Recognizing NIH's Role in Turning Discoveries into Cancer Treatments

By

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ABSTRACT

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.

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

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.

In the 1960s, NIH changed the destiny of biomedical science with groundbreaking discoveries related to the genetic code of DNA translation into proteins via messenger RNA. This discovery has found its place in every field of science and revolutionized the research methodology for finding new medicines and treatments, paving the way for personalized medicine, also known as precision medicine, for various diseases, including cancer. Since then, nothing has remained the same in biomedical science, like a seed in the best soil, and it continues to grow.

1. Methods

1.1 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.

1.1.1 Citeline Pharmaprojects (https://clinicalintelligence.citeline.com/)

This database platform is produced by Citeline/Informa PLC and was used to identify cancer drugs that are developed all around the world.

1.1.2 ClinicalTrials.gov (https://clinicaltrials.gov/)

ClinicalTrials.gov is an online database of clinical research studies and information about their results. This database can be consulted to search for the reason for failed drug development.

1.1.3 SEER Explorer (https://seer.cancer.gov/statistics-network/explorer/)

SEER explorer is cancer statistics explorer network. The data regarding the cancer death rates for breast cancer, prostate cancer and lung cancer were found in this database.

1.1.4 NIH RePORTER

(**https://reporter.nih.gov/**)
This is an electronic tool that provides information regarding NIH-funded research projects, publications and patents resulting from NIH funding.

1.1.5 National Cancer Institute Funding

(**https://www.cancer.gov/about-nci/budget/fact-book/data/research-funding**)
Data regarding the NCI's funding for various research areas are collected from this website.

1.1.6 NIH Technology Transfer

(**https://www.techtransfer.nih.gov/reports/top-20-commercially-successful-inventions**)
Information regarding the National Institute of Health's commercially successful inventions were explored in National Institute of Health's technology transfer website.

1.1.7 NIH Intramural Database (NIDB)

(**https://intramural.nih.gov/search/index.taf)**
Information regarding the outcomes of the Intramural research activities in cancer research were explored in NIH's Intramural Database (NIDB).

1.2 Statistical Analysis

The Spearman's Rho Rank correlation is a non-parametric test used to identify the association between two variables, where the value r = 1 means a perfect positive correlation and the value r = -1 means a perfect negative correlation. We used this tool to examine the relationship between NCI's funding for cancer research and the cancer death rate.

The Spearman's Rho Rank correlation is the most common way of measuring a nonlinear correlation between two variables. All statistical tests were 2-sided, with $P < .05$ considered to be statistically meaningful.[1]

Spearman's Rho Rank Correlation Equation:

$$r = 1 - 6 \sum D2 / (N3\text{-}N)$$

r: Spearman's rank correlation coefficient

D: difference between the two ranks of each observation

N: number of observations

1 Spearman's Rho Calculator. https://www.socscistatistics.com/tests/spearman/default.aspx.

2. Results

2.1 Cancer Drug Development Landscape

The average required time for cancer drug development is approximately 10 years,[2] and the estimated cost of research and development of launching a cancer drug is between $765 million and $4.6 billion.[3] 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 (one-size-fits-all chemotherapy versus precision medicine). For instance, Dinutuximab for childhood neuroblastoma and Durvalumab for non-small cell lung, endometrial, and liver cancers are both immunotherapy drugs that serve as excellent examples for comparing cancer therapeutic drugs. While the research and development of Dinutuximab cost $276 million, the research and development of Durvalumab cost $13.4 billion. Even though both of these drugs are immunotherapy drugs, Dinutuximab is non-precision, in other words, traditional medicine, which is applied with a one-size-fits-all approach. On the other hand, Durvalumab is precision medicine, and using a companion diagnostic (CDx) for PD-L1 during the clinical trials caused higher cost in research and development of this drug.[4]

Cancer drug development is a lengthy process requiring tremendous investment, expertise, and well-established research and development tools. To gain a general perspective on the drug development landscape, cancer drugs launched in the Citeline Pharmaprojects database were examined. The number of cancer drugs launched worldwide was identified. In the Citeline Pharmaprojects database, we searched for cancer diagnostic and therapeutic drugs using the following filter settings: (Drug Disease contains 'cancer') AND (Most Advanced Current Status is 'Launched'). This search yielded 820 cancer diagnostic and therapeutic drugs for various indications, which were launched between 1975 and 2025. The Citeline Pharmaprojects database has two different terminologies: (1) 'Drug Country,' which refers to the country in which the drug was launched, and (2) 'Company HQ Country,' which refers to where the drug company is located. To identify the country that launched the particular drug, we examined the company's HQ Country, as the owner of the drug's intellectual property is the company, regardless of where the drug was launched. The drugs were examined according to the Company HQ Country, and

2 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.

3 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.

4 *Ibid.*

then the top 21 countries that launched the drug were plotted. Countries are involved in the drug launching process in two ways: (1) licensing or (2) originating inventions and intellectual property. Some cancer drug developments are the product of a joint effort by more than one country. In this part of the study, we examined drug development by countries, regardless of their level of involvement in this process. Some of the drugs were developed through a joint effort, and each country was credited for its contribution to the development of that cancer drug.

Not surprisingly, the U.S. has played a significant role in launching 298 out of the 820 cancer diagnostic and therapeutic drugs, equivalent to 36.3% of the total worldwide cancer drug therapeutics.

The Citeline Pharmaprojects databases were searched for cancer diagnostic and therapeutic drugs, and the number of drugs from each country was identified according to the company's headquarters country. The top 21 countries with the highest drug numbers were then plotted in Figure 1.

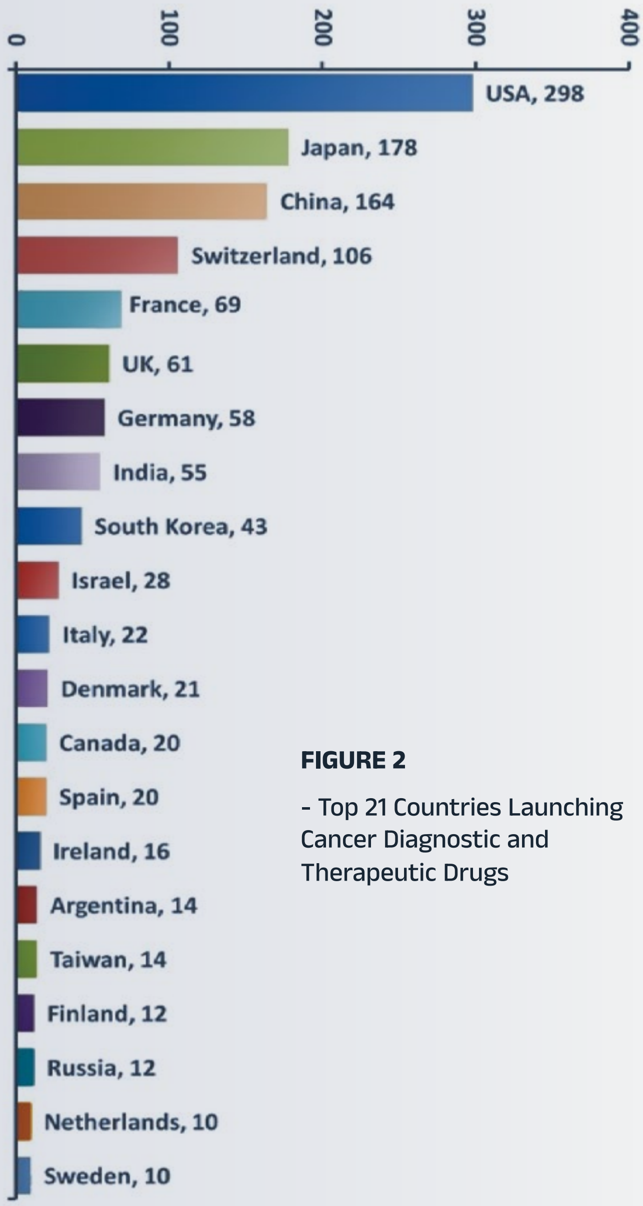


FIGURE 2

- Top 21 Countries Launching Cancer Diagnostic and Therapeutic Drugs

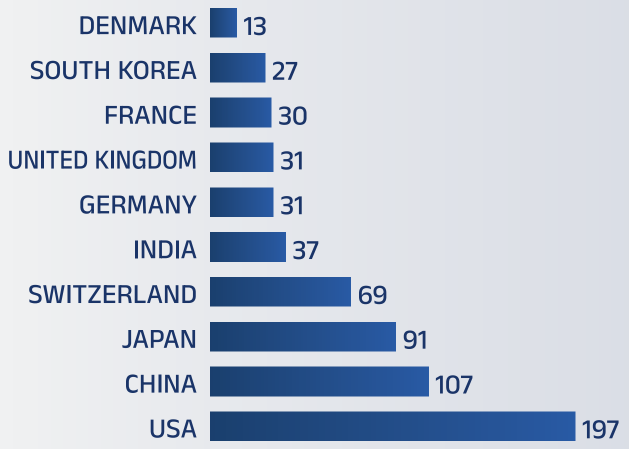


FIGURE 2

- Top 10 Countries Originating Cancer Diagnostic and Therapeutic Drugs

The Citeline Pharmaprojects databases were searched for cancer diagnostic and therapeutic drugs, and the number of drugs from each country as originator were identified. The top 10 countries with the highest drug originator numbers were then plotted in Figure 2.

In this part of the study, we identified the countries that originated cancer diagnostic and therapeutic drugs and plotted the top 20 countries with the highest number of drug originations, in other words, drug inventions. In the Citeline Pharmaprojects database, cancer drug therapeutics-related data also includes information about country whether it is the originator of the drug or licensee of the drug. Therefore, we examined the countries' contribution in the cancer drug development field as "originator" or "licensee." In Figure 1, the countries involved in cancer drug launching are either originators or licensees. The countries that are only originators were also examined and plotted separately in Figure 2. According to these findings, the U.S. is the leading country in drug inventions by originating 24.9 percent of cancer therapeutics. The U.S. is followed by China at 13.9 percent and Japan at 12.7 percent as originators of cancer therapeutic drugs.

As Figure 1 and Figure 2 show, the U.S. leads cancer drug development as an originator as well as a licensee. Being a leading country in cancer drug development requires various high-quality and well-established elements. All these elements serve as the initial and crucial step of the drug process: ***Research*** and ***Development***. NIH has been the important contributor to this aspect for cancer drugs and to treatment for other important diseases. This study aims to uncover and highlight the role of NIH in the U.S.'s success of cancer drug and therapeutics development and in the transformation of discovery to health protocols.

