

ABSTRACT

Keywords: National Institutes of Health, National Cancer Institute, cancer drug development, technology transfer, collaboration, cancer death rate improvement.

The National Institutes of Health (NIH) has been an engine to transform and move innovative life science ideas to bedside solutions for public health since its establishment in 1887. Led by the National Cancer Institute (NCI), NIH’s role in cancer therapeutic development and its largely unseen technology transfer contributions are explored here in three major cancer types: breast, lung, and prostate cancer. The evaluation of publicly available data shows that the NIH, particularly with the activities of NCI, has strongly supported cancer research and has substantially improved public health, saving lives since the 1960s.

INTRODUCTION

Growing, nurturing, and transforming a scientific idea into a medical treatment that saves lives requires an excellent scientific environment consisting of scientific expertise, research tools, and funding—all using the synergy of collaboration around a scientific platform. Therefore, the best metaphor to describe the role of the National Institutes of Health (NIH) in the life sciences should be the seed and mother nature relationship. If we imagine a scientific idea as a seed that needs a nurturing and supportive environment as soil, funding as water, technical expertise to provide the care, and when the care needs further development, bringing advanced resources as a team. All these elements are like growing a seed with the right soil, water, and the right amount of light and care.

The NIH is the world’s largest institution supporting life science innovations to find cures for unmet medical needs. To achieve its mission, NIH provides research funding, scientific expertise, and training for researchers and, importantly, creates a bridge for academia and industry collaboration via cooperative research and collaboration agreements, clinical trials, and technology licensing partnerships. In this study, various databases were used to identify the role of NIH in developing cancer therapeutics and the reflection of this effort on public health.

METHODS

A. Databases : We used multiple databases and resources listed below to understand the current and potential future role of the National Cancer Institute (NCI) and NIH in supporting medical science and cancer therapeutics development.

1. **Citeline’s Phmaprojects** (<https://clinicalintelligence.citeline.com/>) to identify cancer drugs that are developed all around the world.
2. **Clinicaltrial.gov** (<https://clinicaltrials.gov/>) to search NIH supported clinical trials in cancer drug development.
3. **SEER Explorer** (<https://seer.cancer.gov/statistics-network/explorer/>) to search death rates for for breast cancer, prostate cancer and lung cancer.
4. **National Cancer Institute Funding** (<https://www.cancer.gov/about-nci/budget/fact-book/data/research-funding>) to search data regarding the NCI’s funding for various research areas are collected from this website.
5. **NIH Technology Transfer** (<https://www.techtransfer.nih.gov/reports/top-20-commercially-successful-inventions>) to search NIH’s commercially successful inventions.
6. **NIH Intramural Database (NIDB)** (<https://intramural.nih.gov/search/index.taf>) to search outcomes of the NIH Intramural research activities in cancer research.

B. Statistical Method: The Spearman's Rho correlation is a non-parametric test used to examine the relationship between NCI’s funding for cancer research and death rate.

Spearman's Rho Rank Correlation Equation:

$$r = 1 - 6 \sum D^2 / (N^3 - N)$$

r: Spearman's rank correlation coefficient
D: difference between the two ranks of each observation
N: number of observations

RESULTS

1. U.S. Leads in Drug Invention

The average required time for cancer drug development is approximately 10 years [1], and the estimated cost of research and development of launching a cancer drug is between \$765 million and \$4.6 billion [2]. The cost and duration of drug development depend on the disease to be cured. There is a considerable gap in the cost of research and development for therapeutic drugs, depending on the indication for treatment and the type of treatment. In the challenging drug development process, United States leads cancer drug development as an originator as well as a licensee **Figure 1. (A-B)**.

