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Managing Clinical Trials in Bangladesh: Issues, Threats, Opportunities and Approaches

ABSTRACT

Clinical trials, also known as clinical studies, are designed to help us find out how to give a new treatment safely and effectively to people. A clinical trial is an organized research study designed to investigate new methods of preventing, detecting, diagnosing, or treating an illness or disease and attempt to improve a patient's quality of life. The concept of outsourcing for the development and global studies on new drugs has become widely accepted in the pharmaceutical industry due to its cost and uncertainty. Bangladesh is going to be the most preferred location for contract pharma research and development due to its high patient enrolment rate, human resources, and technical skills, adoption/amendment/implementation of rules/laws by regulatory authorities, reliable data quality and changing economic environment. But still 'miles to go' to fulfill the pre-requisites to ensure Bangladesh's success. In spite of all the pitfalls like government policies and weak patent law, lack of ICH-GCP compliant sites, lack of awareness and education amongst patients and bureaucratic hurdle, the country is ambitious and optimist to attract multinational pharmaceutical companies to conduct their clinical trials in Bangladesh.

Background:

Clinical trials are scientific studies in which new treatments – drugs, diagnostic procedures, and other therapies – are tested in patients to determine if they are safe and effective.

As more and more sponsor companies from the US and EU are outsourcing clinical trials to developing countries, Bangladesh as a country has a great potential to be one of the leading clinical trial markets. Looking at the success of India, China, Thailand and other neighboring countries in this region that have been actively involved in clinical trials, Bangladesh too can open itself up to the opportunity in clinical trials and gradually progress to be a favorite destination to conduct clinical trials.

Bangladesh has a very large treatment naive patient population for all therapeutic areas, be it oncology, diabetes, infectious diseases etc and has hospitals and high quality private clinics spanned throughout the country. The majority of physicians in Bangladesh are English speaking making it an attractive place to conduct clinical trials.

Bangladesh with the world's seventh largest population is a rapidly developing country with demands for improved healthcare. Thus demand for clinical research is constantly increasing. With international collaboration growing rapidly, Bangladesh is getting attention from multinational research on its high prevalence of indications such as emerging and re-emerging infections, Cardiovascular, endocrine, Oncology, Neurological, Respiratory, Dermatological, Reproductive and Ophthalmology health.

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With a very large number of drugs, worth more than $50 billion in annual revenues, coming off patent in the next few years, many western pharma companies are now increasingly relinquishing business activities that are not considered core, such as clinical research, and are moving towards contract research. Since in the western countries, clinical research is characterized by extremely high costs and long gestation periods and the same work can be performed in developing countries at a fraction of the cost and much faster, many global pharma companies are increasingly turning their attention to Asia to benefit from low R&D costs in the region and also to gain access to Asia's drug markets. Clinical trials have thus gone 'global,' because CROs find it easier to conduct them in underdeveloped countries, as this is cheaper or has less ethical encumbrances or legal risks. Naïve patient populations, English speaking doctors, low costs and other advantages offered by developing countries have opened up new avenues for the clinical trials market. Hence there is lot of scope for clinical research activities for the South Asian nations if they make use of the upcoming opportunities in this field.

About Bangladesh [1]:

Bangladesh officially known as the People's Republic of Bangladesh is a sovereign state in South Asia. It is governed by a Central Government delegating its power to other administrative divisions. The main economic strength of this country is jute and garment and it maintains a good foreign relation with its neighboring countries. The Government of Bangladesh aimed at improving the healthcare sector by providing the basic health and medical requirements to all people of Bangladesh by means of Primary Healthcare approach. The government formulated the National Health Policy in 1997 and to maintain the health sector, committees have been formed along with inter-ministerial committee in order to decentralize the administration of this sector. Importance has been given to Health research and technology where individual are trained and given the education to meet the standards of health facility today.