2.2. Overview Role of the NIH in Cancer Therapeutics Development

According to statistical estimates, approximately 618,120 people in the U.S. will die due to cancer in 2025;[5] on the other hand, 29,135 people in the U.S. will die in 2025 due to motor vehicle crashes.[6] Cancer-caused death probability is thus higher than that for car accident-caused death. Deaths due to motor vehicle crashes of course are preventable. On the other hand, cancer is oftentimes also both preventable and curable. Therefore, like preventing car accident deaths, the focus on cancer prevention and the development of cancer therapeutics is an important goal for public health. Fortunately, the mortality rate of cancer has been declining because of long-term efforts to create awareness regarding smoking health hazards (which leads to smoking reductions), the discovery of earlier cancer detection methods, and the development of new cancer treatments.[7]

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.[8]

In 1989, the National Center for Human Genome Research (NCHGR) was established at NIH. In 1990, the Human Genome Project (HGP) was developed in collaboration with the U.S. Department of Energy to map the human genome. This initiative ignited all genomic studies and their application in the life science field. The expansion of NCHGR's genome studies through establishing the division of intramural research at the NIH campus in 1993 led to the completion of the Pan-Cancer Atlas by the NCHGR's successor, the National Human Genome Research Institute (NHGRI) and NCI, both part of NIH. The Pan-Cancer Atlas has detailed clinical information on 10,000 tumors from 33 cancer types. The Pan-Cancer Atlas was published as a collection of 27 papers across a suite of *Cell* journals. This phenomenal accomplishment allows scientists to understand human tumor initiation better, leading to better clinical trial designs and improved future cancer treatment.[9]

NIH has been an excellent source for the two essential elements of research and development in cancer drug development: Collaboration and Skilled Expertise. NCI's The Experimental and Therapeutics Clinical Trials Network (ETCTN) is an excellent example of collaboration and skilled medical expertise combined with regulatory and technology transfer agreements. The ETCTN, launched in 2013 by the NCI's Cancer Therapy Evaluation Program (CTEP), became a very successful effort to cultivate collaboration with skilled clinical investigators. Biomarker assay development is the program's major component; therefore, NCI built a centralized mechanism to ensure that assays are analytically validated and fit for the purpose of their use as well as ensuring the availability of all specimens via banking for future use. This system allows ETCTN to acquire high-quality patient tumor specimens for correlative studies and incorporate analytically validated and fit-for-purpose biomarker assays into its programs. Another brilliant part of the NCI ETCTN is that its multi-institutional, multi-disciplinary Drug Project Teams are led by early career investigators, giving enthusiastic early career scientists a great chance to experience clinical study leadership opportunities with the support of senior clinical investigators. NCI's extensive collaborations with industry through a Cooperative Research and Development Agreement (CRADA) and with the research community through the ETCTN allow NCI to facilitate essential studies in the following areas: (1) address unmet medical needs in oncology, (2) engage difficult-to-accrue patient populations in new studies, (3) involve combining agents from different pharmaceutical companies for a single study which is otherwise challenging to complete in the private sector.[10,11]

2.2.1 The Role of NIH in Breast Cancer Therapeutics Development

Breast cancer is the most common cancer in women in the U.S. According to the American Cancer Society's estimates, approximately 316,950 new cases of invasive breast cancer will be diagnosed in women and approximately 42,170 women will die from breast cancer in 2025.[12]

NCI has put forth a tremendous amount of effort to find a 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,

5 Siegel, R.L. *et al., Cancer Statistics, 2025. Ca, 2025.* 75(1): p. 10.

6 National Highway Traffic Safety Administration, part of the U.S. Department of Transportation. https://www.nhtsa.gov/press-releases/nhtsa-2023-traffic-fatalities-2024-estimates.

7 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.

8 Frei III, E. *et al.,* "A comparative study of two regimens of combination chemotherapy in acute leukemia." *Blood, 1958.* 13(12): p. 1126-1148.

9 "NIH completes in-depth genomic analysis of 33 cancer types." https://www.cancer.gov/news-events/press-releases/2018/tcga-pancancer-atlas.

10 Division of Cancer Treatment and Diagnosis, National Cancer Institute. National Cancer Institute early therapeutics clinical trials network program guidelines. *https://ctep.cancer.gov/initiativesPrograms/docs/ETCTN_Program_Guidelines.pdf.*

11 Massett, H.A. *et al.,* "Transforming the early drug development paradigm at the National Cancer Institute: the formation of NCI's experimental therapeutics clinical trials network (ETCTN)." *Clinical Cancer Research, 2019.* 25(23): p. 6925-6931.

12 Siegel, R.L. *et al., Cancer Statistics, 2025. Ca, 2025.* 75(1): p. 10.

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.[13] We searched the NIH RePORTER database for funded breast cancer research projects. We found that 98,323 NIH-funded breast cancer research projects were initiated, 8,966 patent applications were recorded, and these projects resulted in 786,525 publications between 1999 and 2024.

To explore the effect of NCI's funding for breast cancer research from a different angle, we examined the data regarding the NCI funding for breast cancer and the death rate of breast cancer over the years (Figure 3A). We have seen a negative trend between increased NCI funding and the death rate. We plotted these two variables to test whether this trend is statistically meaningful (Figure 6B). We analyzed the correlation between NCI's funding for breast cancer and the breast cancer death rate with Spearman's Rho Rank 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 the 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 3A-B).

13 NIH Health Information. https://www.nih.gov/health-information.

FIGURE 3 - NCI's Funding for Breast Cancer Research and the Breast Cancer Death Rate

(Death Rate refers to "Deaths per 100,000 population (age adjusted)")

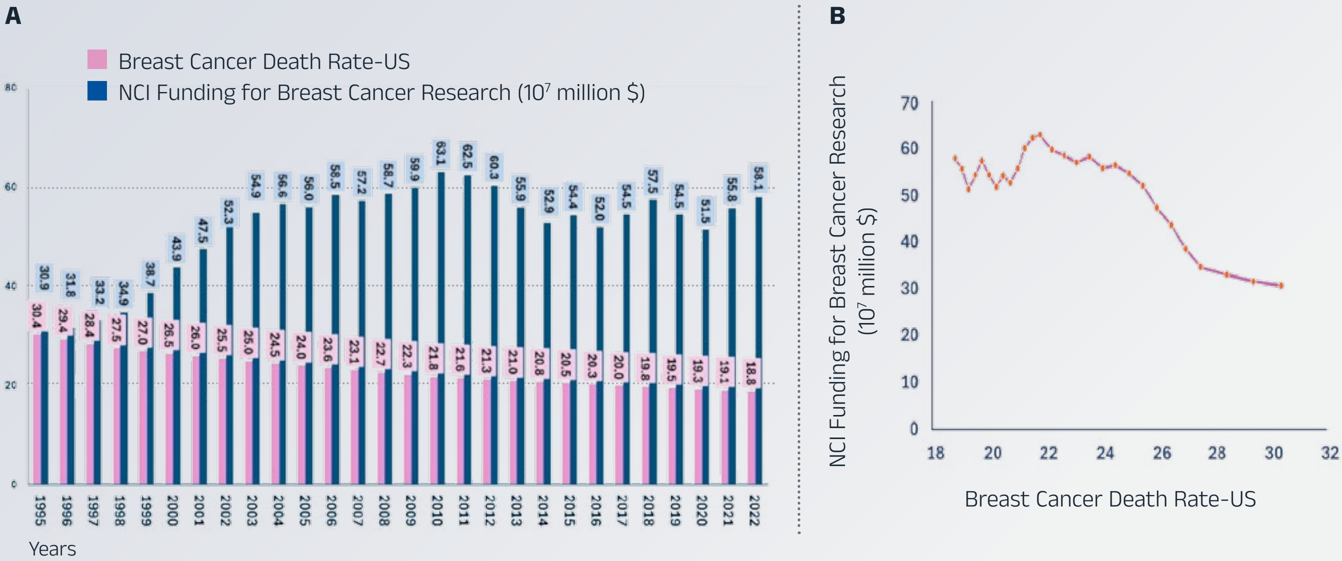
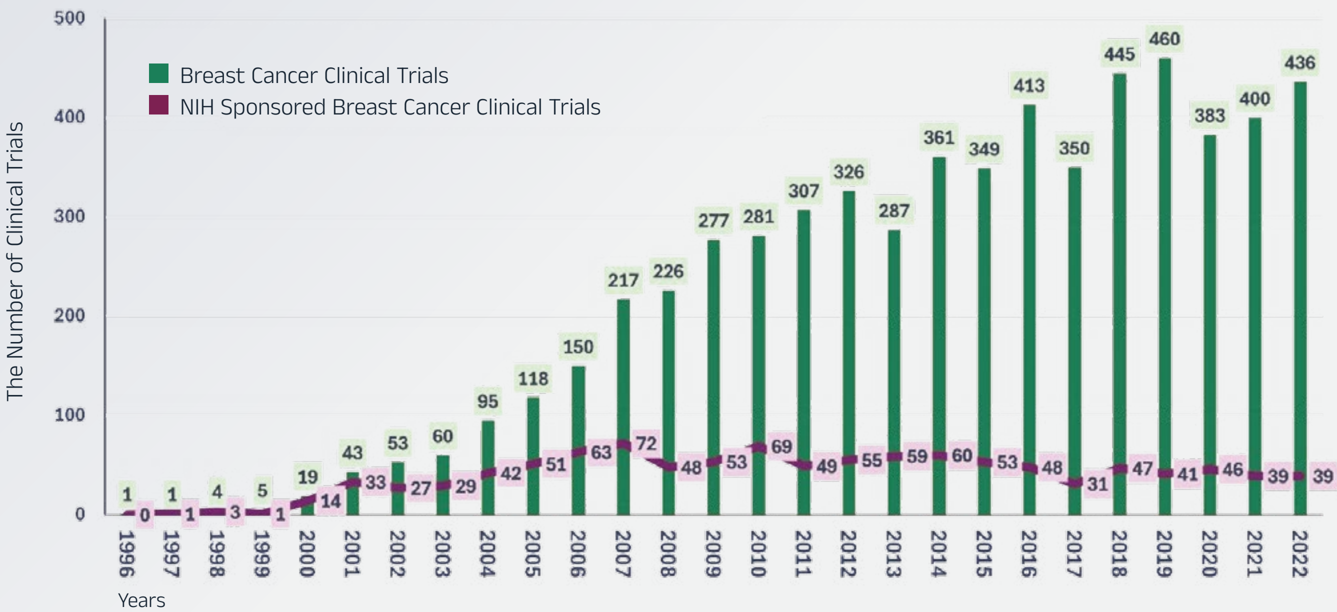


