

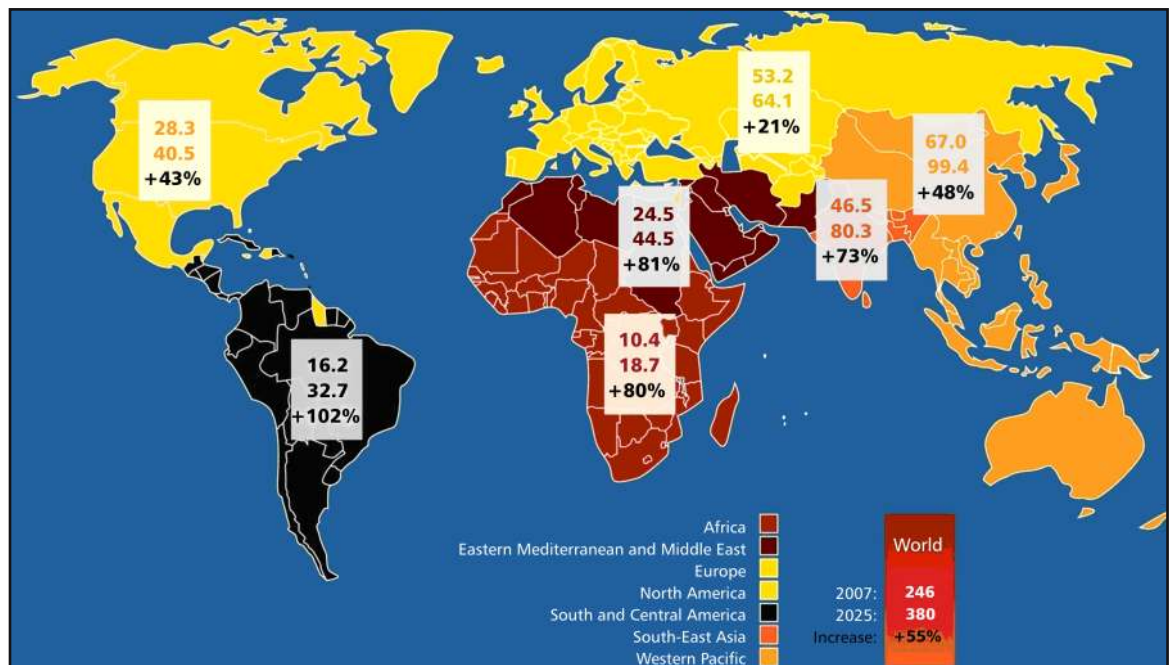
**Diabetes clinical trials
in South East Asia &
the Indian Sub-continent
– *Your Key to success***



SIRO Clinpharm



The exponential growth of diabetes mellitus in the developed as well as developing region poses a significant healthcare challenge for both government and industry. Epidemiological evidence suggests that, without effective prevention and control programmes, diabetes will likely continue to increase globally. It is estimated that some 246 million people or 5.9%, in the age group 20-79 had diabetes in 2007. More than 70% of these live in the developing countries. The worldwide estimate is expected to increase to some 380 million or 7.1% of the adult population by 2025¹. The increase in the number of people with diabetes in each region is shown on the map below.

