



ONCOLOGY India Perspective

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Introduction

1. Cancer is the second leading cause of death globally after cardiovascular diseases.¹ Patients with cancer generally have a poorer prognosis in low-income and middle income countries, including India, because of relatively low cancer awareness, late diagnosis, and the lack of or inequitable access to affordable curative services compared with patients in high-income countries.^{2,3} India has a population of 1.3 billion spread across 29 states and seven union territories, and many of the states are as large as other countries, with varying degrees of development, population genetics, environments and lifestyles, leading to a heterogeneous distribution of disease burden and health loss.⁴
2. The United Nations Sustainable Development Goals target the reduction of premature mortality from non-communicable diseases, which includes cancer, by one-third by 2030 through prevention and treatment.⁵ The National Cancer Registry Programme in India was established in 1981 to generate data on the magnitude and patterns of cancer through population-based registries.^{6,7} The number of registries has grown under this programme, and other population-based registries have also been started in recent years.⁶
3. The India State-Level Disease Burden Initiative is a collaboration with the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD) to produce subnational disease burden estimates for India. This initiative recently reported the variable health transition across the states of India from 1990 to 2016 based on analysis done as part of GBD 2016.^{4,8}

Problem statement

A. Incidence and Prevalence rates

1. All cancers together contributed 5.0% (95% UI 4.6–5.5) of the total DALYs and 8.3% (7.9–8.6) of the total deaths in India in 2016, an increase of 90.9% and 112.8% respectively from 1990.⁹
2. The estimated number of incident cancer cases in India increased from 548 000 (95% UI 520 000–576 000) in 1990 to 1 069 000 (1 043 000–1 101 000) in 2016. The crude cancer incidence rate in India increased by 28.2% (95% UI 19.9–35.5) from 63.4 per 100 000 in 1990 to 81.2 per 100 000 in 2016, but there was no change in the age-standardised incidence rate.⁹
3. The number of deaths due to cancer in India increased from 382 000 (95% UI 351 000–412 000) in 1990 to 813 000 (767 000–850 000) in 2016. The crude cancer death rate in India in 2016 was 61.8 (95% UI 58.3–64.6) per 100 000, as compared with 44.2 (40.6–47.7) in 1990. Male cancer patients had a 12.3% (95% UI 2.9–23.3) increase in age standardised death rate over the 26-year time period, whereas no substantial changes over time were found in female cancer patients.

4. The crude cancer MI ratio in India in 2016 was 0.76 (95% UI 0.72–0.79). The MI ratio was higher in low and lower-middle ETL state groups than the high and higher-middle ETL groups in 2016. The overall MI ratio was significantly higher in males (0.83; 95% UI 0.81–0.85) than females (0.69; 0.64–0.71) in 2016.
5. The leading types of cancer in India in 2016, those responsible for more than 5% of the total cancer DALYs among both sexes combined, were stomach cancer (9.0%), breast cancer (8.2%), lung cancer (7.5%), lip and oral cavity cancer (7.2%), pharynx cancer other than nasopharynx (6.8%), colon and rectum cancer (5.8%), leukaemia (5.2%), and cervical cancer (5.2%)⁹
6. The number of new cases and deaths due to cancer doubled in India from 1990 to 2016, as did the proportional contribution of cancers to the total DALYs and deaths in the country. The crude incidence, mortality, and DALYs from cancer increased substantially over the 26-year time period. However, there was no change in the age-standardised rates for both sexes combined, highlighting the contribution of ageing and population growth to the increasing cancer burden of the country. The age-standardised death rate for cancer increased for males during this period, suggesting differences by sex. Males had higher MI ratios than females in every state of the country. The trends observed in sex-specific and cancer type specific incidence rates over time in India are likely due to a variety of factors, such as population ageing, changes in cancer literacy, detection, health-care access, and a variety of risk factors.⁹

B. Reason for changing trends

Important Reasons and Explanations for Growing Burden of Cancer in India¹⁰

Major Reason	Explanation or Mechanism for Increasing Cancer in India
Increasing population	India's population is growing and is predicted to be greater than China's in two decades. The Empowered Action Group states of North India will experience the biggest increase in population.
Aging as a result of epidemiologic transition	India's population is aging with a decreasing proportion of youngsters and increasing proportion of elders. The fastest transition is in the Empowered Action Group states. Cancer burden will keep increasing with the increasing number of elders in India.
Improved access to less invasive diagnostic tests	More access to computed tomography-guided biopsy and flexible endoscopy-guided biopsy will result in many more deep-seated cancers being diagnosed, which at times could occur just before death
Elderly Indians are seeking better health care	Retired and elderly Indians who used to shy away from Western medicine have started to visit the clinics and are willing to undergo diagnostic procedures, leading to the detection of more cancers.
Reduction in mortality from competing causes	Reduction in mortality from communicable diseases (eg, diarrhoea, lung infections, tuberculosis, malaria) is