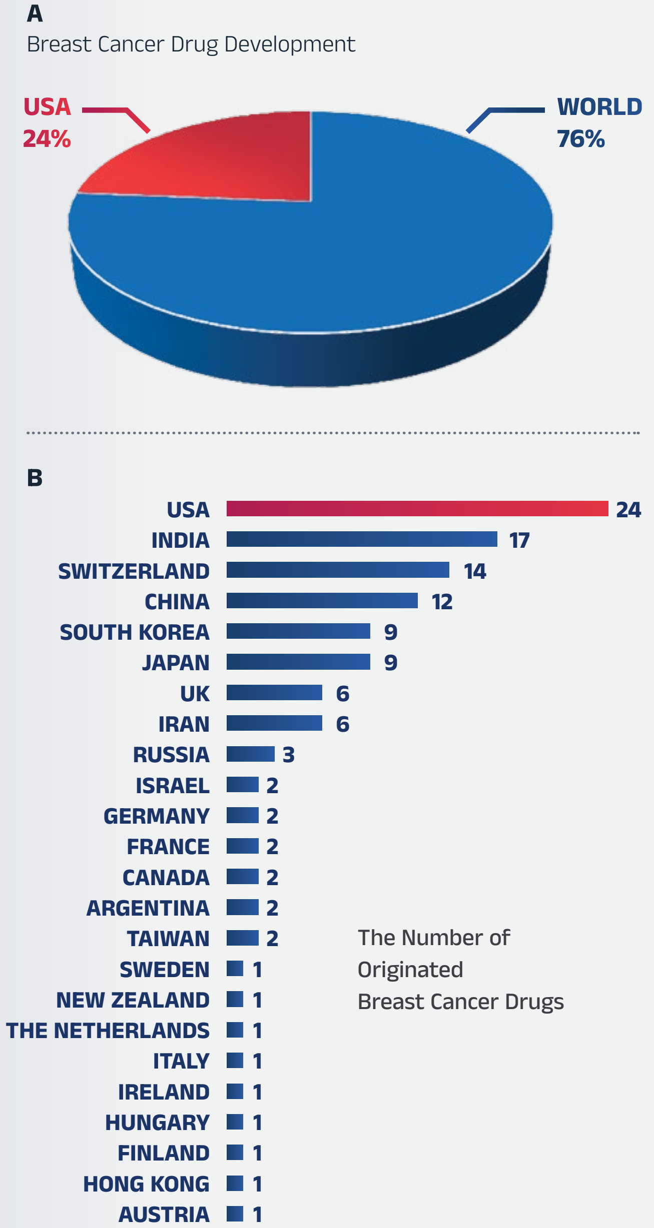
FIGURE 4 - NIH's Role in Breast Cancer Clinical Trials Around the World



We explored the role of NIH in breast cancer clinical trials. In this effort, we searched for completed cancer clinical trials worldwide. 6,067 breast cancer clinical studies have been completed, and NIH has collaborated on 1,073 breast cancer clinical trials since 1998, as shown in Figure 4. This means that NIH has supported 17.7 percent of breast cancer clinical trials worldwide in every way, including collaboration, sponsorship, and funding.

When we examined the U.S.'s role in developing breast cancer therapeutic drugs, we found that 130 were launched worldwide, and 29 of them were launched in the U.S. either as an originator or licensee. This means that 20.8 percent of breast cancer therapeutic drugs were launched by companies located in the U.S. (Figure 5A).

FIGURE 5
- Breast Cancer Drug Development Around the World



During this timeframe, 121 breast cancer drugs were launched, 24 of which were originated in the U.S., which means 19.8 percent of breast cancer drugs were originated in the U.S. The U.S. is followed by India with 17 drugs (14 percent) and Switzerland with 14 drugs (11.6 percent)(Figure 5B). In 1985, the NCI-supported clinical trial results showed that women with early-stage breast cancer who were treated with breast-conserving surgery (lumpectomy) followed by whole-breast radiation therapy had similar rates of overall survival and disease-free survival as women who were treated with mastectomy alone.[14] In 1998, the findings from another NCI-sponsored breast cancer clinical trial proved the importance of the anti-estrogen drug tamoxifen in breast cancer treatment, with a 50 percent decrease in death for the population of women at risk.[15] In 2018, NCI-sponsored clinical trials that used 21 genes associated with a molecular test to assign appropriate and effective treatment to women with early-stage, hormone receptor (HR)-positive, HER2-negative breast cancer. The 21-gene test helps doctors to predict whether chemotherapy will be beneficial for the patients with hormone-positive, HER2-negative, lymph node-negative breast cancer. It is one of the first clinical trials to use a personalized cancer treatment option to decide whether chemotherapy is necessary.[16]

2.2.2 The Role of NIH in Lung Cancer Therapeutics Development

Lung cancer is the second most common cancer in both men and women in the U.S. According to the American Cancer Society's recent statistics, there will be approximately 226,650 new cases of lung cancer (110,680 in men and 115,970 in women) and approximately 124,730 deaths from lung cancer (64,190 in men and 60,540 in women) in 2025.[17] NIH has substantially impacted lung cancer research through NIH funding for research and cancer prevention activities. We searched the NIH RePORTER for NIH-funded lung cancer research projects. We found 80,240 NIH-funded lung cancer research projects corresponding to 7,989 patent applications, and these research projects resulted in 786,525 publications between 1999 and 2024.

Another important NIH effort in lung cancer clinical trials is the NCI-sponsored Lung Cancer Screening Trial (NLST) launched in 2010. The trial uncovered the optimized application of low-dose computerized tomography screening, which can reduce the lung

14 Lichter, A.S. *et al.,* "Mastectomy versus breast-conserving therapy in the treatment of stage I and II carcinoma of the breast: a randomized trial at the National Cancer Institute." *Journal of Clinical Oncology, 1992.* 10(6): p. 976-983.

15 Gail, M.H. *et al.,* "Weighing the risks and benefits of tamoxifen treatment for preventing breast cancer." *Journal of the National Cancer Institute, 1999.* 91(21): p. 1829-1846.

16 Sparano, J. *et al.,* "Clinical outcomes by chemotherapy regimen in patients with RS 26-100 in TAILORx." *Annals of Oncology, 2019.* 30: p. v854.

17 Siegel, R.L. *et al., Cancer Statistics, 2025. Ca, 2025.* 75(1): p. 10.

cancer death rate by 20 percent in current and former heavy smokers.[18]

To explore the effect of NCI's funding for lung cancer research, we examined the data regarding the NCI funding for lung cancer and the death rate of lung cancer between 1995 and 2022 (Figure 6A). We have seen a negative trend between increased NCI funding and the death rate in lung cancer. To test whether this trend is statistically meaningful, we plotted these two variables including NCI funding for lung cancer research and death rate in lung cancer (Figure 6B) and analyzed the correlation between these two variables with Spearman's Rho Rank correlation. The calculated Spearman's Rho ((Rs) = -0.91, and p (2-tailed) <0.001) shows a substantial negative correlation between NCI lung cancer research funding and lung cancer death rate in the U.S. The statistical calculations show these two variables present a substantially negative correlation, which we might interpret as an increase in NCI's funding support for lung cancer research is connected to a decrease in the death rate of lung cancer patients (Figure 6).

18 Team, N.L.S.T.R., "Reduced lung-cancer mortality with low-dose computed tomographic screening." *New England Journal of Medicine, 2011.* 365(5): p. 395-409.

FIGURE 6 - Lung Cancer Death Rate and NCI's Funding for Lung Cancer Research
(Death Rate refers to "Deaths per 100,000 population (age adjusted)")

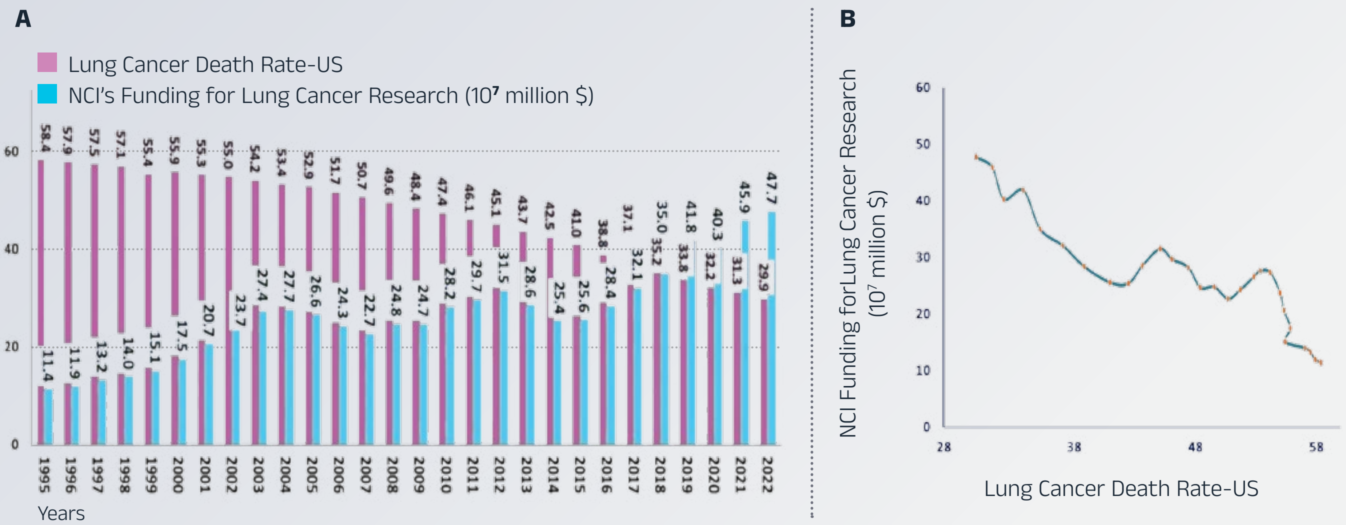
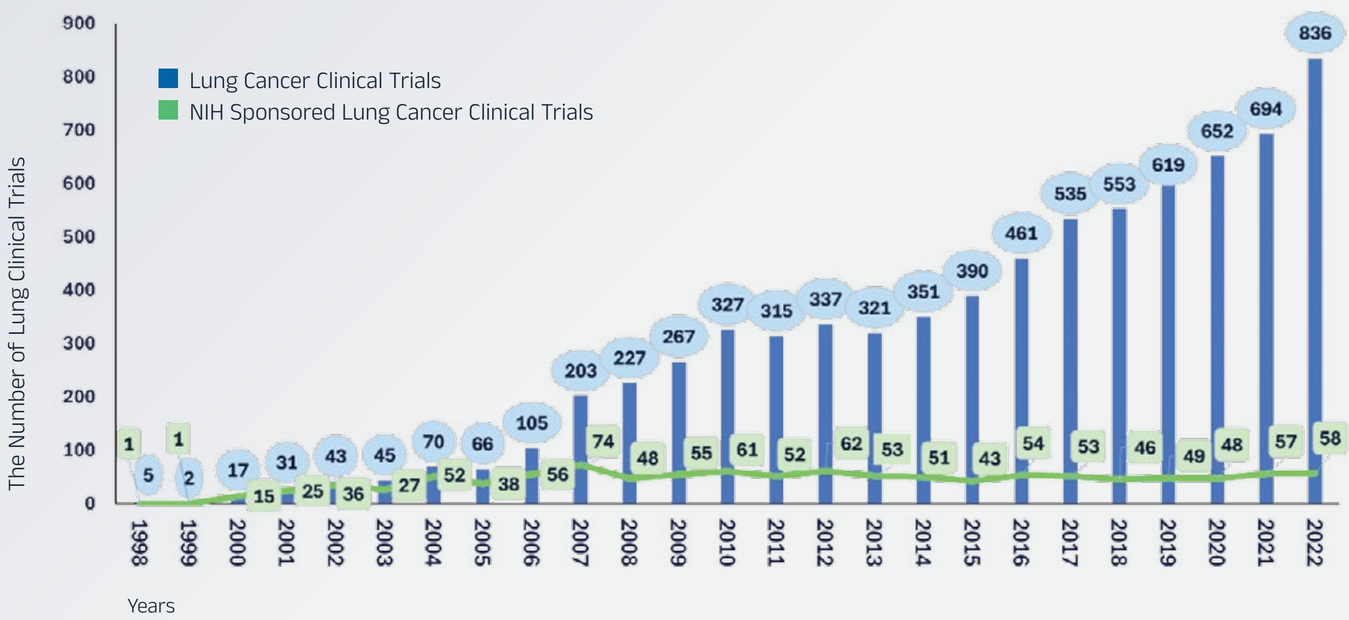


