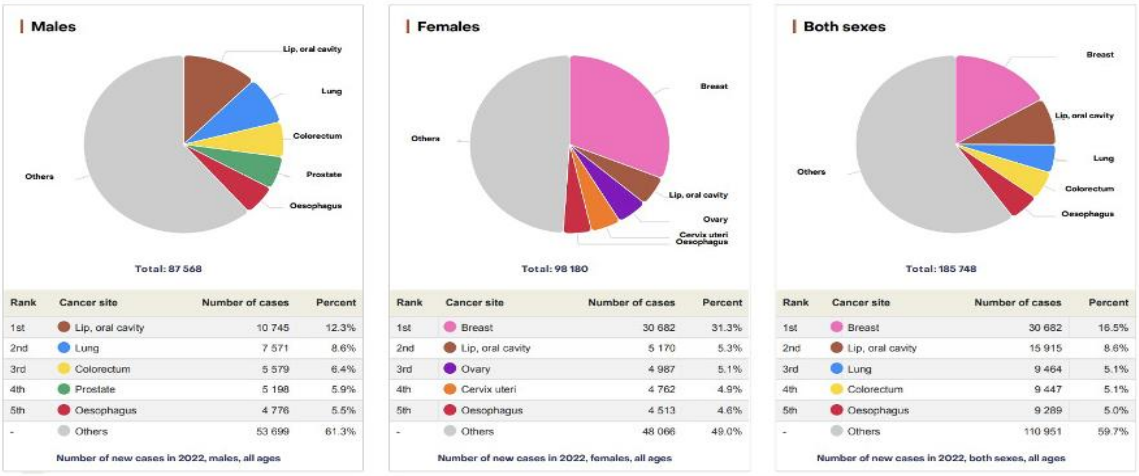


Figure 13:Prevalence of Disease in Pakistan[25]



Rank	Cancer site	Number of cases	Percent
1st	Lip, oral cavity	10 745	12.3%
2nd	Lung	7 571	8.6%
3rd	Colorectum	5 579	6.4%
4th	Prostate	5 198	5.9%
5th	Oesophagus	4 776	5.5%
-	Others	53 699	61.3%

Number of new cases in 2022, males, all ages

Rank	Cancer site	Number of cases	Percent
1st	Breast	30 682	31.3%
2nd	Lip, oral cavity	5 170	5.3%
3rd	Ovary	4 987	5.1%
4th	Cervix uteri	4 762	4.9%
5th	Oesophagus	4 513	4.6%
-	Others	48 066	49.0%

Number of new cases in 2022, females, all ages

Rank	Cancer site	Number of cases	Percent
1st	Breast	30 682	16.5%
2nd	Lip, oral cavity	15 915	8.6%
3rd	Lung	9 464	5.1%
4th	Colorectum	9 447	5.1%
5th	Oesophagus	9 289	5.0%
-	Others	110 951	59.7%

Number of new cases in 2022, both sexes, all ages

Figure 14: Incidence of Top 5 Cancers in Pakistan (Gender-wise Cancer Data 2022)[26]

	New cases				Deaths				5-year prevalence	
Cancer	Number	Rank	(%)	Cum.risk	Number	Rank	(%)	Cum.risk	Number	Prop. (per 100 000)
Breast	30 682	1	16.5	3.7	15 552	1	13.1	2.1	73 903	66.3
Lip, oral cavity	15 915	2	8.6	1.0	10 181	2	8.6	0.68	36 318	15.8
Lung	9 464	3	5.1	0.69	8 307	4	7.0	0.60	12 805	5.6
Colorectum	9 447	4	5.1	0.59	5 235	7	4.4	0.34	20 555	9.0
Oesophagus	9 289	5	5.0	0.62	8 704	3	7.3	0.59	15 099	6.6
Leukaemia	7 722	6	4.2	0.27	5 345	6	4.5	0.21	19 456	8.5
NHL	7 296	7	3.9	0.45	4 344	10	3.7	0.28	18 042	7.9
Liver	6 121	8	3.3	0.44	5 885	5	5.0	0.44	8 519	3.7
Stomach	5 968	9	3.2	0.38	5 093	8	4.3	0.34	9 538	4.2
Bladder	5 391	10	2.9	0.40	3 251	12	2.7	0.24	12 773	5.6
Brain CNS	5 342	11	2.9	0.26	4 407	9	3.7	0.23	15 315	6.7
Prostate	5 198	12	2.8	0.84	2 522	15	2.1	0.37	9 217	7.8
Ovary	4 987	13	2.7	0.61	3 492	11	2.9	0.48	11 195	10.1
Cervix uteri	4 762	14	2.6	0.60	3 069	13	2.6	0.41	11 486	10.3
Larynx	3 987	15	2.1	0.29	2 731	14	2.3	0.21	9 622	4.2
Thyroid	3 135	16	1.7	0.16	688	23	0.58	0.05	8 040	3.5
Corpus uteri	3 037	17	1.6	0.47	1 052	20	0.89	0.17	8 130	7.3
Kidney	2 902	18	1.6	0.18	1 606	18	1.4	0.11	6 748	2.9
Gallbladder	2 841	19	1.5	0.21	2 451	16	2.1	0.18	4 253	1.9
Hypopharynx	1 931	20	1.0	0.13	897	21	0.76	0.06	2 615	1.1