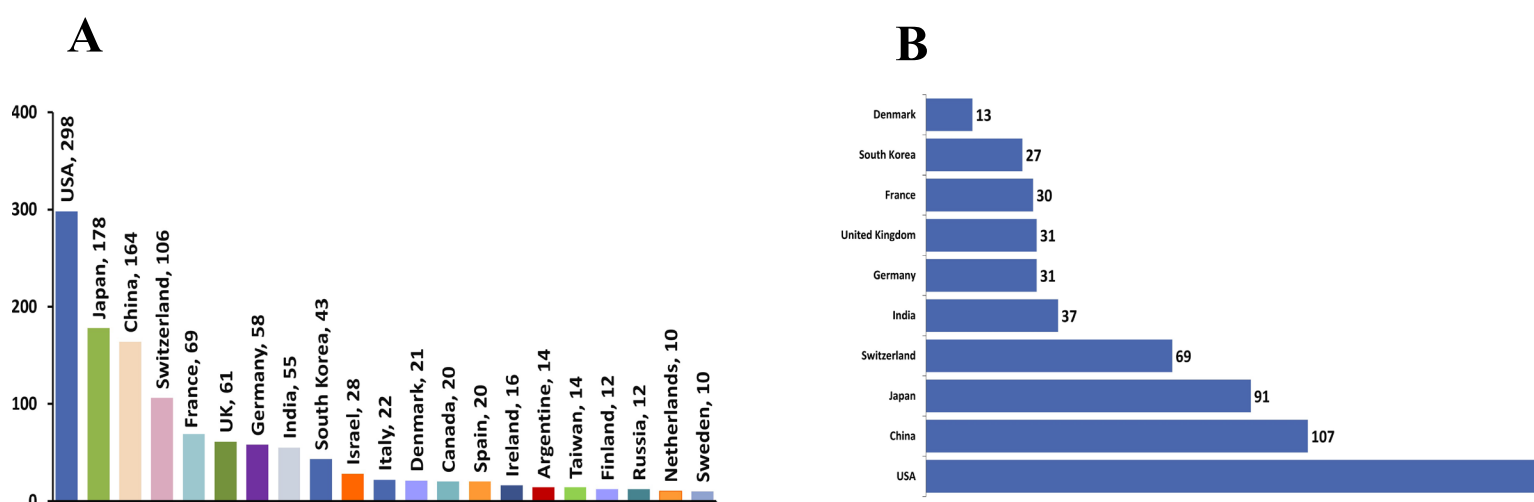


Figure 1. (A) Top 21 countries launching cancer diagnostic and therapeutic drugs **(B)** Top 10 countries originating cancer diagnostic and therapeutic drugs

RESULTS

2. The Role of NIH in Cancer Therapeutics Development

NIH’s effort to treat and cure cancer was initiated in the early 1950s. In 1958, NCI researchers and collaborators worked on the combination chemotherapy with the drugs 6-mercaptopurine and methotrexate for acute leukemia. They showed partial and complete remissions and prolonged survival in children and adults [3]. In 1993, the PanCancer Atlas was completed by the NCHGR’s successor, the National Human Genome Research Institute (NHGRI) and NCI, both part of NIH. The PanCancer Atlas has detailed clinical information on 10,000 tumors from 33 cancer types. This phenomenal accomplishment allows scientists to understand human tumor initiation better, leading to better clinical trial designs and improved future cancer treatment [4].

2.1 NIH’s Role in Breast Cancer Therapeutic Development

NCI has a tremendous amount of effort to find cure for breast cancer and has developed many milestones for breast cancer therapy. NCI contributed to the breast cancer therapeutics in different ways, including the development of the modified radical mastectomy, the discovery of oncogenes, the development of targeted therapies, and improvement in the current therapeutic methods. NIH-supported breast cancer research helped to reduce breast cancer-caused deaths by 42 percent between 1990 and 2019 [5]. We analyzed the correlation between NCI’s funding for breast cancer and the breast cancer death rate with Spearman correlation. The calculated Spearman’s Rho ((Rs) = -0.48166, p (2-tailed) < 0.01) shows a substantial negative correlation between NCI breast cancer research funding and breast cancer death rate, which means that an increase in NCI’s funding support for breast cancer research is connected to a decrease in the death rate of breast cancer patients **Figure 2. (A-B)**. 130 breast cancer drugs were launched worldwide, and 29 of them were launched by the United States either as an originator or licensee **Figure 2. (C)**.