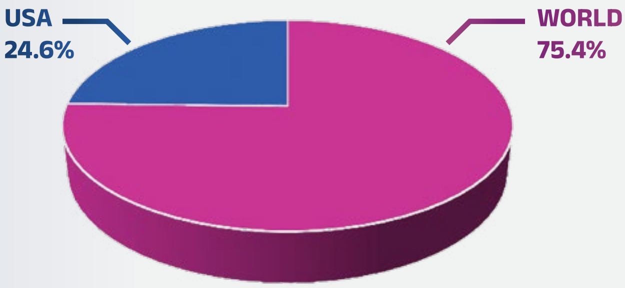
FIGURE 7 - NIH's Support in Lung Cancer Clinical Trials



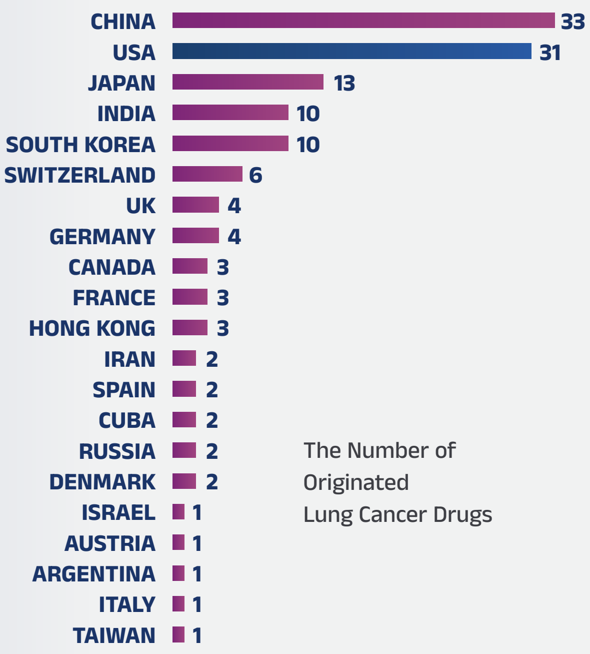
NIH has been supporting clinical trials for lung cancer for a while. According to data found on the website clinicaltrials.gov, 7,472 lung cancer clinical studies have been completed, and NIH has been involved in 1,115 lung cancer clinical trials since 1998. This means NIH supported 14.6 percent of lung cancer clinical trials worldwide (Figure 7).

FIGURE 8
- Lung Cancer Drug Development Around the World

A
Lung Cancer Drug Development



B



After quantifying the NIH effort in support of lung cancer clinical trials, we queried the U.S.'s involvement in developing lung cancer chemotherapeutic drugs. For this purpose, we examined the number of lung cancer drugs launched worldwide and in the U.S. The results show that there are 147 lung cancer therapeutic drugs launched all around the world, and 48 of these therapeutics were launched in the U.S. as an originator or licensee, which means that 24.6 percent of lung cancer therapeutic drugs were launched by companies in the U.S. between 1973 and early 2025 (Figure 8A). 137 lung cancer therapeutic drugs were originated during this timeframe, and 33 of them, equivalent to 24.1 percent of lung cancer drugs, were originated by China. The U.S. followed with 31 drugs (22.6 percent) and then Japan with 13 drugs (9.5 percent)(Figure 8B). Between 1990 and 2003, NIH's efforts in lung cancer research resulted in a decrease in lung cancer deaths in men and women by 54 percent and 30 percent, respectively.[19]

2.2.3 The Role of NIH in Prostate Cancer Therapeutics Development

Prostate cancer is the most common cancer in men, with 313,780 new prostate cancer diagnoses and approximately 35,770 prostate cancer caused deaths projected in the U.S. for 2025. 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. For instance, 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.[20]

Another example is the NCI-sponsored Prostate Cancer Prevention Trial (PCPT) initiated in 2003, and it's results brought forth extraordinary data regarding the therapeutic effect of the drug finasteride, which reduces the production of male hormones in the body and lowers a man's risk of prostate cancer by about 25 percent.[21]

NIH has been playing a role as a pioneer to find a cure with not only intramural research activities but also supporting the extramural research activities through grants for universities and research institutes. According to the NIH RePORTER, 45,583 NIH-funded prostate research projects were initiated, 5,777 patent applications were recorded, and 490,527 research projects were published between 1999 and 2024.

NIH funding is important for both intramural and extramural research activities. To be able to examine the impact of NIH funding on prostate cancer research, the correlation between NCI's funding for prostate cancer research and prostate cancer disease-caused deaths was determined. NCI funding for prostate cancer research and the prostate cancer death rate were plotted between 1995 and 2022 (Figure 9A). As seen in Figure 9A, while NCI's funding for prostate cancer research increased, the death rate for this disease decreased over the years.

As stated above, NCI's funding for prostate cancer research includes intramural and extramural research

19 NIH Health Information. https://www.nih.gov/health-information.

20 National Human Genome Research Institute. https://www.genome.gov/about-nhgri/Brief-History-Timeline.

21 Lucia, M.S. *et al*., "Finasteride and high-grade prostate cancer in the Prostate Cancer Prevention Trial." *Journal of the National Cancer Institute*, 2007. 99(18): p. 1375-1383.

activities. Therefore, intramural and extramural research activities contribute to reducing prostate cancer-related death rates. However, to have a better understanding of a possible correlation between NCI funding for prostate cancer research and the prostate cancer-caused death rate, we plotted NCI funding for prostate cancer research and prostate cancer death rates as seen in Figure 9B, and we analyzed the non-linear data for the NCI funding for prostate cancer research and the prostate cancer death rate with Spearman's Rho Rank correlation. Results of the Spearman Rho correlation indicated that there is no significant relationship between NCI funding for prostate cancer research and the prostate cancer death rate in the U.S. (Rs = .209, p (2-tailed) = .285, p> 0.05).

FIGURE 9 - NCI's Funding for Prostate Cancer Research and the Prostate Cancer Death Rate
(Death Rate refers to "Deaths per 100,000 population (age adjusted)")

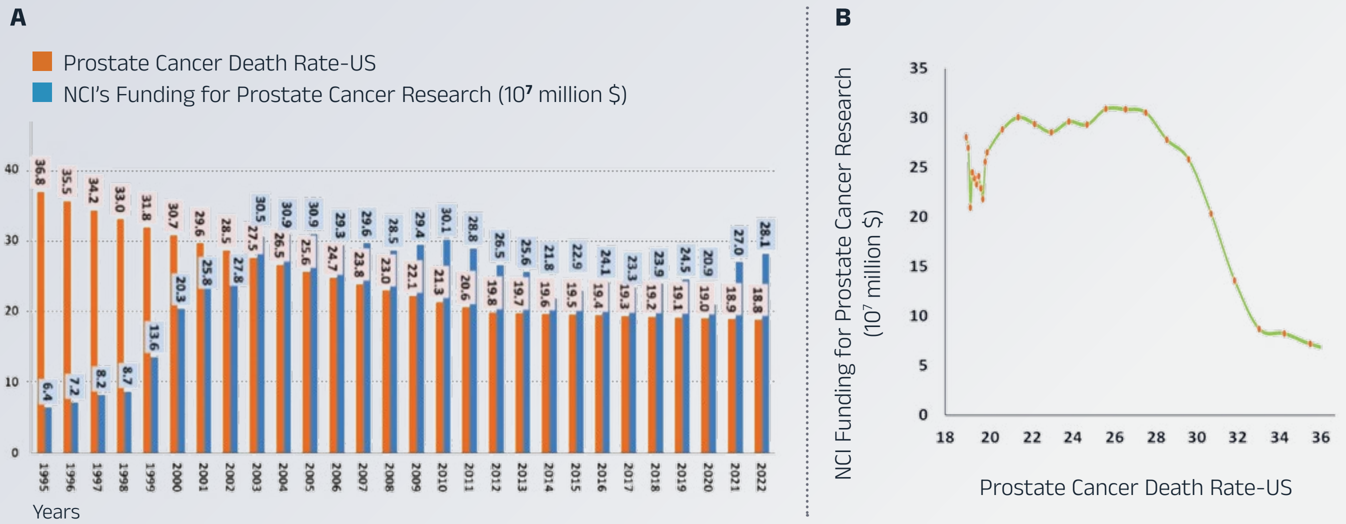
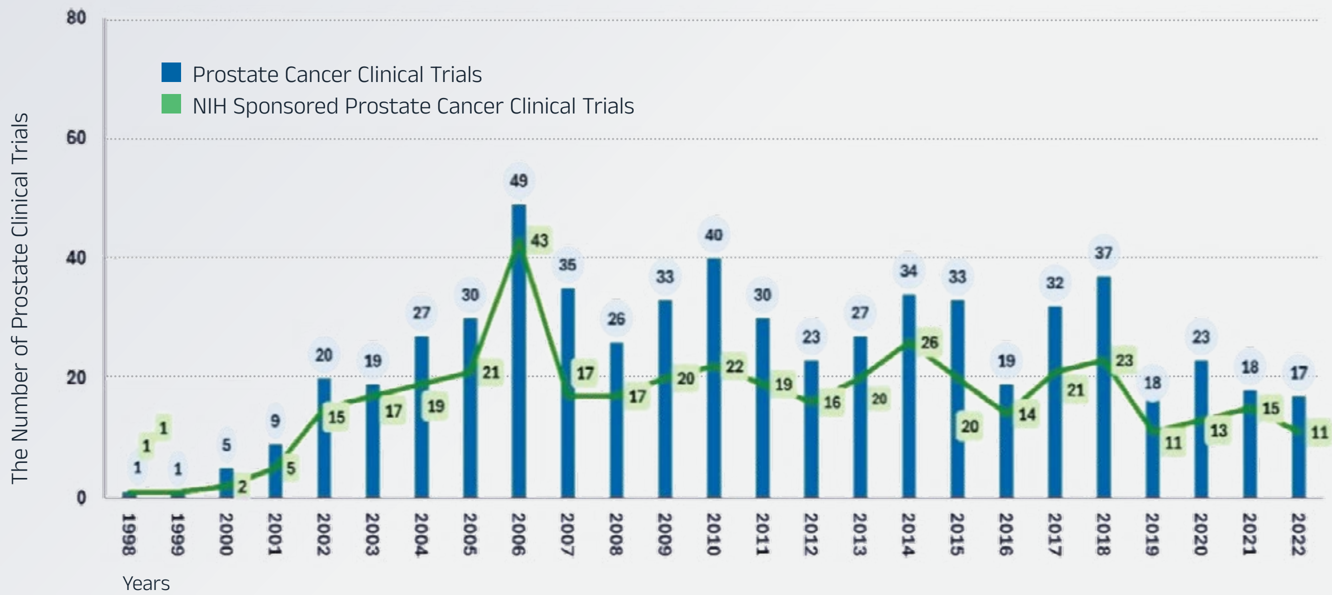


