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Mitigating Social and Economic Burdens: The Role of Genomic Diagnosis and Sequencing in Enhancing Cancer Management in India

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ABSTRACT

Cancer misdiagnosis and mistreatment in India present significant challenges, not only for patients and their families but also for society and the economy as a whole. These issues lead to substantial negative externalities, including a deadweight loss caused by the misallocation of vital healthcare resources. However, advancements in genomic diagnosis and sequencing offer promising potential for improving the accuracy of cancer detection and treatment. This paper explores the field of genomic medicine and evaluates its effectiveness in India, with a focus on how advancements in the country's biotechnology industry can help reduce the socio-economic costs currently borne by the nation.

Key Words: *Genomic Medicine, Genomic Diagnosis, Genomic Sequencing, Cancer, India, Socio-economic Costs, Externalities, Biotechnology*

INTRODUCTION

Genomic medicine is a branch of medicine that involves using a person's genomic information in clinical care (NHGRI, 2019). This field is being increasingly researched, particularly concerning its applications for detecting, diagnosing, and treating diseases and conditions such as Cancer, Congenital Disorders, Endocrine Disorders, and rare genetic disorders. Genomic-based diagnosis, specifically, has the potential to direct therapeutic interventions, predict risk or onset of disease, or detect residual disease (Institute of Medicine (US), 2012). Many techniques may be utilized as part of genomic diagnosis. Genomic sequencing, for instance, is a strong first-line test for diagnosing rare diseases due to its ability to provide an in-depth genetic analysis.

In countries like India, the incorrect detection, diagnosis, and treatment of genetic diseases, such as cancer, are very common. This can directly create economic challenges for the patients in the form of higher and unnecessary treatment costs due to advanced disease progression. However, it can also generate broader economic and societal costs resulting from the inefficient allocation of resources, reduced productivity of the individuals, and the burden on the healthcare systems. Therefore, the application and potential of genomic diagnosis and genomic sequencing in India to overcome these challenges are of key interest. Moreover, the growth of the biotechnology industry in the country is also promising for furthering the development of this application of genomic medicine. In light of the above considerations, this research paper aims to answer the following question; “To what extent can the implementation of genomic diagnosis and genomic sequencing in India mitigate the social and economic costs

associated with the incorrect detection, diagnosis, and treatment of genetic diseases such as cancer?"

This paper argues that genomic medicine, specifically genomic diagnosis enhanced by genomic sequencing, holds great potential to overcome the current socio-economic costs incurred by India regarding the incorrect detection and treatment of cancers.

Exploration of Genomes and Genomic Sequencing

DNA, or deoxyribonucleic acid, is the hereditary material in humans and almost all other organisms found mostly in the nucleus of genes (Genetic Alliance, 2009). A gene is a segment of DNA that codes for a specific protein and allows cells to function, while a genome, pictured in *Figure 1*, is the entirety of the genetic material inside an organism.