Figure 15: Incidence, Prevalence, Deaths and Pakistan (2022)[26]

Table 3: Burden of selected diseases in Pakistan in comparison with neighboring regions[1,27]

Country	Diabetes prevalence as of 2000 (cases)	Hypertension (urban, rural)	% under 5 affected by ARIs in last 2 weeks	% under 5 affected by diarrhea in last 2 weeks	Mortality per 1000 live births	HIV prevalence in 15-49 years (%)
Bangladesh	2.2 (1564)	-	18	6	47	0.02
Bhutan	2.1 (19)	-	-	-	-	<0.10
India	4.0 (22878)	20%, 40%	19	19	48	0.8
Maldives	2.5 (3.2)	-	70	8	-	<0.10
Nepal	2.2 (263)	-	34	27	47	0.5
Pakistan	**7.1 (5310)**	**23%, 18%**	**24**	**26**	**42**	**0.10**
Sri Lanka	2.6 (318)	17%, 8%	-	5	10	<0.10

4.3 Cost efficiency

Low operational cost makes research up to 70% economical than in the US because of cheaper rates in Pakistan, low demand of researchers, cheap laboratory investigations, and other procedures required in trials[28]. The cost of conducting clinical trials in USA ranges between ten and thirty million dollars whereas in Pakistan, same can be completed with a budget of only 1-3 million dollars [29].

Relaxed duties and taxes on import of test articles and supplies There are fund disbursing sources like NIH, HEC, PHRC, Pakistan Science Foundation, Global fund, Islamic development bank, Asian Development bank, Pakistan Society of Internal Medicine, international donors like Fogarty, and Bill and Melinda Gates Foundation. Universities also provide funding to their researchers. For grants <20 million, PSF is followed, and if a a budget is required then HEC can be contacted.

4.4 Regulatory support

DRAP and NBC provide regulatory approval for trials. The first step is the approval of the local Institutional Review Board (IRB), followed by the National Bioethics Committee (NBC). The final step is the application for approval by the Drug Regulatory Authority of Pakistan (DRAP). CT approvals and oversight activities in DRAP are carried out by the Clinical Studies Committee, which falls under the Pharmacy Services Division of DRAP. They provide oversight for the registration and approval of CT Sites and CROs as per the regulations of the DRAP Act 2012 and Bio-study Rules 2017. No person may carry out any CT in Pakistan, for any therapeutic good without a certificate/license issued by the DRAP. A detailed process is given in annexure A. CSC has approved the following agencies for reliance & consideration of relevant CT decisions, reports or other information as provided under Rule 13 (8) of the Bio-Study Rules: The U.S. FDA, The Medicines and Healthcare Products Regulatory Agency UK, The European Medicines Agency, Health Canada, The Therapeutic Goods Administration Australia, and Pharmaceutical & Medical Devices Agency Japan. NBC-PHRC is responsible for the ethical approval of all CTs to be conducted in Pakistan; prior approval from NBC-

PHRC is mandatory for approval to DRAP. However, the application process to NBC and DRAP can be parallel. This can save a significant amount of time for international sponsors.

Timelines for approval are practicality, for an international sponsor, the average timeline for the whole clinical trial application process (from the agreement with a CRO to FPFV – First Patient First Visit) is 5-6 months and then follows as:

- 1 month – Contract signing + Institutional IRB Approvals
- 1.5 to 2 months – NBC
- 2-3 months – DRAP
- 2 weeks - Import License

Since NBC and DRAP submissions can run in parallel, we save up at least a month's time, if both the stakeholders are managed properly with regular communication.