FIGURE 10 - NIH's Support in Prostate Cancer Clinical Trials



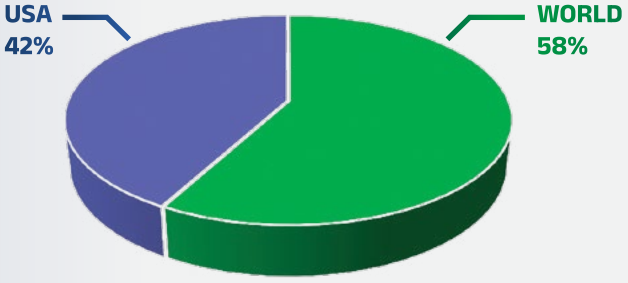
NIH has been putting effort into curing prostate cancer, including NCI's funding for prostate cancer research and support for clinical trials through collaboration and expertise. We explored the role of NIH in prostate cancer-related clinical trials. According to data from the website clinicaltrials.gov, 606 prostate cancer clinical studies have been completed, and NIH has been involved in 409 prostate cancer clinical trials since 1998, as shown in Figure 10. NIH supported 67.5 percent of prostate cancer clinical trials through collaboration, sponsoring, and funding.

To understand the role of the U.S. in prostate cancer drug development, we examined the number of prostate cancer drugs launched worldwide. We found 50 prostate cancer drugs developed worldwide and

21 out of those 50 drugs were launched in the U.S. as originators or licensees. This means that companies in the U.S. launched 42 percent of prostate cancer therapeutic drugs (Figure 11A). 43 prostate cancer therapeutic drugs were country-originated, and nine of them, equivalent to 20.9 percent of prostate cancer drugs, were originated in the U.S. The U.S. is followed by the UK and France with 5 drugs each (11.6 percent) (Figure 11B).

FIGURE 11
- Prostate Cancer Drug Development Around the World

A
Prostate Cancer Drug Development



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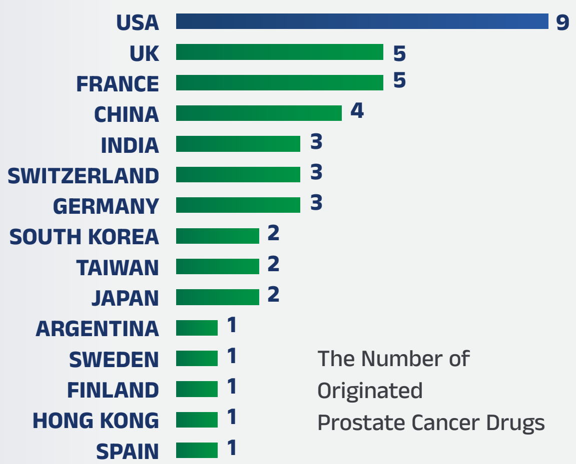


2.2.4 The Role of NCI in Cancer Therapeutic Development

The NCI was initiated as one of the institutes at 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.[22]

NCI has been supporting cancer therapeutic development through these listed main mechanisms for 88 years: (1) Conducting, assisting, and fostering research, investigations, experiments, and studies relating to the cause, prevention, and methods of diagnosis and treatment of cancer; (2) Promoting the coordination of research conducted by the Institute and similar research conducted by other agencies, organizations, and individuals; (3) Providing training and instruction in technical matters relating to the diagnosis and treatment of cancer; (4) Providing fellowships in the Institute from funds appropriated or donated for such purpose; (5) Securing for the Institute consultation services and advice of cancer experts from the United States and abroad; (6) Cooperating with state health agencies in the prevention, control and eradication of cancer.

In this part of the study, we take a closer look at the NCI's contribution to cancer therapeutics development and its impact on public health.

2.2.4.1 The Impact of NCI in Cancer Therapeutic Development

NCI has been supporting cancer therapeutic development from conducting preclinical studies in the laboratory to testing potential therapies in humans. There are many great examples regarding the NCI's contribution in the cancer research ecosystem and in this part of the study we look closer at some of NCI's achievements.

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. One notable example is the NCI DCTD's Cancer Therapy Evaluation Program (CTEP), which is dedicated to developing more effective methods for treating, controlling, and curing cancer. For this purpose, NCI's CTEP coordinates an extensive national program of cancer research to evaluate new cancer therapeutic drugs through translational studies. 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 U.S. 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.[23]

NIH's efforts in genomic studies paved the way for precision medicine through the availability of advanced molecular tools to characterize cancer

22 NCI Funding for Research Areas (2024). https://www.cancer.gov/about-nci/budget/fact-book/data/research-funding.

23 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.

cells. The advanced molecular diagnostic tools and the development of targeted agents have accelerated the application of precision cancer medicine. The NCI has played a pioneering role in precision medicine, launching the NCI-MATCH (Molecular Analysis for Therapy Choice) study, a precision medicine initiative (PMI) sponsored by the NCI. This study recruited over 6,000 patients within less than two years.[24] Later on, NCI carried precision medicine studies to a more advanced level with the development of immunotherapies and the application of agent combinations. The NCI-MATCH study indicated that patients with advanced cancer may benefit from genomic sequencing when planning more effective treatment. The NCI launched the following next-generation precision medicine studies: (1) NCI ComboMATCH study, which tests combinations of specific molecularly targeted cancer therapeutic agents aimed at overcoming primary and adaptive resistance pathways, (2) Immunotherapy-MATCH (iMATCH) for tissue procurement and molecular testing to enhance immunotherapy trials, and (3) MyeloMATCH, the first NCI precision medicine initiative to treat patients with myeloid cancers, which was funded by the NCI from diagnosis throughout their treatment journey.[25,26,27,28] Every precision medicine initiative requires novel and intensive informatics and laboratory support, including diagnostic testing, resources for biopsies, management of biobanks, data storage, and regulatory support. An extensive and efficiently working collaboration network can provide all these necessary elements. Therefore, the NCI has taken several initiative steps and established the Molecular and Immunologic Diagnostic Laboratory Network (MDNet) to provide real-time diagnostic services in support of iMATCH and myeloMATCH, enabling the necessary analyses. These initiatives, along with the tools provided by NCI, have been helping to improve the outcomes of novel therapies and providing convincing evidence that the molecular characteristics of tumors can be used to select the optimal treatment.[29,30] The NCI Central Institutional Review Board (NCI CIRB) is also another initiative sponsored by the NCI for clinical trials in all states and Puerto Rico. NCI CIRB manages multi-site trials under the single IRB by reviewing protocols, consent forms, and other relevant materials for all participating sites, which helps for a more efficient review process with reduced administrative work.[31]

Another great example is the NCI's DCTD Developmental Therapeutics Program (DTP), which is a unique program that supports cancer drug development with no cost services and resources to the academic and private-sector research communities, facilitating the discovery and development of new anti-cancer agents at every stage, from preclinical to first-in-human clinical trial.[32]

To further understand the role of the NCI in the drug development landscape and the fight against cancer, we examined the NCI's funding for cancer

24 Harris, L.N. *et al.,* "The New NCI Precision Medicine Trials." *Clinical Cancer Research, 2023.* 29(23): p. 4728-4732.

25 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.

26 Harris, L.N. *et al.,* "The New NCI Precision Medicine Trials." *Clinical Cancer Research, 2023.* 29(23): p. 4728-4732.

27 Coyne, G.O.S., N. Takebe, and A.P. Chen, "Defining precision: the precision medicine initiative trials NCI-MPACT and NCI-MATCH." *Current Problems In Cancer, 2017.* 41(3): p. 182-193.

28 NCI's ComboMATCH initiative will test new drug combinations guided by tumor biology. https://www.cancer.gov/news-events/press-releases/2023/combomatch-precision-medicine-cancer-initiative.

29 Harris, L.N. *et al.,* "The New NCI Precision Medicine Trials." *Clinical Cancer Research, 2023.* 29(23): p. 4728-4732.

30 Middleton, G., H. Robbins, F. Andre, and C. Swanton, "A state-of-the-art review of stratified medicine in cancer: towards a future precision medicine strategy in cancer." *Annals of Oncology, 2022.* 33(2): p. 143-157.