Major Reason	Explanation or Mechanism for Increasing Cancer in India
	being replaced with mortality from Noncommunicable diseases. Any reduction in the mortality from chronic cardiovascular, lung, and renal disease will place more Indians at risk for cancer.
Cancer transition	Infection-related cancers are being replaced by lifestyle and age-related cancers. Spontaneous decrease in human papillomavirus-related cervix cancer and increase in breast cancer in women and decrease in Helicobacter pylori-related stomach cancer and increase of colorectal cancer in men are two such examples.
Changing social and cultural practices	India's family planning program and right to education are empowering Indian women. An increasing number of women are getting higher education and taking up office work, resulting in later marriages and fewer children. These social changes could increase the risk of breast and ovarian cancer. Indian states with the most successful family planning programs (eg, Kerala) have the highest breast cancer incidence. However, the incidence of cervical cancer continues to be high among the women of less developed states, who marry early and have high birth rates.
Increasing risk from energy imbalance	Increasing economic prosperity and affordability of conveniences among India's middle class have increased the per-capita calorie intake and reduced their physical activity. This is exposing children, youth, and middle-aged Indians to excess fat gain and obesity
Cancer screening	Casual use of cancer screening tests will diagnose many indolent cancers, particularly, breast, prostate, and low-grade neuroendocrine tumors in the upper and lower GI tract.

C. Proposed Solution

1. In the present era of evidence-based medicine, clinical trials are rudimentary for research with results of patient benefit and, should culminate to the development of newer therapeutic regimes. These are scientifically designed to provide effective and safer treatment and, with an aim to change global clinical practice. In India, there are about 800 registered clinical trials of which, approximately three-fourths are funded by the pharmaceutical industry.¹¹ However, the majority of them do not translate in practice changing and if at all the incremental benefits of the newer drugs may not be weighed to its cost-benefit ratio. Among all types of clinical trials, RCT are the gold standard as it minimizes confounding variables, protects identity of participants, addresses ethical concerns, focuses on the benefit to risk ratio and, thereby facilitates accurate data analysis to validate the statistical base so formed.
2. India has the potential to offer the righteous infrastructure for conducting clinical trials aiming at affordable patient care and evidence-based management. Tertiary care cancer facilities are dedicated to this cause.¹² To emphasize these thoughts, other landmark RCT's conducted in such centres need to be mentioned; the "Proluton Trial" for breast cancer

suggested that a single depot injection of progesterone significantly improved the clinical outcomes in node-positive women, as an inexpensive tool in developing countries like India. Finally, the effect of visual inspection with acetic acid screening by primary health workers on the cervix, reduced cervical cancer mortality by 31%. These prospective RCTs have proved to be beneficial and cost-effective, promising a reduction in morbidity and mortality from such cancers.