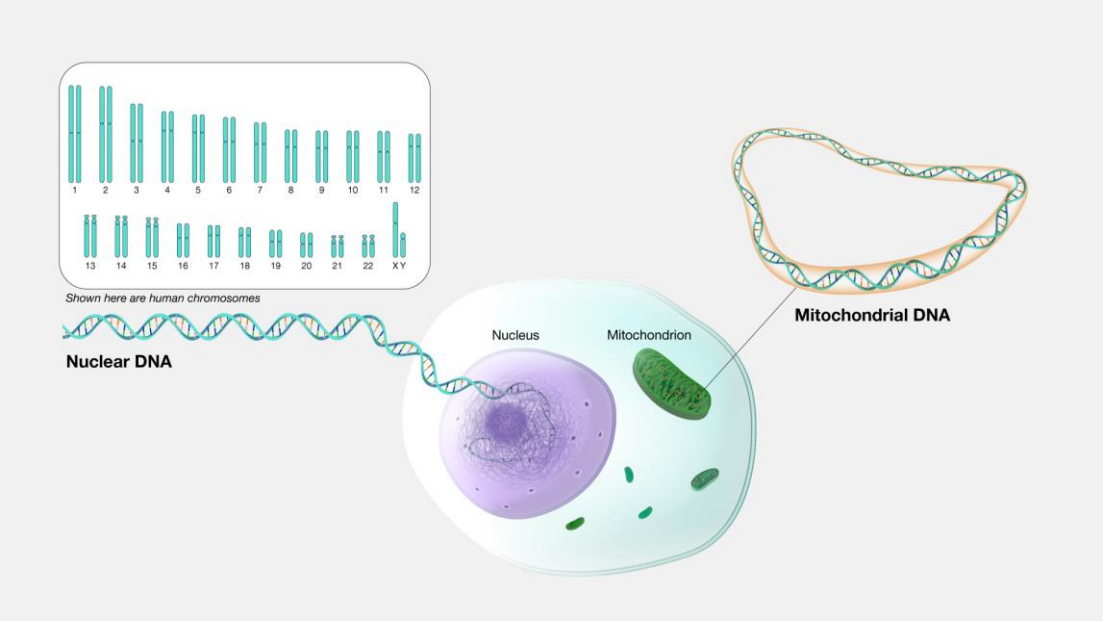

Figure 1 - Yadav, 2020

The human genome consists of 20,000 and 25,000 genes, most of which are the same from person to person. Still, variations may occur due to changes in the sequences of genes in DNA, which can influence someone's health, appearance, and risk of developing certain diseases (Barrell, 2023). In the case of humans, about 2 percent of the genomic DNA sequence varies among individuals.

The Human Genome Project, operated from 1990 to 2003, was a landmark global scientific effort whose signature goal was to generate the first sequence of the human genome (NHGRI, 2022). It provided researchers with basic information about the sequences of the three billion chemical base pairs (i.e., adenine [A], thymine [T], guanine [G], and cytosine [C]) that make up the human DNA (deoxyribonucleic acid) (MedlinePlus, 2021) and covered about 92% of the total human genome sequence because the technologies to decipher the gaps that remained didn't exist at the time. However, scientists knew the last 8% likely contained information important for fundamental biological processes. Hence, the project was further intended to improve the technologies needed to interpret and analyse genomic sequences - to identify all the genes encoded in human DNA and to address the ethical, legal, and social implications that might arise from defining the entire human genomic sequence (NIH, 2022).

In the years since the completion of the HGP, the human genome database, together with

other publicly available resources, has enabled the identification of various genes associated with diseases. Sequencing the eukaryotic genome is difficult due to its large size and number of repetitive sequences. However, due to the improvements and advancements in DNA sequencing technology that followed the HGP, genome sequencing has been made possible even for very large genomes like the human genome (Saraswathy & Ramalingam, 2011). Genomic sequencing is a laboratory method that refers to sequencing the entire genome of an organism instead of sequencing it gene by gene, making it more time efficient and accurate, allowing for more objective and accurate diagnoses for both rare and common diseases, in some cases even before the onset of overt clinical symptoms (NCI, 2011; Fridovich-Keil, 2019). The recognition that human genomes may influence everything from disease risk to physiological response to medications has led to better diagnosis of diseases and disorders, as well as the emergence of the concept of personalized medicine.

The application of Whole genomic sequencing (WGS) to gain a more complete understanding of cancer has been a prime goal of researchers even before 2003 (Lander et al. 2001). However, in line with the advancements highlighted above, post-2003, since 2005, specifically, there have been many large-scale efforts to use genome sequencing to characterize a wide variety of adult and pediatric cancers (Zhao et al., 2018). These efforts included projects such as The Cancer Genome Atlas (TCGA), the International Cancer Genome Consortium (ICGC), and the Catalog of Somatic Mutations in Cancer (COSMIC), among others. The efforts of these projects have progressed our understanding of cancer as a genomic disease and provided data that has proven helpful in the development of tools and resources required to facilitate detection (NCI, 2022). Overall, WGS has been able to offer a base-by-base view of unique mutations present in cancer tissues, enabling the discovery of novel cancer-associated variants, including single nucleotide variants (SNVs), copy number changes, insertions/deletions (indels), and structural variants (NIH, 2022). WGS also provides a comprehensive view of genomic changes in cancer DNA samples compared to normal DNA.

One of the most prominent examples of WGS making cancer detection, diagnosis, and treatment more accurate is the research conducted and findings reported by the Memorial Sloan Kettering Cancer Center (MSK). In 2014, MSK created a test called MSK-IMPACT™ - a comprehensive genetic sequencing tool that analyses over 400 cancer-related genes (Grisham, 2017). This test is designed to identify mutations and other genetic alterations in these genes, which can provide valuable information for diagnosing and treating various types of cancer. The derived information can help doctors determine if an available drug will benefit a patient based on their tumour's genetic profile. Moreover, MSK also realised that the cancer gene panel approach (applied in the test discussed previously) works well with common cancer types such as breast, colorectal, lung, and prostate. However, it is not as useful for matching patients to appropriate therapies for rare cancers in children and young adults. As a result, the center conducted further research using a comprehensive sequencing approach on 114 pediatric, adolescent, and young adult patients. In 2022, MSK successfully reported that their approach identified at least one additional cancer-associated oncogenic variant in 54% of patients (62 out of 114), compared with the current standard genetic sequencing test MSK-IMPACT™. Of these, 33 patients had one or more findings of direct clinical or potentially actionable relevance – evidence of the potential that further research and investment in genomic sequencing can have for solving

cancer among global populations (MSK, 2022).

