Clinical trials and healthcare needs in India: A difficult balancing act but opportunities abound!

Health is the cornerstone of development and “good health is a cornerstone of economic progress, a multiplier of society’s human resources, and indeed, the primary objective of development.”[1] There exists a disproportionally low investment in health research in developing countries compared to their health disease burden globally, popularly known as the 10/90 gap.[2] In 2015–2016, the public health expenditure in India amounted to 1.3% of the Gross Domestic Product, compared with 9.4% in the UK and 11.3% in Germany.[3] Important steps in redressing this imbalance are to promote equity in health research and to strengthen the capacity within developing countries to undertake research that is relevant to them.[4]

Clinical trials are needed globally to reduce disease burden by helping develop safe and effective new therapies and vaccines. As a research tool, clinical trials are fundamental in the effort to develop new products by gaining the data required by regulators, whether for product license extensions, for existing therapies, for common ailments, or to bring cutting-edge new therapies and vaccines into approved use. These solutions may be for non-communicable diseases such as cancer and diabetes, or, as is especially needed in the developing regions of the world, infectious disease. With the evolution of India’s disease burden as well as its pharmaceutical industry, the need for clinical trials has increased manifold. While India has made considerable progress in our fight against several diseases, there still remains a large unmet medical need for many diseases. India has 17% of the global population and 20% of the global disease burden, yet, <1.4% of all global clinical trials are done in India.[5]

In this issue of PICR, Chaturvedi et al.[6] ask the important question whether clinical trials conducted in India match its health care needs? The authors evaluated studies registered in the Clinical Trials Registry of India (CTRI) between 2007 and 2015. Infectious and parasitic diseases had the highest disability-adjusted life years (DALYs) (82,681) and ranked first in disease burden but accounted for only 5% of the total trials ranking 7th according to number of trials. Cancer was ranked first in the number of trials (546/3325; 16.4%) but was ranked 6th based on DALYs (24,015). The authors conclude that since a large number of trials are being conducted on non-communicable diseases, this could lead to a possible conclusion that India is possibly contributing to global research but which may not entirely be necessary for the population and the health needs of the country. A marked skew in the geographical distribution of sites for clinical trials was seen when comparing the number of trials per state in India with the population of that state.

Bajpai[7] also did a search of the clinical trials registered with the CTRI in 2013 and analyzed the typology of drug trials against the top 10 causes of mortality in India. The author makes the assessment that nearly 2/3rd of the trials have been sponsored by private sponsors – drug companies, foreign institutions, or private Indian institutions/persons. The author comments that this is a reflection on the commitment of the government to pitch in as a major sponsor for medical research in the country. The author remarks that as more than 60% of the trials are either phase 3 or phase 4 trials, this is more to do with the fact that India can provide these required patient population rather than due to its technical expertise. Bajpai also states that a very small proportion of the drug trials was concerning infectious diseases (8.6%) and is worrisome that even in the publicly sponsored trials, the proportion concerning infectious diseases was lesser than that in privately sponsored clinical trials.

Western pharmaceutical industry concentrates heavily on developing drugs for non-communicable diseases based mainly on unmet needs in the western hemisphere. An analysis of data from ClinicalTrials.gov[8] shows that there are over 0.2 million clinical studies ongoing currently and 22% are for oncology and an equally impressive 12% for cardiovascular disease whereas only 9% for infectious and parasitic diseases. Given the concerns of ethics, posttrial access, and the extent to which the social value of research gets to the communities that bear risks of the research,[9] there is an inherent hesitation of global pharmaceutical companies to bring their early phase research on compounds for infectious disease in India. Interestingly, endocrinology and metabolic disorders, together with oncology dominate the therapeutic areas, representing almost half of all indications covered by drug discovery projects by India R and D companies, followed
by infections, immunological and rheumatological diseases, neurology and pulmonary and respiratory diseases. All remaining disease areas combined represent <10%. Drug discovery has been considered the least attractive from an investment standpoint, ranking last of 12 options, far behind diagnostics, medical devices, or discovery services. This low attractiveness is compounded by structural weaknesses across the entire sector, such as insufficient understanding of IP protection, regulatory uncertainty regarding clinical trials, unethical practices, or pricing uncertainties. An additional reason why Indian R and D companies develop drugs mainly for non-communicable disease is because they are on the lookout for an interested pharma partner for further development and commercialization of the asset. All this leads to the industry not wanting to take the necessary investment risk on its own with the resultant outcome that the number of Indian R and D companies who have successfully commercialized drugs/vaccines for infectious disease (either alone or in partnership with public institutions) have remained a handful, for example, artemolane with piperaquine for malaria and Risorine for tuberculosis.

In the recent years, several initiatives have been undertaken by various departments of the government, for example, New Millenium Indian Technology Leadership Initiative and Open Source Drug Discovery (OSDD) by Council of Scientific and Industrial Research (CSIR), Government of India, that aim to bridge the gap between public-funded research institutes and private industries toward collaborative drug discovery programs. The Central Drug Research Institute’s main focus was to identify lead molecules for tropical diseases and population control measures from medicinal plants. The search for antimalarials, based on the investigation of *Artemisia annua*, resulted in arteether, for multidrug-resistant or chloroquine-resistant *Plasmodium falciparum*, approved in 1998. CSIR-IIIM, Jammu, in partnership with Cadila Pharmaceuticals, developed a new combination drug for TB in 2009, named Risorine.

OSDD program of CSIR is a team India consortium with global partnership having a vision to provide affordable healthcare to the developing countries by providing a global platform where the best minds can collaborate and collectively endeavor to solve the complex problems associated with discovering novel therapies for neglected tropical diseases such as tuberculosis, malaria, and leishmaniasis.

Drug discovery and development to match India’s healthcare needs:

The Indian drug discovery and development has to cater to affordability and access, on the one hand, and diseases which are more prevalent such as malaria, dengue and tuberculosis. Conducting clinical trials in India indisputably has very positive benefits overall as the research sites gain by working with commercial or not-for-profit sponsors by increasing capacity for research through training and engagement in product development and other global public health initiatives, raising research standards, bringing health improvements and often times investing in research infrastructure in the institution.

The Indian Government aims to stimulate the launch of 2000 startups in life sciences over the coming 5 years and also has a stated highly ambitious target of “one NME per year and 10–12 incremental innovation launches per year by 2030”. Even though daunting, the Indian pharmaceutical R and D efforts have resulted in over 200 preclinical-stage and clinical-stage development compounds which illustrates the tremendous accumulation of R and D capacity and of know-how that has occurred over a time span of two decades. The invigoration of new drug discovery for healthcare needs of the country with allocation of resources, infrastructure, personnel, and strengthening of public-private partnership can provide drug development which matches the healthcare needs as well as has the potential to improve the overall healthcare system in the country.

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