4.5 Human Resource

Pakistan has a pool of PIs and English-speaking professionals with experience in clinical research. There are multiple research training resources in the country. Since 2005, support from academia and CROs has increased providing training in clinical research. Research cooperative groups exist, including the Pakistan Society of Clinical Oncology - Cancer Research Group, Medical Research Society Pakistan, Neurology Awareness & Research Foundation, and Pakistan Society of Cardiovascular and Thoracic Surgeons, which have included clinical research in their programs. Shifa International and Maroof International also provide training for CTs. Metrics Research has been providing internationally accredited certified clinical research professional training since 2008; this is the only internationally accredited certification program in Pakistan with 30 UK CME credit hours and a Canadian Certification. Dimension Research provides training in collaboration with Brookfield University, the UK, and academia in Pakistan.

NIH Field Epidemiology & Disease Surveillance Training Program is regarded as one of the top programs internationally, now converted into a master's degree with the University of Health Sciences. Institutions have linkages with expat Pakistani healthcare professionals motivated to support their home country. APPNA MERIT is playing its role in projecting Pakistan's potential through educational seminars and attracting international sponsors. They work with the Government of Pakistan to resolve regulatory hurdles and facilitate skill transfer to Pakistan.

4.6 Trials Experience

Currently, a total of 2027 trials from Pakistan are registered in clinicaltrials.gov. An analyses of Pakistan trials between 1992-2019 reported that we have gained experience in drug interventions (41.4%), with a focus on treatment (46.7%) and behavioral studies (13.3%). Most studies have taken place in Sindh (53.1%), followed by Punjab (24.8%) and 13.4% of the trials were carried out at multiple locations in Pakistan. The majority of the trials were randomized (66.5%)[4]Many of our sites and CROs have gained experience with clinical studies of all phases. Our sites have experience working with multinational CROs as well.

4.7 Contract Research Organizations

Pakistan has 26 licensed CROs, with key players significantly contributing to the country's clinical research landscape. Metrics Research Pvt. Ltd, operational since 2005, is Pakistan's first full-service CRO, providing end-to-end research solutions. With 80+ professionals, Metrics Research has completed over 100 clinical studies across diverse therapeutic areas, supported by ISO 9001:2015-certified systems and HIPAA/GDPR compliance. Metrics also focuses on capacity building through CPD-certified CCRP training course, having trained over 1,000 healthcare professionals globally. Other local CROs include Dimension Research, Pioneer Research Solutions, DRK Pharma Solutions, CBSCR at ICCBS, Cyntax Health Projects, and newly established Kamal CRO. Multinational CROs active in Pakistan include Parexel, Covance, and Quintiles.

4.8 Infrastructure and Environment

Pakistan has strong IT capabilities with nationwide internet coverage and a robust pharmaceutical industry, ranked 10th most extensive in Asia-Pacific, with over 30 multinationals and 400 local companies generating $1.64 billion annually. The country hosts 80+ DRAP-approved CT sites, three bio-analytical laboratories, and 8 BE/BA study centers, alongside JCI/ISO/DRAP-approved and GCP-compliant healthcare centers and Ethics Committees. Major courier services operate in Pakistan, enabling biological specimen transport to the US within 48 hours under international safety guidelines. Certified central laboratories and advanced CTUs with controlled environments, dedicated staff, and temperature-controlled equipment are available. Metrics Research has developed FDA 21 CFR Part 11, HIPPA, and GDPR-compliant tools and networking capabilities that meet all contemporary standards of data handling compliances. With experience in handling data from over 100 FDA-approved trials in the past couple of years, Metrics has launched the first Pakistani EDC Tool, which is made as per international compliances for the international market. DRK and other CTUs utilize global e-systems such as Rave EDC, Medidata, and CTMS for data capture and trial management. Some sites connect patient data directly with CRAs, monitored by quality assurance mechanisms. Dimension Research has also developed web-based IT systems for pharmacovigilance.

4.9 Institutional Databases

Some Pakistani institutions have developed registries for prevalent diseases, enabling impactful research through collaborations on multicenter studies. Notable studies include thalassemia's genetic inheritance, aplastic anemia epidemiology (with 1324 cases, contributing to European guidelines), multiple myeloma (studied in over 400 patients), and trials on pneumonia, diffuse large B-cell lymphoma, and hypertension. Pakistan also has advanced genetic research facilities, including whole genome sequencers, geneXperts, and biosafety labs at institutions like the National Institute of Health, University of Health Sciences Lahore, LUMS, and the University of Karachi.