Fig 01

Capital	Dhaka
Official Languages	Bengali
Other Languages	English, Chakma and Others
Ethnic Group	98% - Bengali and 2% - Others
Demonym	Bangladeshi
Total Area	147570 km2 (94th)
Population – March 2013 estimate	150,039,000 (8th)
GDP (PPP)	2013 estimate
Total	$324.628 billion[3] (43rd)
Per capita	$2,083[3] (154th)
GDP (nominal)	2013 estimate
Total	$153.58 billion[4] (43rd)
Per capita	$1,044[3] (150th)

Clinical Trials Opportunities in Bangladesh [11]:

According to an article in The Pharma World, leading health Journal in Bangladesh, notwithstanding its potential, clinical research is still underdeveloped in Bangladesh. There is a lack of capacity for bioequivalence studies, no analytical capacity (samples have to be shipped to foreign countries such as India, Singapore for any analytical treatment) and limited bio-banking and documentation of clinical specimens. There is no CRO activity in the country. This cripples the ability of the health and pharmaceutical industry to move forward, severely stunts the professional growth of health care personnel and limits their ability to become competitive for funding in the global arena. Fortunately, with appropriate input from global scientists and consultants, Bangladesh appears very well placed to fill this void and develop world-class clinical research capacity. There is a significant foundation for such clinical research capacity in the health care sector in Bangladesh. Hospitals in the country have the advantage of access to a large population base presenting a range of clinical conditions. These hospitals have talented physicians who are fluent in English and eager to take advantage of opportunities to expand their expertise and scope of activities into state-of-the-art health care research. Moreover Bangladesh has a significant generic pharma industry, currently marketing its products mainly in the domestic market and in non-regulated international markets. Building Contract Clinical Research capacity in Bangladesh will serve the local pharmaceutical companies and allow Bangladesh to take its deserved position in the rapidly-growing global clinical research products and services market. Bangladesh can be the next frontier in the global CRO industry. Based on GDP and the volume of the pharma industry compared to other Asian economies such as India and China, Bangladesh could potentially capture five per cent of the Asian CRO market by 2020. The country is well poised to launch a CRO for multiple reasons that involve both its own fledgling pharma industry as well as the increasing demands in the global market, the article says. The development of a globally-competitive CRO will have an impact beyond the domestic pharma industry. It will attract foreign companies, seeking high quality research at more affordable prices. It will also have a multiplier effect on other areas of the economy that transcend the pharma industry, and contribute to the transition from low-wage labour-intensive activities into higher-wage knowledge-based industries. Building capacity for upscale knowledge industries, including biotechnology and health science, historically has had a remarkable impact on wealth building and human development in the West and is expected to have a similar positive impact in emerging economies [2].

India and Bangladesh Pharma Industry:

In South Asia, India is the leader and other countries like Sri Lanka, Bangladesh, Pakistan and Afghanistan are slowly picking up. Particularly Bangladesh is leading after India in the south. Though at a nascent stage, Bangladesh holds huge potential for the Indian pharma companies to tap. Since a huge potential exists for developing trade and economic relations between the two countries, both the nations should move ahead to tap the emerging opportunities, aver experts [3].

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The clinical studies registered in the *Clinical Trials. Gov* from 2001-2012 by Asian and WHO SEAR countries, and found that Asian countries had the global share of 18.2% of the clinical trial and WHO SEAR countries had only 3.6%, which is 3 and 13 times lower, respectively than those registered by the USA. The top 10 Asian countries had a share of 96.8% of the total registered clinical trials. The trends of registered studies were also increased in the last 12 years in the countries of the WHO SEAR. The number of registered phase3 clinical trials from the SEAR countries was 1626 in the same time frame, which is approximately and one-fifth of the USA trials [4].