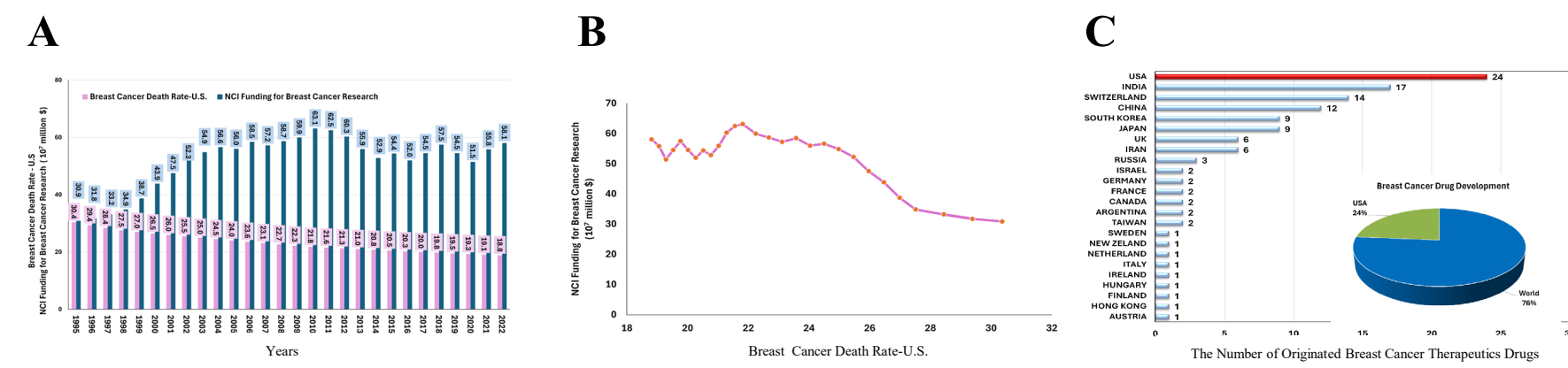


Figure 2. (A-B) NCI’s funding for breast cancer research and breast cancer death rate.(Death Rate refers to “Deaths per 100,000 population (age adjusted)”) (C) Breast cancer drugs development all around the world by licensing or originating

2.2 NIH’s Role in Lung Cancer Therapeutic Development

The NIH has impacted lung cancer research through NIH funding for research and cancer prevention activities. NCI lung cancer research funding and lung cancer death rate was examined via the calculated Spearman’s Rho ((Rs) = -0.91, and p (2-tailed) <0.001). The statistical analysis shows a substantial negative correlation between in the US. these two variables. We might interpret as that an increase in NCI’s funding support for lung cancer research is connected to a decrease death rate of lung cancer patients **(Figure 3.(A-B))**. 137 lung cancer therapeutic drugs were originated, and 33 of them, equivalent to 24.1 percent of lung cancer drugs, were originated by China, followed by the US, with 31 drugs (22.6 percent) and then 13 drugs (9.5 percent) originating in Japan **Figure 3. (C)**.