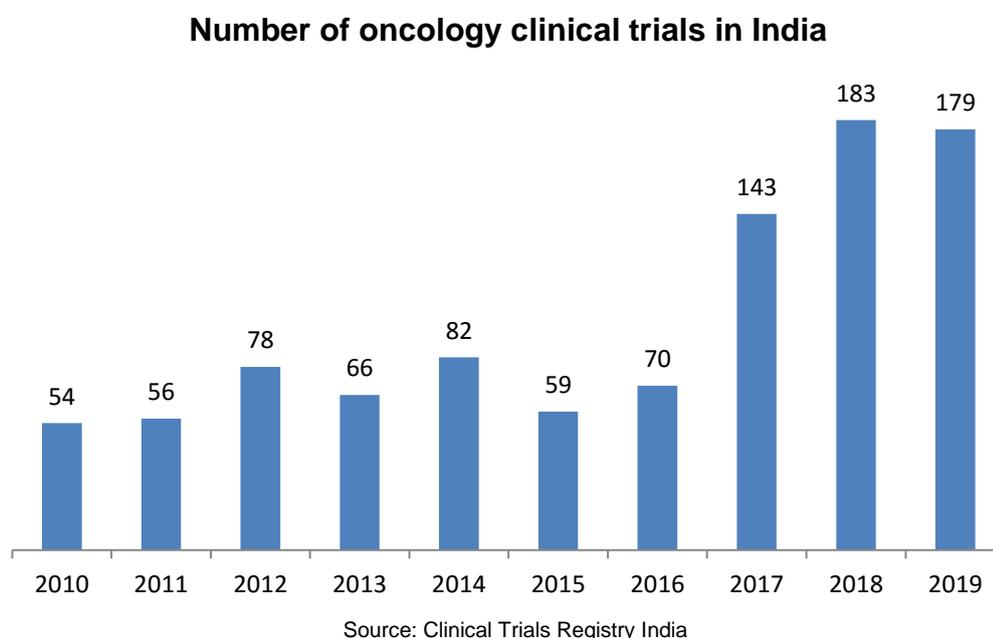
3. With a long standing and well evolved medical education system, the presence of numerous institutions and laboratories with state-of-the-art equipment, the availability of English literate manpower, the low overhead cost, the reservoir of diverse ethnicity harboring naïve plethora of cancers and a solid information technology infrastructure, India is an oasis to conduct clinical trials and to offer cheaper, safer, and effective treatment options to its afflicted population.¹³ Cost reduction, safety, and ease of procurement is of paramount importance to the Indian population and it is imperative to know that more than 70% of the final cost of a product is incorporated and accounted as research expenses.¹⁴ The populous India is a fertile land to promote clinical trials (in keeping with our local disease prevalence) that are mandatory to test their safety, efficacy and adverse effects.¹⁵ With an over 20 billion (Indian rupees) pharmaceutical industry, India is one of the top five manufacturers of bulk drugs in the world and, is among the top 20 pharmaceutical exporters in the world. India, with its open direct foreign investment policies has created more lucrative opportunities in clinical research to lure more talented professionals into the field of research, thereby making it an emerging nucleus for collaborative Research and Development.
4. To encourage clinical research, the government has lifted import duties on clinical trial supplies and has granted permission for export of clinical trial specimens approved by the Drug Controller General of India (DCGI).^{12,16} Clinical trials have also been exempt from sales taxation. To avoid the general public from exploitation by pharmaceutical and similar industries, the Medical Council of India is the statutory body responsible for patient safety and disciplining investigator for violations; thus Investigator-initiated trials should be promoted in high-volume academic centres. One such initiative is the recent creation of National Cancer Grid, India formed in August 2012 comprising of more than 60 Regional Cancer Centers across the country to promote and safeguard the uniformity of “Patient care,” “Education and Training,” and “Collaborative research.”^{15,17} Other agencies such as Indian Council of Medical Research (ICMR), Department of Biotechnology and the Wellcome Trust and Department of Science and Technology have emerged as the major funding agency to support national and international trials.^{15,18}
5. By 2009, India had become one of the most preferred countries to conduct clinical trials and this resulted in several incidents of unethical practice and did not protect the safety of our vulnerable population.¹⁹ Though the ICMR has been in place since 1949, it was not till 2005 that strict measures were set in accordance to the principles of the Declaration of Helsinki 1964 (7th revision — 2013), the Indian Good Practice guidelines and the

International Conference on Harmonization, for conducting clinical trials to protect the safety of the participants; now its implementation is being looked after by the DCGI.^{12,20} For added authenticity, the Clinical Trials Registry India, a part of Primary Register of the International Clinical Trials Registry Platform makes it mandatory for all investigators to register prospectively their trials under the national registry and provide complete disclosure of the trial data set items.²¹ To encourage those interested in medical trials, organizations like Institute of Clinical Research India, the Academia of Clinical Excellence and the Bioinformatics Institute of India are offering education and courses related to clinical research, data management and patient safety.¹²

D. Conclusion

Indian population has unique cancers such as tobacco related head-neck cancers which are in higher number than in the west and provide an ideal opportunity for researchers to fill the void in the existing literature. Extrapolating western data to the Indian population may not be applicable at all times. There should be a uniform and widespread dissemination of high-quality cancer care through the collaborative initiative. There should also be an evidence-based practice grounded on meaningful clinical research relevant to Indian population and directed towards their problems. And to have more effective, affordable, and easily accessible medical treatment for cancer, more RCTs are necessary in India.

Recognising this need, clinical trials in oncology have been on the rise. Trials in this area have more than tripled over the last 10 years in India.



In addition, the cost of conducting a clinical trial in India is one-third of that in Australia and one-fifth of that in the US.