5. Challenges and Mitigation Strategies

5.1 Education and Awareness of Participants

Pakistani patients' education and awareness regarding CTs are minimal. For example, patients often consent without fully understanding the implications of the various clauses in the ICF. Differences in cultural, moral, and ethical values between potential participants and sponsors may sometimes create misunderstandings regarding the participants' expectations in a clinical trial. This early phase issue can be easily overcome with increasing awareness of the globally applicable participant's rights in a human trial. More importantly, several initiatives are now being taken (patient advocacy groups formed by Ziauddin University Hospital, Karachi e.g.) to overcome these teething problems.

5.2 Funding and Resources

Limited funding is available and is also, sometimes, not utilized based on research priorities. The clinical research industry stakeholders struggle due to investments required to increase education and awareness in the healthcare communities, as well as the general masses.

There is insufficient contribution of the local pharma industry in terms of monetary investment for clinical research and understanding the epidemiology of the diseases in Pakistan. There is, however, increasing interest from the local herbal/ alternate remedy manufacturers in adopting a regulated clinical study path to improve their export business.

Most research funding comes from the researchers themselves. The science and technology ministry has budgets, but there is a dire need for a clear disbursement strategy. Funding by the Global Fund, Islamic Development Bank, Asian Development Bank, etc., is also available but not streamlined. According to an analysis, trial sponsors in Pakistan have mostly come from the non-governmental, non-industry category (66.5%).

Some donors, such as the Bill & Melinda Gates Foundation, Welcome Trust, and Fogarty, are interested in funding, but only a few centers of excellence do well to attract these grants, while many others fail to grab the opportunity. Also, the research priorities of donors might not be in line with our research needs, failing to develop the interest of our researchers and not utilizing the opportunity well.

5.3 Infrastructure

Pakistan has limited institutions with JCI accreditation i.e. Agha Khan University Hospital Karachi, Shifa International Hospitals Ltd. Islamabad, Shaukat Khanum Memorial Cancer Hospital and Research Centre Lahore and Shaukat Khanum Memorial Cancer Hospital and Research Centre Peshawar[30,31]

There is a lack of established outsourcing mechanisms for sites having limited experience, resources and support staff for managing phase-III trials; however, international vendors for the ancillary services for clinical trials (insurance, transport, storage of IMP, central labs etc.) are readily available.

Frequent power breakdowns and internet disruptions in the country make it difficult

to communicate and conduct trial activities; however, all approved centers for clinical trials by DRAP have a power and internet back-up strategies in place, largely overcoming this hurdle.

EMR is not established in most hospitals, which is a requirement in every trial for electronic source document verification. However, many hospitals have recently started investing in a proper EMR and the outlook looks promising for big tertiary care hospitals of Pakistan.

5.4 Contract Research Organizations

There is absence of any international alliances between multiple CT centers which are approached by CRO or sponsors to aid participant enrolment in Pakistan. At the moment, CROs and trial sites report a shortage of clinical research specialists, especially registered nurses, trained for research. CROs express need for more sites compliant with ICH-GCP guidelines to cater to the massive trial potential in Pakistan.

No government policies for CRO promotion exist, while huge investment is required from CRO businesses. While issuing licenses to CROs and sites is an excellent initiative to maintain the quality of work, DRAP is grossly understaffed to cater to these needs, which can result in lengthy approval timelines. CROs are also struggling to align the national pharmaceutical industry's expectations in terms of service provisions for clinical research, and there are unrealistic expectations from the local industry about the scope of work and ethical and regulatory requirements for conducting clinical research in Pakistan.

5.5 Hesitancy to Conduct Clinical Trials in Pakistan

Clinical trials hold a unique and pivotal position as the cornerstone of evidence-based medicine. It is crucial to evaluate the safety and efficacy of interventions, including drugs, devices, and treatment protocols, before their widespread adoption. However, a significant knowledge gap exists within the health sector in Pakistan, particularly regarding the distinctions between medical research, clinical trials, and health services research. This lack of clarity often hinders researchers and institutions from aligning their work with the appropriate research framework, compromising their contributions' quality and relevance.

A recent analysis of clinical trials (CTs) in Pakistan reveals that most trials conducted have relatively low participant numbers, with a mean of 58 participants, and most trials (47.2%) fall within the range of 101–1000 participants. In addition, issues such as inadequate blinding are prevalent, with 34% of studies showing no blinding, 17.3% employing single blinding, and only a tiny fraction implementing more rigorous designs, such as double, triple, or quadruple blinding. The presence of missing data in 23.2% of trials further highlights the challenges in maintaining research integrity. Additionally, very few trials focus on diagnostic interventions, basic sciences, education, or counseling, and none target genetics all of which are critical areas for advancing the medical field in Pakistan[31].