The Landscape of Cancer in India

The graph below presents information regarding the 2022 age-standardized incidence rate (ASIR) by five-year age group and gender for India.

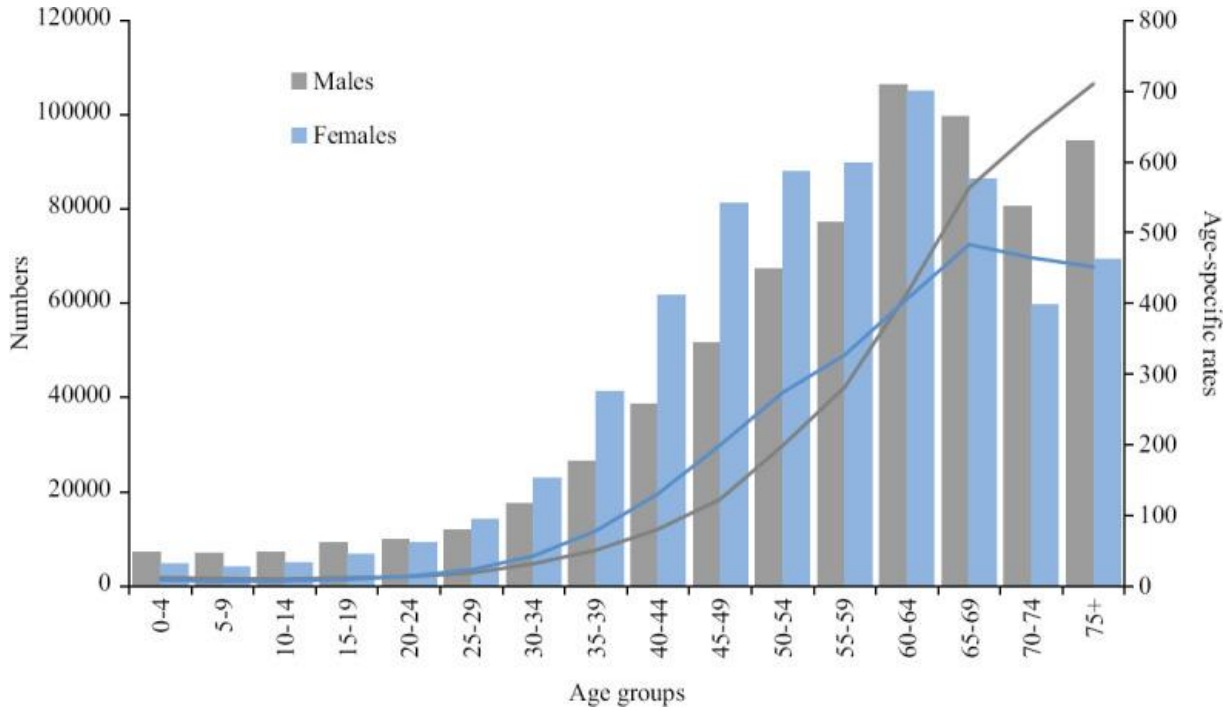

Figure 2 - Sathishkumar et al., 2022

India reports more than a million new cancer cases every year. While this rate has still not surpassed those of some developed countries - for instance, India reports 100 cases for every 100,000 people while the US reports 300 (WCRF, 2022) - experts expect this trend to change due to what is being termed an "epidemiological transition" (Yadavar, 2023). According to a report published, chronic conditions like cancer are now so prevalent that they have reached "critical levels." Cancer cases in the country are expected to rise at a rate surpassing global averages - from 1.39 million in 2020 to 1.57 million by 2025 (Rajvanshi, 2024). Moreover, India also bucks the global trend of men generally reporting a 25% higher incidence of cancer than women. Instead, according to a study published in the Lancet Oncology, women in India have a higher diagnosis percentage (Dhillon et al., 2018). Another critical demographic aspect of cancer in India is the lower median age of those being impacted by cancer than in the US, UK, and China. For example, while the median age for lung cancer is 70 in the US, 68 in China, and 75 in the UK, in India it is 59 (Rajvanshi, 2024).