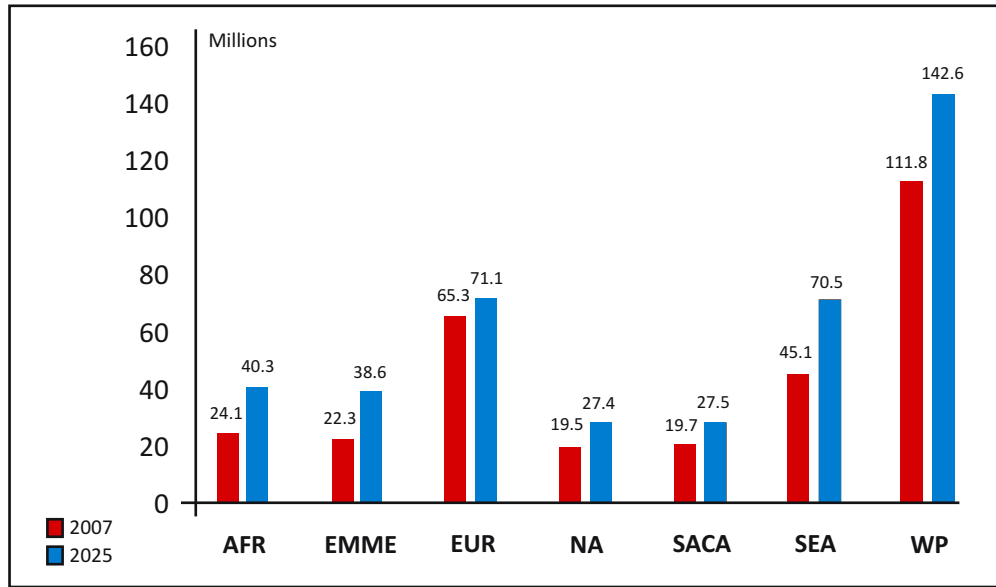


Source: International Diabetes Atlas

From the map it can be concluded that it is the developing countries that presently face the greatest burden of diabetes mellitus. Fast pace of economic growth in the Indian sub continent and South-East Asia has led to rapid urbanization and a significant change in the lifestyles of the urban populace. These changes which include change in diet, increased level of stress and/or sedentary lifestyle have contributed to the increased prevalence of diabetes mellitus in these regions. Also, along with diabetes mellitus, lesser forms of glucose intolerance, particularly impaired glucose tolerance (IGT), can now be found in almost every population in the world. IGT is now recognized as being a stage in the transition from normality to diabetes. Thus, individuals with IGT are at high risk of progressing to Type 2 diabetes.



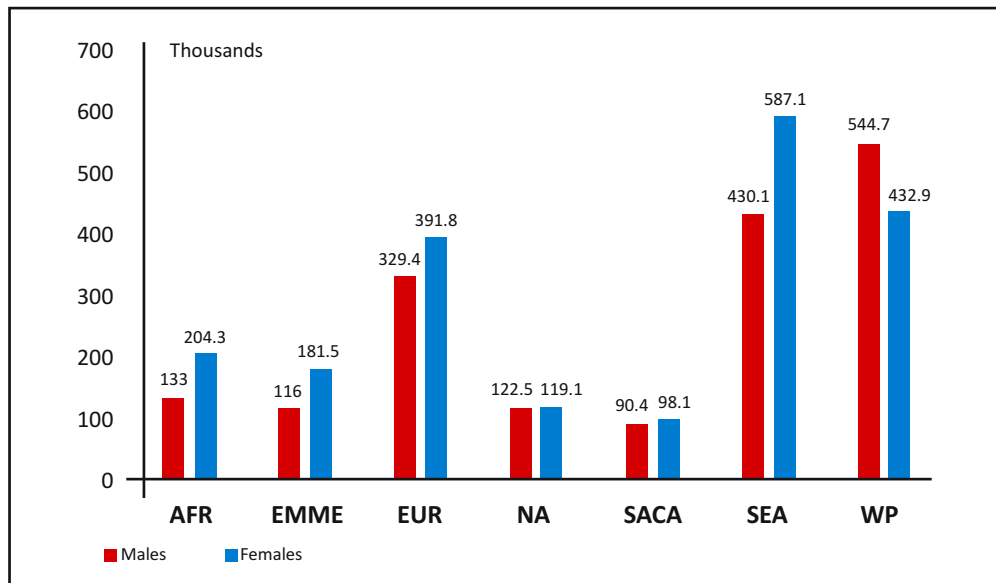
The chart below shows the number of people with IGT (20-79 Age Groups) by region, 2007 and 2025².



Source: International Diabetes Atlas

Today, diabetes mellitus accounts for 6% of mortality worldwide with about 3.8 million deaths in 2007 alone³.

The chart below shows the region wise deaths attributable to diabetes mellitus.



Source: International Diabetes Atlas

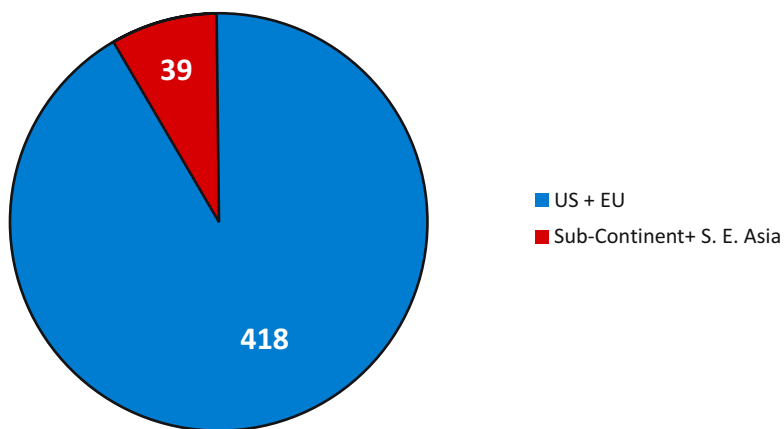


It is evident from the chart that the Asian region leads the world in mortality caused by diabetes. Significant number of the populace of the Indian sub-continent & South-East Asia do not have access to recently launched anti-diabetic drugs. This high unmet need makes drug development in this field a very promising endeavor.