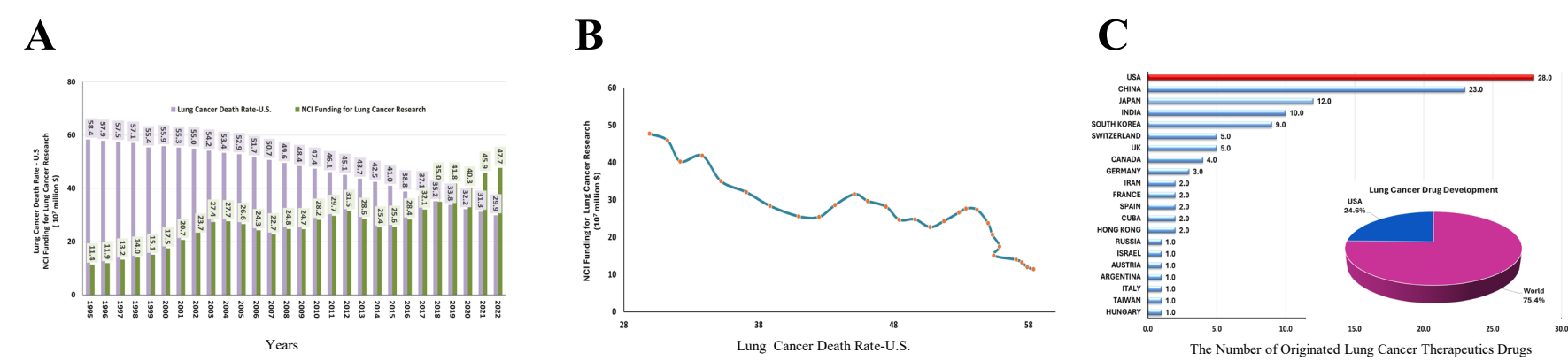


Figure 3. (A-B) NCI’s funding for lung cancer research and lung cancer death rate.(Death Rate refers to “Deaths per 100,000 population (age adjusted)”) (C) Lung cancer drugs development all around the world by licensing or originating.

2.3 NIH’s Role in Developing Therapies for Prostate Cancer

NIH’s involvement in the prostate cancer research field has brought new ideas to the light, with practical applications to the bedside for the unmet medical needs of patients. In 1996, NCHGR in collaboration with other researchers identified the location of the first major gene that provides the first evidence of specific genes for prostate cancer [6]. We analyzed the non-linear data for the NCI funding for prostate cancer research and prostate cancer death rate with Spearman correlation. Results of the Spearman correlation indicated that there is no significant relationship between NCI funding for prostate cancer research and prostate cancer death rate in the United States **Figure 4. (A-B)**. 21 out of 50 prostate cancer drugs launched in the United States as originators or licensees. This means that companies in the United States launched 42 percent of prostate cancer therapeutic drugs. **Figure 4.(C)**.

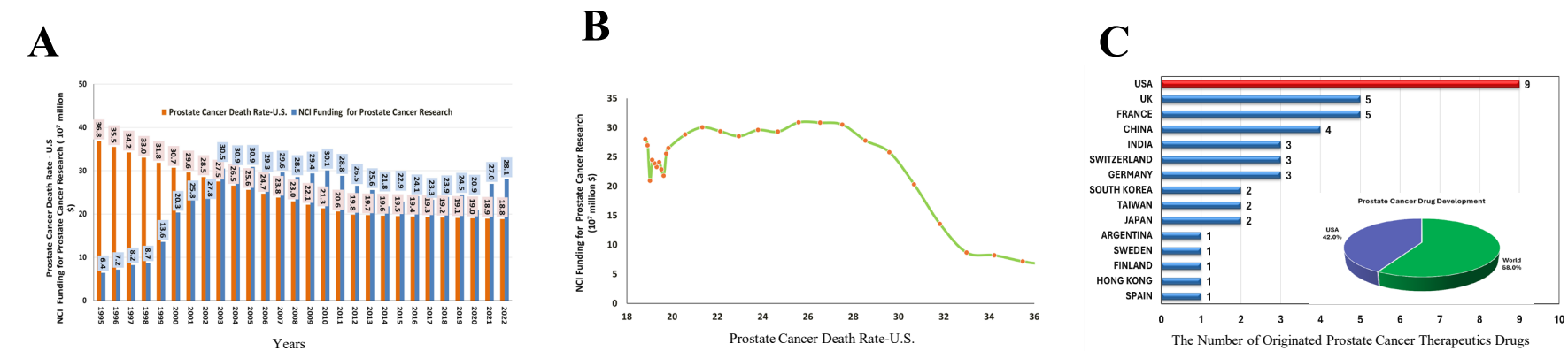


Figure 4. (A-B) NCI’s funding for prostate cancer research and prostate cancer death rate.(Death Rate refers to “Deaths per 100,000 population (age adjusted)”) (C) Prostate cancer drugs development all around the world by licensing or originating.