Despite these challenges, Pakistan remains strategically positioned to become a more prominent player in the global clinical trial industry. The country's diverse population and varied healthcare needs offer significant opportunities for research. However, the underrepresentation of clinical trials in the country suggests that the

full potential of Pakistan’s research infrastructure has yet to be realized. This underutilization is evident when comparing Pakistan's performance in the clinical trial landscape, where it occupies a middle position among Organization of Islamic Cooperation (OIC) member states.

Bridging the knowledge gap surrounding clinical trials is essential not only for enhancing research collaboration but also for attracting sponsors and elevating the overall quality of research in the country. Strengthening the clinical trial infrastructure in Pakistan would contribute to aligning its research with international standards, ultimately benefiting the global medical community and improving local healthcare outcomes.

5.6 Environment

Pakistan’s health sector, though historically challenged by fragmented systems and limited government spending—less than 3% of GDP—has taken a positive and promising turn. This shift was outlined in the National Health Vision 2016-2025, where Pakistan’s federal and provincial governments made a joint commitment to increase health expenditures nationally from under 1% of GDP to 3%. This ambitious strategic direction is already showing results, with significant growth in research outputs since 2018. The rise of medical schools, international collaborations, and a growing focus on clinical research demonstrate the nation's commitment to strengthening its healthcare system and advancing clinical research for the benefit of its population[32].

Pakistan’s pharmaceutical industry faces challenges, including reliance on imports for 95% of active ingredients, delays in licensing by DRAP, and the absence of FDA-approved companies. There is no biotechnology industry or effective commercialization pathway for research. These hurdles, however, should not be a deterrent to the local pharmaceutical industry, which has witnessed a remarkable increase in the exports of generic molecules to many parts of the world. A greater focus on post authorization studies (Phase IV trials to document the efficacy and safety of the marketed molecules in the local population) and quality indices (bioequivalence and bioavailability studies of all marketed products) can support the commercial objectives of the industry.

6. Recommendations

6.1 Stakeholder Involvement

- Take the education sector on board as a stakeholder in clinical research initiatives and improve health literacy for the population.
- Expand the scope of trials by covering areas that are under-researched, such as herbal medicine, biosimilar, proteomics, genomics, BA/BE studies, biomarkers of unique diseases and epidemic-prone diseases, pharmacogenomics, and dose reduction studies.
- Focus more on phase II and III trials. In Pakistan, much work is being done at the T0 level of translational research, i.e., basic sciences research, but is not translated well into T1 and T2 research, where the pharmaceutical industry should be engaged.
- Trials should be approached with better management and partnerships. Sites should be linked with outsourcing services like volunteer recruitment.
- Besides commercial research projects, we should also promote investigator-initiated trials, designing the protocol ourselves and not waiting for commercial project to be offered. Our local pharma industry can play an important role in that by sponsoring these initiatives and more importantly, helping investigators identify the key research areas of focus for the Pakistan healthcare landscape.
- Develop a formal platform where all the stakeholders of clinical research can meet periodically to discuss and resolve the challenges faced practically. The ACRP initiative can really help us in aligning this.
- Electronic applications and systems (that are already in place) can be more formalized for regulatory approvals to increase the transparency of the processes.

6.2 Training and Capacity Building

- Train CROs to plan and execute trials effectively, avoiding a “could do all” approach. Focus on niche areas, ethical projects, and collaboration among CROs to build trust and ensure sustainable growth.
- Adapt online courses for local challenges in trial conduct. Include biostatistics, epidemiology, genetics, and IT skills in medical curriculums. Promote diaspora engagement (e.g., APPNA MERIT) for capacity building, guest lectures, and research grants.
- Strengthen research infrastructure by mandating research staff in medical colleges. Offer faculty time off for research and rotations, fostering critical thinking and innovation. Promote research commercialization and integration into institutions.

- Encourage site collaborations through designated liaisons and training in collaborative ethics. Introduce KPIs for collaborative research projects and flexibility in authorship credits to minimize conflicts.
- Invest in site development and accreditation by international bodies (e.g., Alliance for Clinical Research Safety). Establish a national clinical trial registry and disease registries (e.g., for cancer, genetic diseases). Develop EMR systems linked to the National Health Information System.
- Support pharma industries by addressing drug pricing and expediting licensing for new products. Promote biosimilar patents, local raw material production, and public-private partnerships for vaccine R&D and biological production.
- Create a leadership body engaging stakeholders (CROs, hospitals, pharma, IT, patients, government). Define national research priorities, address gaps in research sites, and establish a network to link academia, industry, and policymakers.