In spite of the rapid growth of diabetes in the populations of the Indian subcontinent and South-East Asia, these regions are not adequately represented in global clinical trials. Historically, this has been due to the fact that most of the sponsors conducting clinical research in diabetes mellitus have been from the developed world. Also, their target regulatory agencies have traditionally been in the developed world viz. USFDA, EMA, PMDA Japan.

The chart below shows the number of clinical trials in diabetes registered in 2010 in the developed markets of USA and EU vis-à-vis. the Indian subcontinent and South-East Asia⁴.

Clinical Trials in Diabetes Mellitus



Source: www.clintrials.gov



Advantages offered by Indian Subcontinent and South-East Asia:

There are several reasons to consider the Indian Subcontinent and South-East Asia for clinical trials.

- Faster patient recruitment due to:
 - Large and increasing population of patients with Type II Diabetes Mellitus
 - Relatively less competition for patients
 - Availability of treatment naive patients
 - High patient-to-site ratio as compared to developed markets
- Highly motivated and skilled clinical investigators
- Significant cost savings
- Conducive regulatory scenario
- Potentially large commercial markets for new drugs to be launched

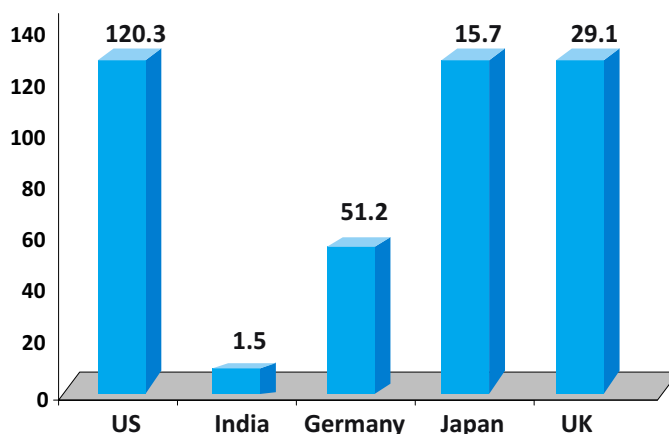
Faster patient recruitment:

Increased demand for clinical trial subjects along with a concurrently lower participation rate in developed markets has led to an acute shortage of trial subjects which threatens to significantly slow down ongoing medical research. Research conducted by a consulting firm suggests that it would take 5.8 years to fully enroll all currently open Phase III trials if only US sites were used as compared to 1.9 years using both US and other global sites⁵.

Faster patient recruitment is one of the most important success factors for a clinical trial. The Indian sub-continent & South-East Asia with their large populations can help to reduce the recruitment timelines for global studies. As evident from the aforementioned charts, the Indian subcontinent and South-East Asia have a large pool of treatment naive patients which may benefit from improved access to medications through participation in clinical trials. With an average trial density of 1.5⁶, there is less competition for recruitment of patients as compared to those in developed markets. Quicker patient recruitment offers multifold benefits viz. faster completion of a clinical trial, reduced cost of drug development and longer post-approval patent term for recoupment of R&D investments.



Trial density



Source: www.clintrials.gov

Highly motivated and educated clinical investigators:

Primary investigators are a critical cog in the clinical trial machinery. Access to high quality investigators is paramount for the success of any clinical trial irrespective of geography. The Indian Sub-continent & South-East Asia is home to large numbers of western educated investigators. These investigators are highly motivated to participate in clinical trials. Research has shown that the main reasons for an investigator to participate in a clinical trials are⁷:

- Access to new and innovative compounds for their patients
- Prestige in associating with global bio-pharmaceutical companies
- Academic interest of the investigator
- Monetary compensation

Also, there are many investigators available in these regions with firsthand experience in participating in ICH-GCP compliant global clinical trials. In light of these reasons, it is easier to recruit clinical investigators who are not only motivated to recruit patients but also adhere to the clinical trial protocol thereby ensuring high quality of data.



Cost Savings:

Conducting clinical trials in the Indian Sub-continent and South-East Asia has shown to produce savings in not just cost but also in time. On an average, a delay of 1 day in the clinical trial costs the sponsor about \$1 million. Sponsors conducting clinical trials in the Asian regions can not only expect expedited timelines but also cost savings to the tune of 30-40% as compared to USA and Western Europe. These savings are mainly attributed to the lower costs of medications, site fees, investigator fees, travel etc.