RESULTS

3. The Role of NCI in Cancer Therapeutic Development

NCI has been supporting cancer therapeutic development for 88 years. The NCI was initiated as one of the institutes at the NIH with the National Cancer Institute Act, Public Law 244 to conduct, assist, and foster research, investigations, experiments, and studies relating to the cause, prevention, and methods of diagnosis and treatment of cancer [7].

- ❖ NCI’s Division of Cancer Treatment and Diagnosis (DCTD) has numerous activities focused on the development of novel diagnostics and therapies for cancer, with a primary goal of reducing the time required to bring the most effective cancer therapeutic drugs and biomarkers to bedside treatment.
- ❖ NCI’s CTEP plans reviews and coordinates clinical trials for investigational cancer therapeutic drugs from the early stage of protocol development through the preparation and submission of Investigational New Drug Applications (INDs) to the US Food and Drug Administration (FDA). NCI’s CTEP also serves as a liaison to the FDA for the extramural clinical research community and industry collaborators. Furthermore, NCI’s CTEP also manages tracks, and reviews clinical protocols, as well as regulatory compliance for clinical trials [8]
- ❖ The NCI has played a pioneering role in precision medicine, launching the NCI-MATCH (Molecular Analysis for Therapy Choice) study. This study recruited over 6,000 patients within less than 2 years [9].
- ❖ We analyzed correlation between the cancer-caused death rate correlates and NCI funding by using Spearman analysis. The statistical analysis outcomes ((Rs) = -0.76, and p (2-tailed) < 0.001) show that the association between NCI’s funding for cancer research and cancer-related death rate might be considered substantially important **Figure 5. (A-B)**.
- ❖ There are currently 42,802 completed cancer clinical trials worldwide. In this enormous amount of work and effort in clinical studies, NIH alone supported 7,525 cancer clinical trials, 17.6 percent of the whole clinical trial effort

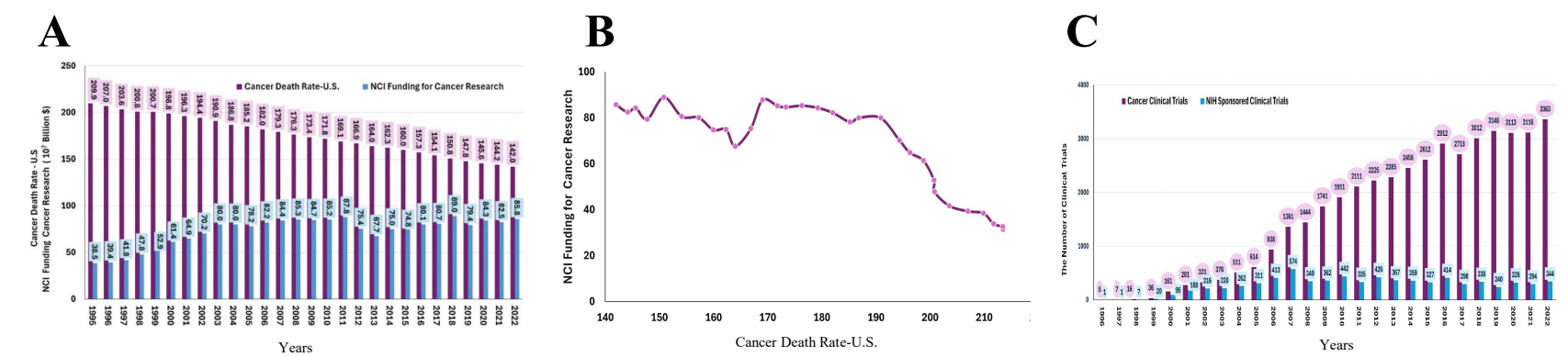


Figure 5. (A-B) Cancer death rate and NCI’s funding for cancer research.(Death Rate refers to “Deaths per 100,000 population (age adjusted)”) C. NIH’s support in cancer clinical trials