31 NCI Central Institutional Review Board https://www.ncicirb.org/.

32 The NCI Development Therapeutics Program (DTP). https://dtp.cancer.gov/.

FIGURE 12 - Cancer Death Rate vs. NCI's Funding for Cancer Research
(Death Rate refers to "Deaths per 100,000 population (age adjusted)")

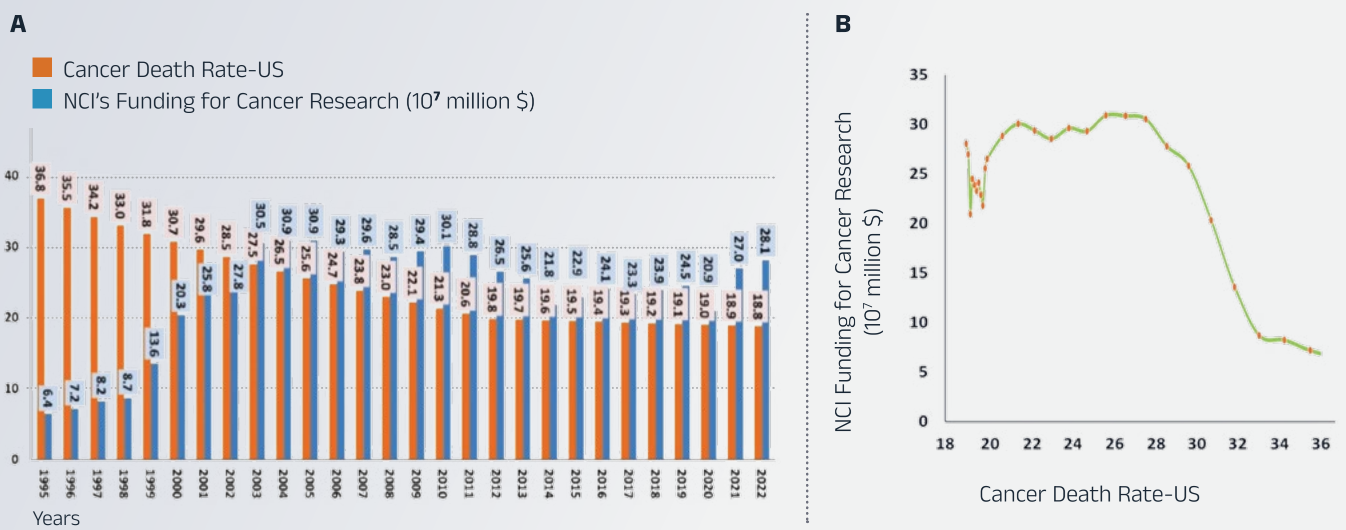
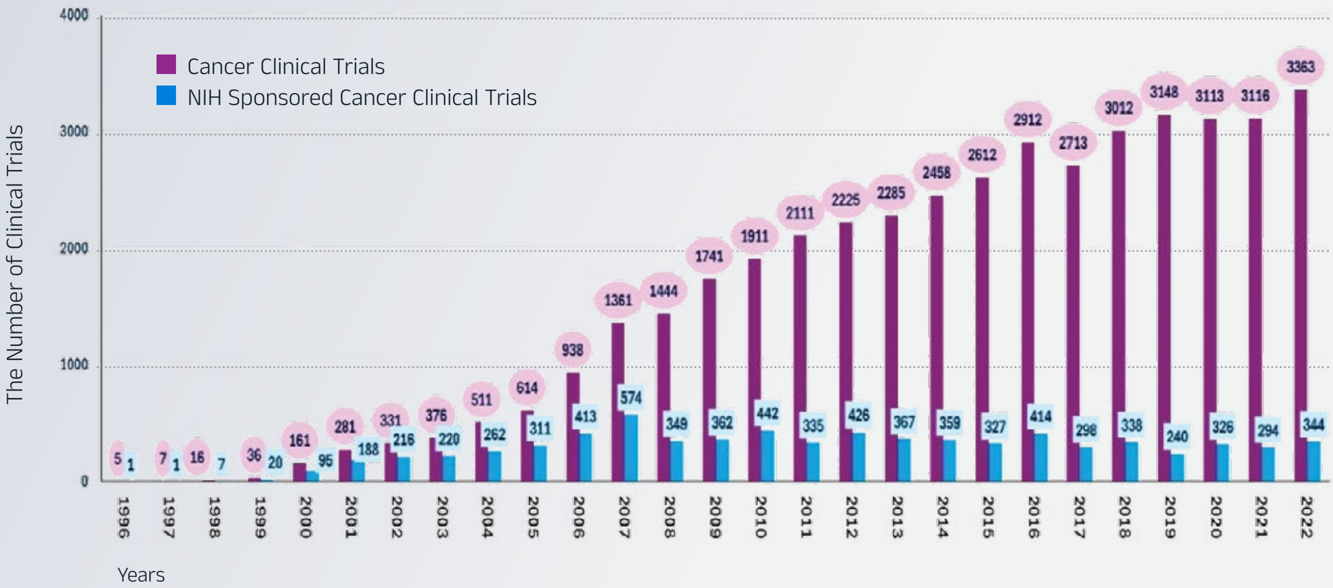


FIGURE 13 - NIH's Support in Cancer Clinical Trials



research and NIH's involvement in cancer clinical trials. In this part, we examined the role of NCI's yearly budget, covering intramural and extramural research activities in cancer-caused deaths in the U.S. For this purpose, we plotted the NCI's annual budget and cancer death rate between 1995 and 2022. While there is a slight increase in the NCI budget, there is also a slight decrease in the cancer-related death rate in the U.S. (Figure 12A). To analyze whether the cancer-caused death rate correlates with NCI funding for cancer research, these two variables were plotted for better observation. The statistical correlation was tested using Spearman's Rho Rank correlation analysis (Figure 12B). 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 the cancer-related death rate might be considered substantially important.

To identify NIH's role in supporting cancer clinical trials, we examined cancer clinical trials completed worldwide. 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 13).

Every step of NCI's effort in cancer therapeutic drug development requires collaborative work, which is established on various technology transfer agreements, including the Clinical Trials Agreement (CTA), the Cooperative Research and Development Agreement (CRADA), and the Material Transfer Agreement (MTA).

2.2.4.2 The Role of NCI in Cancer Prevention

Cancer prevention is one of the key components with a focus to reduce the risk of developing cancer through making healthy choices. After the National Cancer Act was signed in December 1972, the NCI Director was allowed to establish not only national cancer research centers, but also national cancer control programs.[33] Since then, the multidisciplinary effort of the NCI to find cures for all kinds of cancer types goes hand in hand with cancer prevention. NCI initiated implementation science in cancer prevention and control through conducting research, supporting the research with funding and expertise, and building partnerships to achieve more impactful benefits in this field.[34] Healthy lifestyle choices, including managing healthy weight, avoidance of smoking, adding physical activities in daily routines, limiting alcohol, protecting against oncogenic virus infection through respective prophylactic vaccination, and eliminating occupational exposure can help reduce the chance of developing cancer.[35,36]

In the 1970s, NCI heavily supported nutrition related studies for cancer prevention research following the 1971 Cancer Act, also known as the War on Cancer.[37,38] In 1982, a smoking, tobacco, and cancer intervention research program was launched by NCI. In 1983, NCI created the division of Cancer Prevention and Control (DCPC) and initiated two programs: (1) Diet and Cancer and (2) Chemoprevention, into which

33 National Cancer Institute Division of Cancer Prevention. https://prevention.cancer.gov/about-dcp/history-and-timeline.

34 Neta, G. *et al.,* "Implementation science in cancer prevention and control: a decade of grant funding by the National Cancer Institute and future directions." *Implementation Science, 2015.* 10: p. 1-10.

35 Lippman, S.M. and W.K. Hong, "Cancer prevention science and practice." *Cancer Research, 2002.* 62(18): p. 5119-5125.

36 Sei, S. *et al.,* "NCI Resources for Cancer Immunoprevention Research." *Cancer Immunology Research, 2024.* 12(4): p. 387-392.

37 NCI Division of Cancer Prevention. https://prevention.cancer.gov/about-dcp/history-and-timeline.

38 Cantor, D., "Between Prevention and Therapy: Gio Batta Gori and the National Cancer Institute's Diet, Nutrition and Cancer Programme, 1974–1978." *Medical History, 2012.* 56(4): p. 531-561.

the NCI put substantial effort.[39] The Diet and Cancer program focused on epidemiologic and experimental studies to identify how cancer development was influenced by dietary factors. NCI's effort to identify the connection between cancer and dietary factors brought the importance of diet to the light and ignited public attention.

In 1982, NCI commissioned the National Academy of Sciences to summarize all knowledge related to the diet's role in cancer development.[40,41] In 1984, NCI's DCPC initiated clinical trials in chemoprevention and diet and nutrition, and preclinical efficacy and toxicology studies.

NCI launched its Smoking, Tobacco, and Cancer Program (STCP), and it became one of the NCI's top priorities.[42] This program aimed to decrease the smoking or tobacco usage-related cancer incidence and mortality. In 1991 the American Cancer Society (ACS) and the DCPC started the American Stop Smoking Intervention Study (ASSIST). ASSIST is one of the great examples of effective public/private partnership between NCI and ACS. This study funded 17 state health departments; it was completed in eight years. ASSIST became one of the most extensive intervention research programs in the world. NCI performed all these efforts with a robust collaboration effort.[43] NIH and FDA's partnership to promote tobacco control regulatory research for cancer prevention and control-related research is another great example of a collaborative effort.[44]

NCI's DCPC started the Chemoprevention Program, which aims to identify agents that will prevent, halt, or reverse carcinogenesis. In 1991, this program initiated 27 intervention clinical trials, including synthetic retinoids and natural chemoprevention substances including vitamins A, C, E, B12, folate, and beta-carotene.[45] In 1993, NCI's DCPC initiated the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trials. PLCO had an enrollment of 154,877 women and men between 1993 and 2001, and follow up continued for nearly 30 years. The primary results of PLCO yielded 300 peer-reviewed scientific publications. PLCO has been a great resource for the research community all around the world with its data, biospecimens, and clinical outcomes.[46] In 1997, DCPC was reorganized into the Division of Cancer Prevention (DCP) and the Division of Cancer Control and Population Sciences (DCCPS). DCP is dedicated to cancer prevention, while DCCPS explores population genetics, epidemiology, behavior, society, and the welfare of cancer survivors.

DCP launched various research programs to promote immunoprevention research in collaboration with the extramural research community and other NIH institutes, including the National Institute of Allergy and Infectious Diseases (NIAID), for novel vaccine adjuvants. The PREVENT preclinical drug development program is one DCP initiative, and it is the only research program designed to advance innovative cancer preventative agents, including molecularly targeted small-molecule agents and vaccines. The most recent and promising outcome of the PREVENT program is taking the first steps toward creating a vaccine to prevent cancer in people with Lynch Syndrome, an inherited condition that elevates a person's risk of colorectal, endometrial, and other types of cancer.[47,48,49,50,51]

These are only some of the critical milestones that NCI achieved and played a proactive role in the challenging, collaborative, work-loaded field of cancer prevention and control.