6.3 Adopting a Risk-Based Approach to Clinical Trials

Traditional monitoring methods rely heavily on intensive on-site visits and 100% SDV, regardless of a study's inherent risk level. While these methods are resource-intensive, they have shown limited improvements in overall data quality. Recognizing these challenges, the ICH GCP guidelines were revised in 2017 to promote a risk-based approach to monitoring. RBM focuses resources on high-risk aspects of trials while employing centralized and adaptive monitoring strategies. This dynamic approach ensures that monitoring practices are continuously refined based on ongoing risk assessments. To facilitate the implementation of RBM, numerous tools and guidance documents have been developed, including the ECRIN RBM toolbox, ICH GCP E6(R2) and the soon to be implemented R3 guidelines, the FDA's guidance on risk-based monitoring, and the Swiss Clinical Trial Organization's RBM framework. These resources provide structured methodologies for integrating RBM into CT workflows.

For Pakistan, adopting a risk-based approach to monitoring is not just advantageous but essential. Traditional monitoring practices, which are costly and resource-intensive, pose significant challenges in Pakistan's resource-constrained healthcare and research system. By embracing RBM, Pakistan can:

1. **Optimize resource utilization:** Efficiently allocate limited resources, ensuring high-risk trials receive necessary attention without overburdening low-risk studies.
2. **Enhance trial quality and compliance:** Improve adherence to international standards, attracting global sponsors and increasing Pakistan's visibility in the clinical research landscape.
3. **Strengthen data integrity:** Leverage centralized monitoring and advanced analytics to ensure robust, high-quality trial outputs.

4. **Reduce costs:** Lower monitoring expenses, making CTs more sustainable and cost-effective.

This shift to RBM will strengthen the credibility of Pakistan's CTs and position the country as a competitive and reliable destination for high-quality clinical research.

6.4 Ethical and Regulatory Compliance

- Considering unannounced audits for checking compliance with ICH-GCP principles and greater liability on the sponsor and the CROs, India managed to revive its lost reputation after violating ethics principles in trials.[ii]
- In the opinion of a credible stakeholder from clinical trial sites, there is room for improvement in the fair distribution of funds in the research team (from PI to nurses, technicians, receptionists, etc.).
- Budget release to the sites should be linked to precise deliverables and not registrations without proper electronic entries.
- Strengthening the role of national, provincial, independent, and institutional ethics committees and data safety monitoring boards. All IRBs in the country should also be inspected and issued official licenses to benchmark to an international standard. They should be supported in seeking accreditation from AHRPP, the internationally accepted accrediting body.

6.5 Government Policy Support

- The government should provide tax breaks for R&D and duty-free import of biologicals, like India's duty exemptions on investigational products and research services.
- The Health Ministry can play a more active role in supervising the healthcare R&D industry. Better supervision and input are needed to ensure that government policies are conducive to international sponsors and investors alike.
- Technical capacity of DRAP should be enhanced by including vaccine specialists, physicians, virologists, immunologists, etc., expanding its expertise beyond pharmacy.
- The Biosafety Study Rules 2017 need a few important revisions to align with international practices. Some key recommendations include:
    - Current rules are not clear about the regulatory pathway for Phase IV and observational studies. Only interventional studies should be mandated to go through the regulatory processes for registration of CTs across all phases.
    - The central process for IND import license should be considered to improve efficiency. Local DRAP offices need to be approached currently, this results in some duplication of paperwork.
    - A rule of separate timelines for CT approval should be considered rather than the same process for each application. It is recommended

to relax the timelines for reviews of Phase IV and BA/BE studies to encourage the local industry.

- Close out of trials are tagged with an official DRAP visit for IP reconciliation. This can be done remotely as well to enhance efficiency as this step usually results in unnecessary delays.

- Data integrity and IP protection are essential. Countries like Jordan saw significant growth in their pharmaceutical market and exports by improving IPR enforcement, attracting global pharma companies (Reference: WTO Cell, TDAP, 2008).

Implementing these recommendations requires government commitment and leadership from the medical community. Pakistan, despite limited resources, can leverage its human capital to enhance clinical research by adopting strategies from countries like the US, Australia, India, and China, emphasizing quick approvals, tax incentives, and stringent data protection.