4. Summary of NIH’s dedication to prevent and cure cancer disease

- ❑ New research and development approaches via NIH’s Intramural Research Program as seen in **Figure 6**.
- ❑ Licensing new technologies from NIH research for commercial development and public benefit.
- ❑ Cultivating collaboration with universities, research institutes and companies.
- ❑ Supporting cancer research with funding.
- ❑ Providing expertise for the research community.
- ❑ Making research materials available for the research institutes and universities
- ❑ Putting effort to repurposing of commercially available therapeutics for the new indications.
- ❑ Establishing synergy within the research community with an effort to shorten drug development process
- ❑ Training future doctors, nurses, scientists.
- ❑ Taking initiative steps to share data with research community to be used in secondary research purposes.
- ❑ Having a mission to create public health awareness to prevent cancer via health information initiatives.

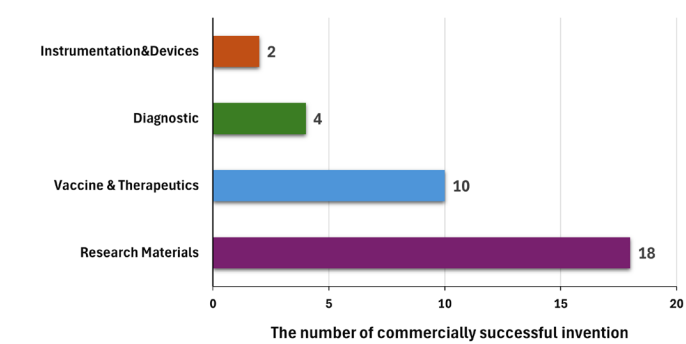


Figure 6. Commercially successful inventions developed by the NIH’s intramural research (Data originated from NIH Technology Transfer website, <https://www.techtransfer.nih.gov/reports/top-20-commercially-successful-inventions>)

5. Conclusion

Cancer drug development requires a tremendous amount of time, funding, and excellent expertise. In **Figure 7**, all the elements NIH has been using for cancer drug development are illustrated. These elements can be brought together and made to perform most efficiently only through well-established collaborations guided by the technology transfer function. Since “it takes a village” to launch a cancer therapeutic drug, NIH has been the most important part of this village in transforming discoveries into for practical application to the bedside for patient’s health.



Figure 7: Summarized elements of cancer drug development

6. References

1. Uygur, B., J. Duberman, and S.M. Ferguson, *A guide to time lag and time lag shortening strategies in oncology-based drug development. Journal of commercial biotechnology*, 2017, 23: p. 75.
2. Henderson, R.H., et al., *Delivering the precision oncology paradigm: reduced R&D costs and greater return on investment through a companion diagnostic informed precision oncology medicines approach. Journal of Pharmaceutical Policy and Practice*, 2023, 16(1): p. 84.
3. FREI III, E., et al., *A comparative study of two regimens of combination chemotherapy in acute leukemia. Blood*, 1958, 13(12): p. 1126-1148.
4. *NIH completes in-depth genomic analysis of 33 cancer types.* https://www.cancer.gov/news-events/press-releases/stories/2023/03/23_genomics_33_cancers
5. NIH Health Information, <https://www.nih.gov/health-information>
6. National Human Genome Research Institute. <https://www.genome.gov/about-nihgr/Brief-History-Timeline>
7. NCI Funding for Research Areas, <https://www.cancer.gov/about-nci/budget/fact-book/data/research-funding>, 2024.
8. Ansher, S.S. and R. Scharf, *The Cancer Therapy Evaluation Program (CTEP) at the National Cancer Institute: industry collaborations in new agent development. Annals of the New York Academy of Sciences*, 2001, 949(1): p. 333-340.
9. Harris, L.N., et al., *The New NCI Precision Medicine Trials. Clinical Cancer Research*, 2023, 29(23): p. 4728-4732.