The biggest concern with these rising cases is that many shortcomings in the diagnosis and treatment of cancer have been identified in India. There have been repeated reports of misdiagnosis of cancer among patients across the country. In 2019, in Kerala, for instance, a 38-year-old woman had to undergo chemotherapy at Government Medical College Hospital, Kottayam, after being wrongly diagnosed with breast cancer (The Hindu, 2019). Moreover, in 2023, a Kannada film actor was wrongly diagnosed with end-stage cancer by a Bengaluru diagnostic center,

driving her into severe mental agony and depression (Peter, 2023). A study by Singh et al. (2009) also found that in the Indian context, misdiagnosis of lung cancer as pulmonary tuberculosis is widespread, which leads to delayed diagnosis. Other than incorrect or delayed detection and diagnosis, mistreatment of cancer is also common in the country. For instance, a study by Onco.com, reports that over 15% of cancer patients in India were getting completely wrong treatment, 7% were given incorrect chemotherapy drugs, and 41% did not undergo complete tests (BioSpectrum, 2019).

This misdiagnosis and consequent mistreatment can create many costs for both the patient and their family, as well as the economy and society, which can be better understood through the concept of negative externalities. These externalities represent the unintended costs imposed on society beyond the private costs that the individual patients incur. For instance, while the patient will have to bear the private costs of the medical expenses of misdiagnosed treatments, including surgeries, hospital visits and stays, and medications, the social costs are significant and present themselves in the form of: a strain on the health care system due to repeated visits and treatments, reducing the availability for other patients the higher healthcare costs at a national level, diverting resources from other vital areas a decrease in workforce productivity due to a large number of people being out of the workforce or unproductive due to prolonged incorrect treatment increase in mental health issues among the patients and their families due to the stress, anxiety and uncertainty created by the financial and psychological impact of the misdiagnosis and mistreatment

The above explains why the private cost of healthcare may be significant in light of misdiagnosis and mistreatment. Still, the social costs surpass the same and create something known as a deadweight loss i.e. the loss of economic efficiency due to the misdiagnosis and mistreatment leading to over-provision of incorrect healthcare services.

The above can also be represented in a graph as seen in *Figure 3.* Due to the misdiagnosis and mistreatment, the marginal social costs (MSC) are higher than the marginal private costs (MPC). The market equilibrium (Q1) occurs where the demand (D) intersects the MPC, leading to overconsumption of healthcare services.

The optimal level of healthcare (Q*) would be lower if the external costs were considered. The deadweight loss illustrates the inefficiency and societal burden due to the external costs of misdiagnosis and mistreatment in the healthcare system.

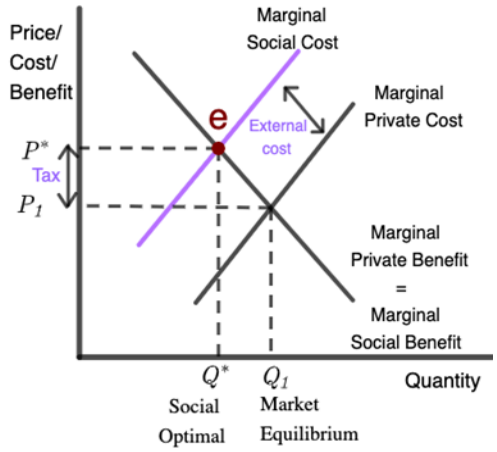

Figure 3

Implications and Potential of Genomic Sequencing for Cancer Diagnosis, Detection, and Treatment in India

Biotechnology is concerned with harnessing cellular and biomolecular processes to develop technologies and products that help improve our lives and the health of our planet (BIO, 2024). DNA sequencing is the foundation for all modern biotechnology, and developments in this technology facilitate genomics advances. Therefore, any advances in the country's biotechnology industry will hold promising results for genomic medicine's application.

India's bio-economy industry has grown from US$ 10 billion in 2015 to US$ 130 billion in 2024 and is expected to reach US$ 300 billion by 2030 (IBEF, 2024). The number of biotech startups has gone from a meagre 52 in 2014 to 5300 plus in 2022 (Desai, 2023). Furthermore, according to Invest India (2020), India is Asia's third-largest destination for biotechnology and one of the top 12 destinations worldwide. India's rise as a go-to destination for bio innovation and biomanufacturing is a highly anticipated and sought-after outcome, with biotechnology emerging as a sunrise sector in the country (Desai, 2023). The Indian biotechnology industry mainly develops domestic talent and demonstrates value-based care. The government has successfully initiated growth in this industry through various flagship programs such as 'Make in India' and 'Startup India' (IBEF, 2024). Overall, the biotechnology sector, mainly due to its multidisciplinary approach, holds the potential to provide an array of solutions for challenges in various sectors such as health, agriculture, environment, energy, and industrial processes. Specifically, however, the advances in biotechnology have and may be expected to continue enabling progress in developing and applying genomic diagnosis and sequencing.