7. Opportunities for Growth of the Pakistani Clinical Trial Market

A CSC has been nominated to address the application backlog, and the processes are streamlined now in 2025. There is a transparent calendar for these review meetings, which are conducted on the scheduled dates. Stakeholders can align their efforts in accordance with the published calendar to efficiently submit their applications. The Supreme Court has also played a pivotal role in facilitating research by resolving delays caused by bureaucratic hurdles. We need to invest in hospitals with the potential to develop as clinical trial sites and many private institutes have been developing this approach recently. A genetic reference lab and research center are also planned at Health Services Academy Islamabad in collaboration with China. With construction underway, NIH has allocated land for a technology hub, genomics center, biobank, and R&D facilities. Moreover, the public sector is also catching up, which can help us improve the catchment of more common diseases in the community for clinical trials.

8. ACRP International Ambassador Club

The ACRP International Ambassador Club, established in March 2024, provides a platform for clinical research professionals worldwide to collaborate and advance their professional development in alignment with the club's mission. As part of the ACRP, a global non-profit organization, it offers valuable resources for individuals and organizations in the life sciences sector.

8.1 Introduction to ACRP

The Association of Clinical Research Professionals (ACRP), established in 1976, is the premier international non-profit organization dedicated solely to representing, supporting, and advocating clinical research professionals. With over 16,500 members across 72 countries, ACRP promotes excellence in clinical research through education, certification, and community engagement.

8.2 Establishment of ACRP Ambassador Club

To extend its mission globally, ACRP created the International Ambassador Club, an initiative to bring together clinical research professionals worldwide to promote professional development, collaboration and uphold high standards in research practices. Pakistan and Japan are the only two countries with established Ambassador Clubs, highlighting their commitment to advancing clinical research and promoting global cooperation.

8.3 Leadership in Pakistan

The leadership of the ACRP Ambassador Club in Pakistan consists of professionals from academia, sponsors, Clinical Trial Organizations (CROs), Clinical Trial Units (CTUs) and major stakeholders, all led by Dr. Baber Saeed Khan as the founding President. His leadership and passion for advancing clinical research are instrumental in positioning Pakistan as a contributor to the global research community while promoting professional growth and creating opportunities for researchers to excel on the international stage.

8.4 Purpose of Establishing the ACRP Ambassador Club

The ACRP International Ambassador Club has been created so that international clinical research professionals come together in support of professional development purposes that align with ACRP's not-for-profit mission. ACRP is the only non-profit organization solely dedicated to representing, supporting and advocating for clinical research professionals. ACRP supports individuals and life science organizations globally by providing community, education and credentialing programs. ACRP is a registered charitable organization whose mission is to promote excellence in clinical research and whose vision is that clinical research is performed ethically, responsibly and professionally everywhere in the world.

8.5 Objectives of the ACRP Ambassador Club

1. **Support Professional Growth:** Members have access to a wide range of top-tier clinical research training programs tailored for professionals at all levels and they are internationally recognized, including:

- **ACRP Certified Professional (ACRP-CP®):** Recognizes clinical research professionals of all types. Eligibility requires 3,000 hours of verifiable work experience related to human subject research. Candidates must pass the standardized ACRP-CP® Certification Exam.
- **Certified Clinical Research Coordinator (CCRC®):** Designed for research coordinators, demonstrating proficiency in essential knowledge and skills. Eligibility requires a combination of education and experience. Candidates must pass the CCRC® Certification Exam.
- **Certified Clinical Research Associate (CCRA®):** Validates expertise in monitoring and overseeing clinical trials. Eligibility requires specific educational and professional experience. Candidates must pass the CCRA® Certification Exam.
- **Certified Principal Investigator (CPI®):** Focused on equipping principal investigators with specialized skills. Successful completion of the CPI® Certification Exam is necessary to earn this credential.

2. **Promote Networking and Collaboration:** The club creates platforms internationally for professionals to share experiences, build connections and collaborate on research initiatives.
3. **Promote Advocacy and Best Practices:** The club serves as a representative body to advocate for clinical research professionals while promoting ethical standards and global best practices in research.

8.6 Advantages of Membership in the ACRP Ambassador Club

Membership in the ACRP International Ambassador Club offers numerous benefits:

- **Authentic and Validated Training:** The club promotes authentic, validated and internationally accepted training and certifications in clinical research, ensuring members receive education that meets global standards.
- **Enhanced Quality of Research:** By providing a workforce trained to international standards, the club improves the quality of clinical research conducted in Pakistan. This ensures adherence to ethical practices and enhances the credibility of research outputs.
- **Collaboration with Institutions:** The Ambassador Club actively collaborates with institutions to train individuals for certifications, fostering a skilled workforce capable of conducting high-quality research.
- **Exclusive Access to Educational Resources:** Members can utilize ACRP's comprehensive library of webinars, certifications and training programs to stay updated on the latest clinical research advancements.
- **Global Networking Opportunities:** The club facilitates meaningful connections among clinical research professionals in Pakistan, Japan and beyond, encouraging the exchange of knowledge and collaborative projects.