Clinical studies registered in WHO SEAR countries – 2001 - 2012

Countries	All clinical studies	Phase I clinical trials	Phase II clinical trials	Phase III clinical trials
Bangladesh	141 (3.7%)	13 (4%)	26(3.4%)	33 (2%)
Bhutan	2 (0.05%)	0	0	0
India	2160 (56.9%)	237 (73.8%)	457 (59.7%)	969 (59.6%)
Indonesia	186 (4.9%)	7 (2.2%)	23 (3%)	84 (5.2%)
Korea DPR	1 (0.03%)	0	1 (0.1%)	0
Maldives	1 (0.03%)	0	0	0
Myanmar	7 (0.2%)	1 (0.3%)	1 (0.1%)	4 (0.2%)
Nepal	29 (0.8%)	1 (0.3%)	8 (1%)	9 (0.6%)
Sri Lanka	28 (0.7%)	1 (0.3%)	4 (0.5%)	12 (0.7%)
Thailand	1240 (32.7%)	61 (19%)	245 (32%)	515 (31.7%)
Timor-Leste	1 (0.03%)	0	0	0
Total	3796	321	765	1626

Asia is home to 60% of the world's population, and thus shoulders a significant proportion of the global disease burden and lags behind most other regions in its overall health attainments. Large hospital infrastructures and an increasing pool of trained and motivated clinical researchers have offered a tremendous market potential for clinical trials in the region. These have pulled towards increased pharmaceutical research and offer prospective study sites which provide an opportunity to cost effectively recruit more patients within the timelines of the trial. An important indicator of this is the growing R&D investment in Asian Markets, and CRO services are also forecasted to grow 20% by 2015. However, there are several factors and problems responsible for the successful implementation of clinical trials in Asia which are related to managerial, ethical, clinical scientific, regulatory reasons as well as physician/investigators and trial subjects. Managing clinical trials requires efficient trial management strategies including standard trial management guidelines and robust methods of implementation and evaluation [4].

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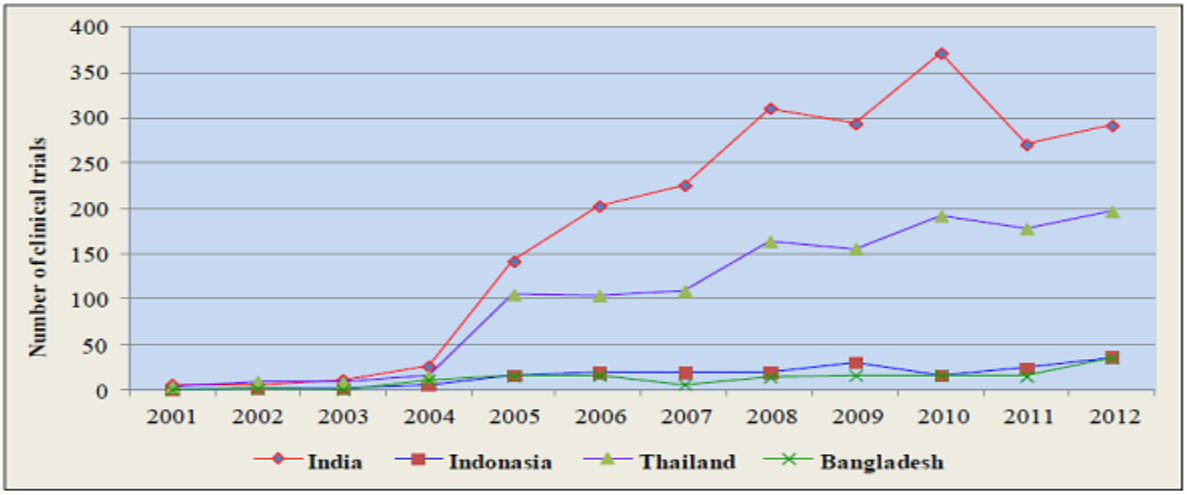

Trend of clinical trials registered in selected WHO SEAR countries - 2001 - 2012

Issues and approaches in managing clinical trials at Bangladesh:

Key factors	Issues and approaches
Project planning and management	Strategic and operational management plan - Objectives, resources, and time frame - Ethical and scientific issues - Day-to-day running of the trial Competent trial team - Responsibilities: responsibility, authority and delegation Monitoring – delivered as planned - Risk assessment, QA management systems Monitoring Robust statistical analysis plan Clinical Trial regulations/guidelines - National/regional/international - GCP and local regulations - GLP certified labs
Physician participation	Time constraints -Reward and recognition Financial: pay increase, promotion, grants for attending conferences -Non-financial: recognition/awards