On 3rd January 2020, for instance, a genome sequencing and analysing project was initiated by DBT and led by the Centre for Brain Research at the Indian Institute of Science, Bengaluru, in hopes of helping in understanding the nature of different diseases in the Indian population and developing predictive diagnostic markers (Bajaj, 2020). India's population of 1.4 billion comprises over 4,600 population groups, many of which are endogamous (intermarried), leading to genetic diversity and disease-causing mutations (Dutt, 2024). An India-specific genetic database is crucial because it will pave the way for more targeted and effective healthcare solutions for genetic mutations like cancer.

The strides India is expected to make in the biotechnology sector and their progress with the Genomic Project - detailed above - will enable the sequencing of genomes and greater integration into the country's healthcare industry. The larger scale production of these genomic sequences will be critical for developing India's specific cancer genome database, and this database will be useful in developing cancer-specific biomarkers for early detection and personalized treatment of patients (PTI, 2023). WHO has stated that a true definition of biomarkers includes "almost any measurement reflecting an interaction between a biological system and a potential hazard, which may be chemical, physical, or biological. The measured response may be functional and physiological, biochemical at the cellular level, or a molecular interaction" (Slikker, 2017). Biomarkers identified will be critical for developing Real-time quantitative PCR (RT-qPCR) and sequencing-based early diagnostic kits (PTI, 2023). Furthermore, identified drug targets can be used to develop novel anti-cancer therapeutics for pancreatic cancer and pediatric leukaemia. As stated by principal investigator S Mahalingam, Department of Biotechnology, IIT Madras, "The preclinical cancer models will be of immense help for drug screening and understanding the in-vivo cancer pathogenesis.

The successful development of an organoid will facilitate high-throughput cancer drug screening. A similar approach will be extended to other cancers prevalent in India, which will help initiate a start-up company on cancer therapeutics and diagnostics" (PTI, 2023).

The above will be of great value as it can significantly reduce the socio-economic costs currently associated with incorrect diagnosis and/or treatment. It will enable not only more affordable medication but also increase the accuracy of detection.

CONCLUSION

India witnesses a large number of cancer cases every year. This number will only grow in the future, putting the country at risk of what has been identified as an epidemiological transition. The most significant danger of this is that because India, unfortunately, witnesses a significant level of cancer misdetection, misdiagnosis and mistreatment, the aforementioned can create several socio-economic costs both for the patients and also for the wider economy and society. This paper aimed to evaluate to what extent genomic sequence, as a technique of genomic diagnosis, can help overcome these socio-economic costs by making cancer detection diagnosis and treatment more accurate in the country.

As analysed in the paper, cancer is a genetic disease, and the high levels of interbreeding in the Indian community can lead to significant levels of genetic mutations giving way to a large number of cancer cases. Reports of individuals across the country being misdiagnosed and mistreated for cancer are a pressing issue. From an economic perspective, the patients have to bear significant costs. The costs to the economy and society come in the form of decreased productivity of the misdiagnosed patients, increasing the burdens on the healthcare systems and opportunity costs, generating negative externalities i.e. wherein the social costs surpass the private costs. This represents a deadweight loss to society due to the misallocation of resources and must ideally be amended.

Fortunately, with the Indian biotechnology industry experiencing rampant growth and the increasing research into genomes in India, the country's healthcare industry can expect to benefit greatly from the application of genomic diagnosis and genomic sequencing to make the detection, diagnosis, and treatment of cancer more accurate. This can be facilitated by developing cancer-specific biomarkers, which can then be used to develop technologies such as sequencing-based early diagnostic kits. In line with this, the implementation of genomic diagnosis and genomic sequencing can mitigate the social and economic costs associated with the incorrect detection, diagnosis, and treatment of genetic diseases such as cancer in India to a great extent.

To facilitate the above, however, it is essential for investments in health infrastructure, promoting preventive healthcare measures, and addressing health inequities to be prioritized by the government and the respective ministries. Continuing research and advances can also lower sequencing costs, which may be vital considering the economic context of India.

Declaration by Authors

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