- **Enhanced Professional Recognition:** Certifications such as ACRP-CP®, CCRC®, CCRA® and CPI® are internationally recognized, enhancing career prospects by demonstrating adherence to high professional standards.
- **Location-Based Benefits:** Members in specific regions may enjoy reduced membership rates and access to localized resources, ensuring accessibility and inclusivity.

8.7 Pakistan's Involvement

Pakistan's membership in the ACRP International Ambassador Club underscores its growing role in the global clinical research landscape. The local chapter actively engages professionals through workshops, seminars and networking events, focusing on training and development to align with international standards. Under Dr. Baber Saeed Khan's leadership, the club is promoting a new era of clinical research excellence in Pakistan, encouraging the adoption of best practices and contributing to global research efforts.

The ACRP International Ambassador's Club represents a vital effort to support clinical research professionals worldwide. By providing authentic training, promoting collaboration and improving the quality of research, the club plays a vital role in shaping the future of clinical research in Pakistan and beyond.

8.8 Call to action

Clinical Research professionals are encouraged to become members of the ACRP and the ACRP Ambassador Club. They may do so individually or as an institution. By doing so they will have access to the various professional development opportunities offered by both ACRP and its Ambassador Club. They will also remain updated with the latest international developments related to clinical research.

9. Way Forward

Many international sponsors are now convinced about reducing the research gap in LMICs due to the high disease burden in these countries, and their attention can be gained to improve awareness regarding CTs in our population.

Contribution from PHRC can be expected in the future. In the past, it has been in terms of evidence generation and offering research grants to organizations. Now, it is a part of NIH and renamed Health Research Institute. Its new role is to fund research only instead of conducting it, and funds are given by scoring research based on priorities and incentivization.

International pharmaceutical companies are realizing they can't ignore the Indo-Asian population, and recently, many trials have shifted to South Asia. Pakistan can also expect to get investment opportunities and boost its economy via advancement of its clinical trial industry.

10. Conclusion

In conclusion, Pakistan has a unique opportunity to become a key player in the global clinical research landscape. By leveraging its human capital and implementing policies that streamline processes, ensure data integrity, and incentivize investment, the country can address existing gaps and attract more international sponsors. A collaborative approach, driven by motivated leadership and strategic partnerships, is essential for creating a robust research ecosystem. With ongoing developments and growing global interest in LMICs for clinical trials, Pakistan is well-positioned to advance its clinical trial industry, fostering innovation, economic growth, and improved health outcomes.

11. Annexure

11.1 Regulatory Process

i. Clinical trial approval

For DRAP approval, required documents include: investigator brochure, final approved protocol, informed consent form, fee challan for regulatory approval and import license, CEC approval, list of participating countries, trial phase, drug quantity, site details, PI resume, ethics committee approval with member list, GMP certificate with CPP/free sale certificate (if the drug is marketed in the origin country), pre-clinical/safety data, adverse event reporting form, patient enrollment numbers, monitors/CRA/CRO names, evidence of registration in the origin country, Pakistan registration letter (if applicable), study drug label sample, and authorization letter for drug import. Shelf life should ideally be ≥75%, but short-expiry drugs may be imported based on study requirements.

Applications for clinical trial sites (Form I), trial authorization (Form II), and site license renewal (Form III) per Bio-Study Rules 2017 are available at DRAP offices or the website. IRB/IRC of public or private institutions provides ethical clearance and periodic reviews. Applications to IRBs and NBC can be submitted in parallel.

ii. IMPs import approval

Approved CT may apply for an import license on Form-4 of the Drugs (Import & Export) Rules 1976 if the importation of IMPs is required for the trial. Form-4, along with all the necessary documents and prescribed fee, may be submitted to respective field offices of DRAP. The approval for importation of IMPs will be dealt with/ approved by the Quality Assurance and Lab Testing Division of DRAP after approval of the conduct of clinical studies. After fulfillment of all formalities, an import license on Form-6 of the Drugs (Import & Export) Rules 1976 will be issued with a 2-year validity. If a trial duration is more than 2 years, the applicant may renew the import license by submitting Form-4 under the Drugs (Import & Export) Rules 1976 to respective field offices of the DRAP. The clinical research wing of the health ministry takes care of the regulatory approval process. Separate approval is not required for the export of biological materials from Pakistan.

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