3. Discussion

Finding new early cancer detection methodologies and curing deadly cancer disease is a complex transformation process of an idea into a discovery, similar to growing a seed into a fruitful tree; it requires a well-established ecosystem with many high-quality elements. To save lives, putting effort in every way into life science is an inevitable requirement for improving current medical practice and developing future therapeutic approaches, not only for cancer but any medical field. NIH's dedication to prevent and cure cancer disease can be summarized through several various powerful mechanisms.

39 Greenwald, P., "NCI cancer prevention and control research." *Preventive Medicine, 1993.* 22(5): p. 642-660.

40 Lippman, S.M. and W.K. Hong, "Cancer prevention science and practice." *Cancer Research, 2002.* 62(18): p. 5119-5125.

41 Greenwald, P., "NCI cancer prevention and control research." *Preventive Medicine, 1993.* 22(5): p. 642-660.

42 *Ibid.*

43 National Cancer Institute. ASSIST: Shaping the Future of Tobacco Prevention and Control, 2005: https://cancercontrol.cancer.gov/brp/tcrb/monographs/monograph-16.

44 Tobacco Regulatory Science Program (TRSP) National Institutes of Health Office of Disease Prevention, 2013: https://prevention.nih.gov/tobacco-regulatory-research.

45 Boone, C.W., G.J. Kelloff, and W.E. Malone, "Identification of candidate cancer chemopreventive agents and their evaluation in animal models and human clinical trials: a review." *Cancer Research, 1990.* 50(1): p. 2-9.

46 National Cancer Institute Division of Cancer Prevention. https://prevention.cancer.gov/about-dcp/history-and-timeline.

47 Sei, S. *et al.,* "NCI Resources for Cancer Immunoprevention Research." *Cancer Immunology Research, 2024.* 12(4): p. 387-392.

48 PREVENT Cancer Preclinical Drug Development Program (PREVENT). https://prevention.cancer.gov/research-areas/networks-consortia-programs/prevent.

49 Leoni, G. *et al.,* "A genetic vaccine encoding shared cancer neoantigens to treat tumors with microsatellite instability." *Cancer Research, 2020.* 80(18): p. 3972-3982.

50 "Technology Transfer Considerations." https://prevention.cancer.gov/research-areas/networks-consortia-programs/prevent/tech-transfer-considerations.

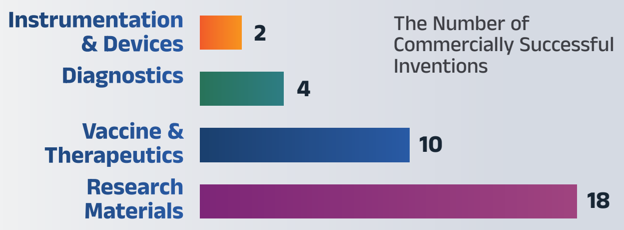
51 "Could a Vaccine Prevent Colorectal Cancer in People with Lynch Syndrome?" https://www.cancer.gov/news-events/cancer-currents-blog/2019/vaccine-prevents-colorectal-lynch-syndrome.

NIH's Intramural Research Program

(1) Bringing Forward New Research and Development Approaches via NIH's Intramural Research Program

NCI's funding supports both intramural and extramural research activities. One important success outcome for intramural research is intramural research-derived inventions. NIH's intramural research activities have brought many commercially successful inventions as a cure for an unmet need or as a research tool to excel in cancer research outcomes. According to the published data at the NIH Technology Transfer website,[52] NIH intramural researchers developed 18 research materials that were included in the annual "Top 20" list of commercially successful inventions of NIH. Highly used and standardized research tools help to create a new research perspective and importantly accelerate the development of cancer therapeutics (Figure 14).

FIGURE 14 - Commercially Successful Inventions Developed by the NIH's Intramural Research



Data originated from the NIH Technology Transfer website, https://www.techtransfer.nih.gov/reports/top-20-commercially-successful-inventions

According to the metrics published at the NIH technology transfer website, the NIH technology transfer office processed 6,082 invention disclosures and executed 5,164 license agreements between 2006 and 2024. We searched the NIH Intramural Database (NIDB) for NIH-funded cancer research outcomes, and we found that NIH intramural investigators performed 2,117 cancer-related projects and produced 5,893 recorded annual reports between 1999 and 2024.[53]

TABLE 1 - FDA-Approved Products for Cancer Therapeutics Based on License Agreements from NIH's Intramural Research Program

INVENTION	DRUG TYPE	DISEASE	NOVELTY	STATUS
Amtagvi®	T cell immunotherapy	Metastatic melanoma for adult patients	The first and the only one-time, individualized T cell therapy to receive FDA approval for a solid tumor cancer	Launched in 2024 with Iovance as NIH licensee
Abecma®	Chimeric antigen receptor (CAR) T-cell therapy	Multiple myeloma	Treatment for adult patients with relapsed or refractory multiple myeloma who have received at least four prior therapies	Launched in 2021 with Bluebird Bio as NIH licensee
Tecartus®	CD19-directed genetically modified autologous T cell immunotherapy	Mantle cell lymphoma and B-cell precursor acute lymphoblastic leukemia	Treatment of mantle cell lymphoma and B-cell precursor acute lymphoblastic leukemia	Launched in 2020 with Kite Pharma as NIH licensee
Lumoxiti®	CD22-directed cytotoxin	Relapsed or refractory hairy cell leukemia	Treatment of adult patients with relapsed or refractory hairy cell leukemia who received at least two prior systemic therapies	Launched in 2019 with AstraZeneca as NIH licensee
Gardasil 9®	Vaccine for human papilloma virus (HPV)	Human papilloma virus (HPV)	An improved vaccine to protect against human papilloma virus (HPV) for use in males and females aged 9 to 45. Gardasil 9 prevents certain cancers and diseases caused by the nine HPV types covered by the vaccine	Launched in 2019 with Merck & Co. as NIH licensee
Yescarta®	Chimeric antigen receptor genetically modified autologous T cell immunotherapy	B-cell lymphoma	The treatment of adult patients with relapsed or refractory large B-cell lymphoma	Launched in 2018 with Kite Pharma as NIH licensee
Cervarix®	Vaccine for human papilloma virus HPV16 and HPV18	Human papilloma virus HPV16 and HPV18	A bivalent human papilloma virus (HPV) vaccine that protects against infection by HPV16 and HPV18 viruses. Infections from these viruses have been etiologically linked to cervical cancer	Launched in 2006 with GlaxoSmithKline as NIH licensee

52 NIH Institute of Health Technology Transfer website. https://www.techtransfer.nih.gov/metrics/inventions-and-licenses.

53 NIH Intramural Database. https://intramural.nih.gov/search/index.taf.

TABLE 2 - FDA-Approved Products for Cancer Therapeutics Based on License Agreements from NIH's Intramural Research Program

INVENTION	DRUG TYPE	DISEASE	NOVELTY	STATUS
Gardasil®	Vaccine for human papilloma virus HPV16, HPV18, HPV6, and HPV11 to prevent cervical cancer	Human papilloma virus (HPV): HPV16, HPV18, HPV6, and HPV11	Vaccine to protect against cervical cancer, currently approved for use in females aged 9 to 26. Gardasil® prevents infection against four forms of human papilloma virus (HPV): HPV16, HPV18, HPV6, and HPV11	Launched in 2006 with Merck as NIH licensee
Kepivance®	Human keratinocyte growth factor protein produced using recombinant DNA technology	Mouth sores	A recombinant human keratinocyte growth factor (KGF) decreases the incidence and duration of severe mouth sores in patients with hematologic cancers who receive myelotoxic therapy	Launched in 2005 with Amgen as NIH licensee
Velcade®	Targeted cancer therapeutic drugs	Multiple myeloma	Proteosome inhibitor	Launched in 2003 with Millennium Pharmaceuticals as NIH licensee
Zevalin®	Monoclonal antibodies with the cell killing ability of radioactive atoms	Non-Hodgkin's lymphoma	The first radioimmunotherapy to be approved by the FDA	Launched in 2002 with IDEC as NIH licensee
Thyrogen®	A recombinant form of human thyroid stimulating hormone	Thyroid cancer	A recombinant form of human thyroid stimulating hormone to use in follow-up screening of patients who have been treated for thyroid cancer. This permits these patients to avoid the debilitating effects of thyroid hormone withdrawal while undergoing standard diagnostic procedures	Launched in 1998 with Genzyme as NIH licensee
Taxol®	A compound derived from the bark of the Western Yew tree	Advanced stage epithelial ovarian and breast cancers	A new method of administration significantly improved the treatment of cancerous tumors	Launched in 1996 with Bristol-Myers Squibb as NIH licensee
Fludara®	A DNA polymerase inhibitor (fludarabine)	B-cell leukemia	DNA polymerase inhibitor (fludarabine) to have potent activity in the treatment of B-cell leukemia	Launched in 1991 with Berlex as NIH licensee

(2) Licensing New Technologies from NIH Research for Commercial Development and Public Benefit

The NIH Technology Transfer Office executed 4,873 licensing agreements between 2006 and 2023 for its intramural research program, but that does not tell the entire story.[54] These license agreements transfer new discoveries made in the areas of vaccines, diagnostics, therapeutics, devices and research tools to industry for further development, and, if successful, these are then launched into the market as products available to the public. While many of the license agreements relate to cancer in the areas of research tools, diagnostics and other products, it is particularly useful to note that the FDA-approved products listed in Table 1 and Table 2 are for cancer therapeutics based on license agreements from NIH's intramural research program:[55]

54 NIH Institute of Health Technology Transfer website. https://www.techtransfer.nih.gov/metrics/inventions-and-licenses.