Conducive Regulatory Scenario:

Over the past several years governments in Indian Sub-continent and South-East Asia have framed policies to encourage conducting clinical trials in their countries. Today, these countries have a strong regulatory and ethical oversight than in the past. Asia has diverse regulatory systems and navigating all of these would be a challenge for any sponsor. Given below is a snapshot of the regulatory timelines a sponsor can expect in this region¹⁰.

Country	GCP Adoption	Approval Process	Regulatory Approval Timeline
India	2001	Parallel Approval	~120 days
Indonesia	2001	N/A	~90 days
Malaysia	1999	Parallel Approval	~100 days
Philippines	1993	Parallel Approval	~100 days
Singapore	1998	IRB approval --> Reg. Approval	~30 days
Thailand	2000	Parallel Approval	~110 days

The experience gained through conducting clinical trials is being leveraged for evolving new regulations which try to strike a balance between patient safety and in attracting more number of clinical trials.



Large markets for new drugs:

The large populations of South-East Asia & Indian Sub-continent not only are a source of clinical trial subjects but also future customers of cutting edge medical innovations. The rapid economic growth in this region has led to the development of a large middle class which craves for access to new and innovative medicines. Although these potential consumers earn far less as compared to those in the developed regions in absolute terms, they are quickly acquiring the buying power especially when purchasing power parity is considered. Estimates by a global bank suggest that about 60 million Indians (roughly equal to the population of the UK) can already afford to buy western medications⁸. With majority of the demand for new medications to come from these regions, it would be prudent for global sponsors to use these regions not just for faster patient recruitment but also as a beachhead for new business.

Challenges in conducting trials in South-East Asia & the Indian sub-continent:

Although significant potential exists in conducting clinical trials in these regions, there are also some potential challenges. Some of them are:

- Experience in conducting clinical trials as compared to the West
- Language and cultural differences
- Logistical challenges

Experience in conducting clinical trials:

Although there are over 500,000 medical professionals in India, not all of them would have experience in participating in clinical trials. This would entail significant hand holding and knowledge sharing on part of the sponsor. Conducting frequent investigator training and refresher sessions would be one way to address this. The site CRA has to be in constant touch with the investigator to prevent issues coming up. Development and dissemination of clinical trial related literature also helps in increasing awareness amongst the investigators.

Language and cultural barriers:

Countries in South-East Asia & the Sub-continent possess diverse cultural identities with hundreds of languages and thousands of dialects. Successful implementation of trials in this region would require innate understanding of the culture and languages involved. The clinical trial documents need to be in the appropriate languages in which the trial needs to be conducted. Also, the differences in languages, dialects and literacy levels across these regions throw up a formidable challenge to the process of informed consent.



Logistical hurdles:

Many of the countries in these regions do not have well developed infrastructure. Transport connectivity may be an issue in some of these countries. The knowledge and understanding of various import regulations is also a challenge. Most regional CROs do not even have a clinical trials supplies facility of their own and tend to outsource the task thus increasing the need to coordinate further risking the timelines.

Tackling the challenges:

As demonstrated in the previous sections, conducting clinical trials in the regions of South-East Asia and the Indian Sub-continent provide numerous benefits to the sponsors. However, there are also certain challenges, insufficient knowledge of which may cause significant impediment in the completion of the trial. The ideal way for a global sponsor to address these challenges is to partner with a clinical research organization (CRO) with innate knowledge of these regions. An experienced CRO with a strong regional presence can effectively help a global sponsor in navigating the potential pitfalls of conducting a trial in this fast growing region.



List of Acronyms:

- AFR – Africa
- EMME - Eastern Mediterranean and Middle East
- EUR – Europe
- NA – North America
- SACA - South and Central America
- SEA – South-east Asia
- WP – Western Pacific

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About the Authors



Ajit Nair, PhD

President - Global Operations

Ajit Nair is the President of SIRO Clinpharm's Global Operations. He provides leadership, vision and direction to the growth of SIRO's global operations and is focused on creating an efficient and responsive organization to service the growing client pool at SIRO. He looks at strategic issues concerning integration across various operational geographies and global delivery models.



Rajendra Talele

Senior Vice President – Clinical Operations Asia & Europe

Mr. Talele is responsible for overseeing the execution and operational excellence of Clinical Research, including Clinical Project Management, Clinical Monitoring and Clinical Documentation departments. He has over 16 years of experience working with the pharmaceutical industry and clinical research organizations based out of India.