E. References

1. Cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990 to 2016: a systematic analysis for the Global Burden of Disease study. *JAMA Oncol* 2018; published online June 2. DOI:10.1001/jamaoncol.2018.2706.
2. Chalkidou K, Marquez P, Dhillon PK, et al. Evidence-informed frameworks for cost-effective cancer care and prevention in low, middle, and high-income countries. *Lancet Oncol* 2014; 15: e119–31.
3. Sivaram S, Majumdar G, Perin D, et al. Population-based cancer screening programmes in low-income and middle-income countries: regional consultation of the International Cancer Screening Network in India. *Lancet Oncol* 2018; 19: e113–22.
4. India State-Level Disease Burden Initiative Collaborators. Nations within a nation: variations in epidemiological transition across the states of India, 1990–2016 in the Global Burden of Disease Study. *Lancet* 2017; 390: 2437–60.
5. United Nations. Sustainable Development Goals.
6. <http://www.un.org/sustainabledevelopment/health/> (accessed March 11, 2018).
7. Indian Council of Medical Research. Three-year report of population-based cancer registries 2012–2014: incidence, distribution, trends in incidence rates and projections of burden of cancer. Bengaluru: National Centre for Disease Informatics and Research, ICMR, 2016.
8. Indian Council of Medical Research. National cancer registry programme: population-based cancer registries. <http://www.pbcrcindia.org/> (accessed March 11, 2018).
9. Indian Council of Medical Research, Public Health Foundation of India, Institute for Health Metrics and Evaluation. India: Health of the Nation's States—The Indian State-Level Disease Burden Initiative. New Delhi: ICMR, PHFI and IHME, 2017.
10. *Lancet Global Health* 2018; published online Sept 12. [http://dx.doi.org/10.1016/S2214-109X\(18\)30387-5](http://dx.doi.org/10.1016/S2214-109X(18)30387-5), [http://dx.doi.org/10.1016/S2214-109X\(18\)30407-8](http://dx.doi.org/10.1016/S2214-109X(18)30407-8), and [http://dx.doi.org/10.1016/S2214-09X\(18\)30409-1](http://dx.doi.org/10.1016/S2214-09X(18)30409-1)
11. *History of the Growing Burden of Cancer in India: From Antiquity to the 21st Century* Robert D. Smith¹ and Mohandas K. Mallath, MD, DNB² ascopubs.org/journal/jgo on August 2, 2019; DOI
12. Gupta YK, Padhy BM. India's growing participation in global clinical trials. *Trends Pharmacol Sci.* 2011;32:327–9.
13. Maiti R., *MR Clinical trials in India.* *Pharmacol Res.* 2007;56:1–10. Epub 2007 Feb 20.
14. Sariola S, Ravindran D, Kumar A, Jeffery R. Big-pharmaceuticalisation: Clinical trials and contract research organisations in India. *Soc Sci Med.* 2015;131:239–46.
15. Prinja S, Bahuguna P, Pinto AD, Sharma A, Bharaj G, Kumar V, et al. The cost of universal health care in India: A model based estimate. *PLoS One.* 2012;7:e30362.
16. Burt T, Gupta YK, Mehta N, Swamy N, Vishwas, Speers MA. Ethics standards (HRPP) and public partnership (PARTAKE) to address clinical research concerns in India: Moving toward ethical, responsible, culturally sensitive, and community-engaging clinical research. *J Clin Res Bioeth.* 2014;5:195.
17. Nundy S, Gulhati CM. A new colonialism? – Conducting clinical trials in India. *N Engl J Med.* 2005;352:1633–6.
18. Pramesh CS, Badwe RA, Sinha RK. The national cancer grid of India. *Indian J Med Paediatr Oncol.* 2014;35:226–7.
19. Dandona L, Katoch VM, Dandona R. Research to achieve health care for all in India. *Lancet.* 2011;377:1055–7.
20. Selvarajan S, George M, Kumar SS, Dkhar SA. Clinical trials in India: Where do we stand globally? *Perspect Clin Res.* 2013;4:160–4.
21. Imran M, Najmi AK, Rashid MF, Tabrez S, Shah MA. Clinical research regulation in India-history, development, initiatives, challenges and controversies: Still long way to go. *J Pharm Bioallied Sci.* 2013;5:2–9.
22. Sil A, Das NK. How to register a clinical trial in India? *Indian J Dermatol.* 2013;58:235–6.

F. Abbreviations

1. MI=mortality-incidence. *MI ratio is calculated by dividing crude death rate per 100 000 by the crude incidence rate per 100 000
2. DALYs=disability-adjusted life-years
3. ETL=epidemiological transition level
4. (UIs) = uncertainty intervals