	Research area -Physician interest -Clear potential to improve patient care Training Regular feedback
Patient recruitment	Provision of greater amounts of information -Hard to reach patient groups Patient education about treatment/improving health -Cutting edge care and latest treatment Reduce practical issues such as inconvenience, cost -User friendly procedures
Collaboration	Collaborative group or network Representative from each participating sites Regular meeting, effective feedback
Communication	Method of communication - Technology: E-mail, SMS, Face-book, twitter, blogs Listening to problems and resolving any issues quickly - Regular feedback and staff satisfaction
Administrative support to trial team	Centralized support services outside the physician group Clerical and other administrative tasks - Human subject approvals, institutional agreements - Progress reports to funding agencies - Communications among the research team
Efficient systems for data management	Robust computerized systems and procedures Monitor day-to-day running of the trial - Recruitment, randomization procedures and data management - Electronic data capture - Reduce workload
Education and training for trial team	Degree/diploma/certificate course Short-term courses: workshops Online/distance learning
Publication and dissemination	Made widely available

	- Journals, trial registers, conference presentations Multi-centre trial - Local dissemination and presentation - Standard guidelines for reporting clinical trials

As market is expanding in Bangladesh, SWOT analysis is play vital role to highlight the positive and negative issues for expanding clinical research markets. It is very encouraging that the opportunities are far greater than threats and that the strength outweighed the weaknesses. If Bangladesh is able to address these issues adequately, the region will be the 'research hub' for all types of clinical trials in near future [4].

SWOT analysis for emerging clinical trial market in Bangladesh:

Strengths	**Weakness**
• Lower trial cost per patient compared to the US and EU • Large patient pool with high enrolment • Wider coverage of ethnic populations • Drug naïve patients • Disease pattern and diversity • Government support	• Lack of awareness about clinical trials/clinical research • Lack of trained clinical research professionals • Patients participation and compliance • Smaller hospitals with inadequate research set-up • Ethical and scientific issues - Delayed project approval process • Regulatory affairs frameworks and systems - Implementation of ICH-GCP and local regulations • Outsourcing risk assessment • Communication problem
Opportunity	**Threats**
• Emerging markets • Interested international pharmaceutical and • biotech companies • Fast patient recruitment with relatively low costs	• Lack of regulatory and ethical approval frame works • Limited well trained personnel • Administrative bureaucracy • Political unrest • Cultural barriers

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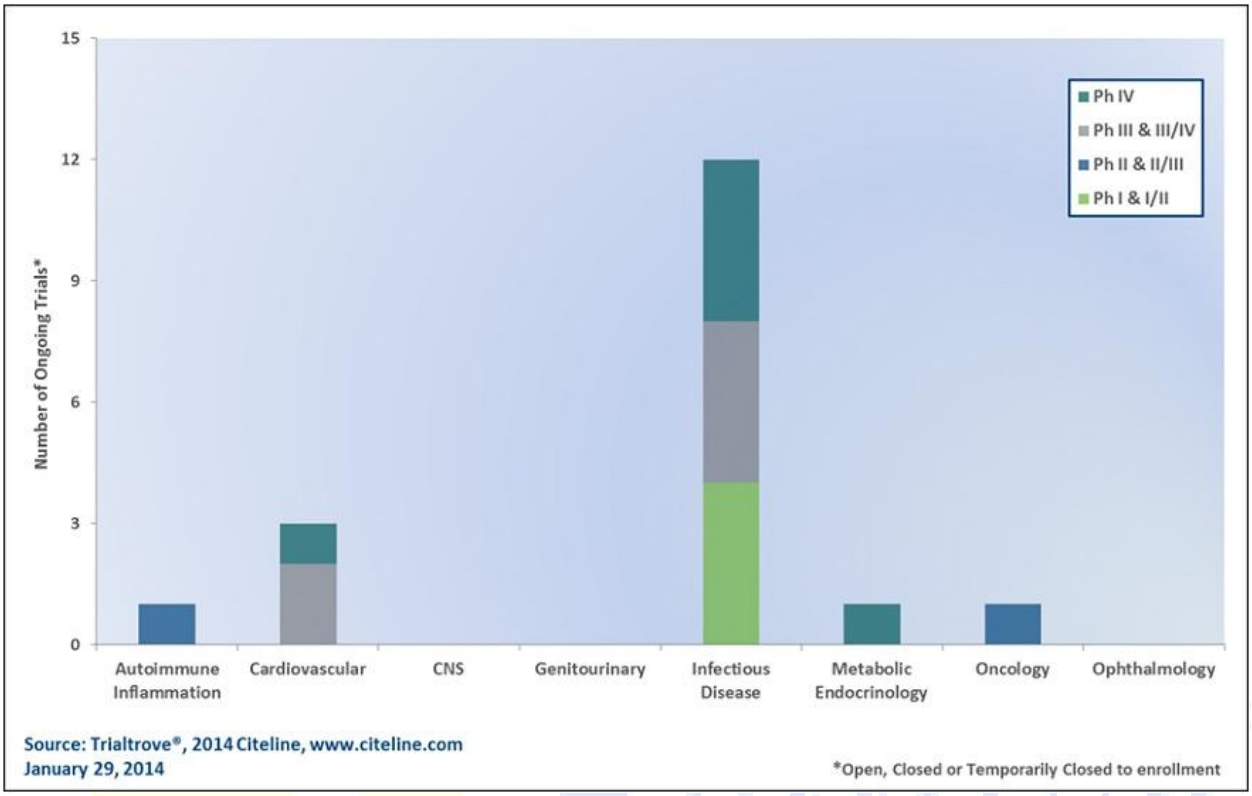
Clinical trials statistics in Bangladesh[1]:



Need to plug loopholes

The future progress of clinical trials in Bangladesh, the regulatory set up needs to be tightened up. It is essential to make trial regulation less complicated and more readily adaptable to risk, and for having guidelines that are globally applicable and adaptable to all types of trial. Such guidelines would be as easily applied to pragmatic trials of existing treatments or disease management questions as they would be for trials of new drugs and vaccines.

Since developing countries have needs and abilities distinct from those of more developed countries, these countries should be allowed to work with sufficient leeway to address issues specific to these regions. Bringing the clinical trials enterprise of developing countries back into the hands of local populations could have widespread benefits, feel some of the experts.

If the loopholes are plugged and existing laws are stringently implemented to ensure that clinical trials are conducted with utmost transparency and diligence, the prospects for clinical trials would be quite high in Bangladesh, they opine.

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CRO's aim should be to:

1. Enhance Bangladesh public health and education in clinical research
2. Establish Bangladesh as a viable partner in worldwide clinical research
3. Develop and improve infrastructure in its research, in its medical scientific community within its centers of medical excellence
4. Aims to manage and setup training structures on ICH GCP. Promote various institutes to provide postgraduate courses in CR. This will empower local doctors, nurses, graduates and medical students all over Bangladesh.

Conclusion:

In Bangladesh, in spite of all the present pitfalls, the country is certainly gearing up to attract more and more researchers from around the world to conduct their clinical trial studies. Laws are being amended to facilitate the entry of global clinical trials and the regulatory system is being polished. The current situation improves by massive and concerted efforts are on to train research professionals and increase the base of investigators and supporting staff. Bangladesh is already off the starting blocks and gearing up for an inundation of clinical research trials and this will ensure the timely conduct and completion of the clinical trials and at the same time generate high quality data for international submission. Bangladesh is poised to offer the global pharmaceutical industry high quality and cost effective contract services(a proven track record for some of these services and an enthusiasm to expand into services at the higher end of the value chain.) to support drug discovery, clinical trial conduct, data management and manufacturing. An increasing number of international pharmaceutical companies will seek to establish outsourcing arrangements in variety of forms after uphold international intellectual property laws with high ethical standards. The primary driver for outsourcing will change from cost saving to the quest for high quality and speed as the sector matures. Bangladesh's more ambitious pharmaceutical companies to fulfill their aspirations of becoming players in global pharmaceutical industry through a thriving contract Skills developed by Bangladesh workforce.

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