55 *Ibid.*

(3) Cultivating Collaboration with Universities, Research Institutes and Companies

Licensing, CTAs, DUAs, and CRADAs are all great examples of cultivating collaboration performed by the technology transfer offices at NIH. Each of these technology transfer agreements opens doors for a collaboration that might lead to a great invention; when the complexity of scientific problems such as cancer is considered, collaborative work becomes more important and inevitable. Searching for a cure for this deadly cancer is one of humanity's most complex scientific problems, and a multidisciplinary approach through collaboration might bring a solution. NIH has been supporting and taking the initiative to collaborate with academia, research institutes, and companies. There are many great examples of NIH collaboration efforts. The NCI-supported Pediatric Preclinical In Vivo Testing (PIVOT) program is one of the great examples of collaboration. NCI's (PIVOT) consortium consists of a coordinating center and seven academic research programs specializing in

FIGURE 15 - The Summary of Numbers of NIH-Funded Cancer Research Outcomes

DISEASE	RESEARCH PROJECTS	PATENTS	PUBLICATIONS	CLINICAL TRIALS
All Cancer Types	649804	28944	1449085	7525
Breast Cancer	98323	8966	789525	1073
Lung Cancer	80240	7989	816169	1115
Prostate Cancer	45583	5777	490527	409

(Data originated from NIH RePORTER)

basic research and preclinical testing of treatments for the most common pediatric cancers. NCI's PIVOT program aims to identify new cancer therapeutics for the selected childhood cancers and develop preclinical data that will be useful to childhood cancer researchers in prioritizing new agents for clinical evaluation. NCI's PIVOT program has collaborated with more than 80 pharmaceutical companies over the last 15 years and it systematically evaluates novel agents against genomically characterized childhood solid tumor and leukemia in vivo models.[56,57,58]

(4) Supporting Cancer Research with Funding

NIH has been funding extramural cancer research in universities and small companies as well as its intramural research program. The outcomes of NIH funding support for cancer research communities were searched in NIH RePORTER. It was found that NIH-funded cancer research yielded 649,804 research projects; 1,449,085 publications; 28,944 patents; and 7,525 clinical trials. As mentioned in our earlier findings in NIH RePORTER for breast, lung, and prostate cancer, we summarized NIH-funded research outcomes for breast cancer, lung cancer, and prostate cancer separately, as seen in Figure 15.[59]

The NIH intramural research program activities also bring many ideas to light through practical applications, and the IRP recorded 5,831 invention disclosures between 1999 and 2024.

The RxPONDER (Rx for Positive Node, Endocrine Responsive Breast Cancer) clinical trial founded by NCI is an excellent case study of such a valuable research investment.

Initially, National Comprehensive Cancer Network Guidelines recommended endocrine therapy and adjuvant chemotherapy for women with lymph node-positive, hormone-receptor-positive (HR (+)) breast cancer. However, despite the benefit of increasing disease-free survival (DFS), chemotherapy caused significant toxicities in patients who might not benefit from adjuvant therapy. In this clinical trial, the recurrence score based on the 21-gene breast cancer assay has been tested to predict for each patient whether chemotherapy will benefit women with lymph node-positive HR (+) breast cancer. The cost of the RxPONDER clinical trial was estimated at $27 million, and the expected value of research outcomes of the trial ranged between $450 million and $1 billion. The primary objective of this trial was to assess survival. However, this clinical trial was projected to feature a return on the investment of 17 to 39 times the NIH clinical trial cost.[60] This clinical trial was not just a lifesaving study for the participants but also improved the lives of future patients through changing the medical practice.

The impact of NIH scientific grant funding on patenting by pharmaceutical and biotechnology organizations has also been explored. In this current study, these bibliometric data were used to link specific grants to private sector innovations. A $10 million increase in NIH funding in a research area was found to result in a net increase of 2.3 patents. This means that every two to three NIH-funded grants generate 2.3 additional patents.[61] When these results are reflected in sales of the patented drugs, it was found that every one dollar in NIH funding might result in 1.40 dollars in patented drug sales. This is another excellent example of the NIH's contribution to the U.S.'s leadership role in cancer drug development.

(5) Providing Expertise for the Research Community

One of the most valuable elements of facilitating new drug discovery is expertise, which takes decades to acquire. NIH is one of the best scientific environments for doctors, nurses, clinicians, and scientists to share and expand their expertise through collaboration with pharmaceutical companies and

56 Pediatric Preclinical In Vivo Testing Consortium (PIVOT). https://preclinicalpivot.org/about-pivot/.

57 NCI Initiative to Speed Development of Childhood Cancer Therapies (2015). https://www.cancer.gov/news-events/cancer-currents-blog/2015/pptc-awards.

58 NCI Pediatric Preclinical in Vivo Testing (PIVOT) Program. https://ctep.cancer.gov/MajorInitiatives/Pediatric_PIVOT_Program.htm.

59 "NIH completes in-depth genomic analysis of 33 cancer types." https://www.cancer.gov/news-events/press-releases/2018/tcga-pancancer-atlas.

60 Wong, W.B. *et al.,* "The value of comparative effectiveness research: projected return on investment of the RxPONDER trial (SWOG S1007)." *Contemporary Clinical Trials, 2012.* 33(6): p. 1117-1123.

61 Azoulay, P., J.S. Graff Zivin, D. Li, and B.N. Sampat, "Public R&D investments and private-sector patenting: evidence from NIH funding rules." *The Review of Economic Studies, 2019.* 86(1): p. 117-152.

academia. The NIH scientific community has always been closely engaged with the research community through collaboration. All the collaborative efforts are established through various technology transfer agreements, and these agreements then formally bring the finest expertise on the topic into the discussion. Confidential Disclosure Agreements (CDAs) facilitate information exchange under confidentiality terms. Material Transfer Agreements (MTA) and Data Usage Agreements (DUA) are established to exchange materials and data, Clinical Trials Agreements (CTA) and Cooperative Research and Development Agreements (CRADA) are established to perform research in conjunction with the expertise needed to make the best of the collaboration effort.

(6) Making Research Materials Available for the Research Institutes and Universities

NIH has been very supportive of sharing research materials with the scientific community. If the research material is discovered and/or developed at NIH, these materials could be shared via a MTA with the research community. Besides this, NCI has many examples for material sharing programs with the research community. CTEP has the National Clinical Trials Network (NCTN) and the Experimental Therapeutics Clinical Trials Network (ETCTN) programs. Under these programs, clinical agents are available for clinical or non-clinical research use after receiving the NCI and collaborator company's approval for the proposed research.[62] The NCI Formulary is another excellent example. It was launched by CTEP in 2011. Since then, research synergy has been created to perform combination studies focusing on different agents targeting molecular pathways from collaborating pharmaceutical companies.[63] For this purpose, CTEP negotiated and executed NCI Formulary CRADAs with pharmaceutical collaborator companies. These CRADA agents are available to the NCI-funded ETCTN and NCTN institution academic investigators to conduct clinical trials in the U.S. or to any investigators for preclinical research. CTEP's efforts help the researcher to obtain agents by eliminating the lengthy agent access process between individual researchers and pharmaceutical companies and to offset the cost to purchase the agents.

NCI's Office of Cancer Clinical Proteomics Research (OCCPR) brings another material source for the research community. NCI OCCPR is part of the NCI's DCTD with a mission to improve prevention, early detection, diagnosis, and treatment of cancer. To serve this purpose, OCCPR launched an antibody program aimed at producing and characterizing standardized affinity agents for cancer-associated targets. These antigens and antibodies are now available to the scientific community for research purposes.[64]

Another great example is the NCI's Proteomic Data Commons (PDC). One of the critical roles of the PDC is to make available cancer-associated standardized biospecimen, clinical, and proteomic data to the research community. PDC is an excellent resource for understanding the functional role of proteins in cancer development, risks, and treatment design.[65]

(7) Putting Effort to Repurposing of Commercially Available Therapeutics for the New Indications

Drug repurposing refers to the use of an approved drug for a new disease indication. Because approved drugs have already been tested in humans, their approval for a new indication can be started earlier and approved by the FDA sooner. Therefore, repurposing a drug is an efficient way to cure a disease with a short-time drug development process at a lower cost.

The National Center for Advancing Translational Sciences (NCATS), one of NIH's institutes, launched an initiative to bring pharmaceutical companies and scientists together to repurpose abandoned compounds in May 2012. This initiative aimed to accelerate drug discovery and development.[66,67] NCATS established two research programs for drug repurposing: Toxicology in the 21st Century (Tox21) and Biomedical Data Translator (Translator). Tox 21 can manage 10,000 compounds, including 3,700 FDA-approved and investigational drugs, according to their bioactivity in vitro setting.[68] NCATS's advanced computerized technology can test thousands of drug candidates simultaneously, analyze the data, and predict which drug candidates can be repurposed for the new indication. One of the success stories of this initiative is the combination of berzosertib and topotecan. NCATS's drug repurposing effort led this combination to a clinical trial of small cell lung cancer.[69] NCATS and the NCI scientists developed a screening method to predict how to efficiently combine three or more cancer drugs.

62 Division of Cancer Treatment and Diagnosis, National Cancer Institute. National Cancer Institute early therapeutics clinical trials network program guidelines. https://ctep.cancer.gov/initiativesPrograms/docs/ETCTN_Program_Guidelines.pdf.

63 NCI FORMULARY. https://nciformulary.cancer.gov/.

64 NCI's Office of Cancer Clinical Proteomics Research (OCCPR). https://proteomics.cancer.gov/about/office-overview.

65 The National Cancer Institute's Proteomic Data Commons (PDC). https://pdc.cancer.gov/pdc/about.

66 Allison, M., "NCATS launches drug repurposing program (2012), *Nature Publishing Group U.S. New York.*

67 Liu, F. *et al.,* "Exploring NCATS in-house biomedical data for evidence-based drug repurposing." *PLOS One, 2024.* 19(1): p. e0289518.

68 *Ibid.*

69 "Drug Testing Approach Uncovers Effective Combination for Treating Small Cell Lung Cancer." https://ncats.nih.gov/news-events/news/2021/drug-testing-approach-uncovers-effective-combination-for-treating-small-cell-lung-cancer#:~:text=The%20NCI%20researchers%20tested%20the,25)%20improve%20in%20some%20way.

This new method helps medical practitioners find the most effective drug combinations at safe concentrations and exposures.[70]

(8) Establishing Synergy Within the Research Community with an Effort to Shorten Drug Development Process via Renovation of Clinical Trial Timelines

To transform new therapeutic approaches into the standard of care for cancer patients, they need to be approved by regulatory authorities following clinical trials that demonstrate the efficacy and safety of the treatment. Sufficient patient enrollment is one of the most important factors to run clinical trials successfully as sufficient patient enrollment leads to statistical certainty of the treatment outcome. However, sufficient patient accrual has been an issue for the successful completion of many clinical trials.[71] To address this obstacle, CTEP established and organized the Operational Efficiency Working Group (OEWG) in 2008 to accelerate the timely accrual and completion of NCI-sponsored clinical trials. The OEWG established new strategies and guidelines within the research community, resulting in robust communications, improved progress monitoring, and protocol-tracking web sites. Initial OEWG results showed that with these improvements, development times for phase I–II studies are reduced from a median of 541 days to a median of 442 days, an 18.3 percent decrease. Development times for phase III trials were reduced from a median of 729 days to 395 days, a 45.7 percent decrease.[72]

(9) Training Future Doctors, Nurses and Scientists

NIH is one of the best scientific environments for future doctors, nurses, clinicians, scientists, and other future employees in life science fields. NIH researchers are pioneers in their fields. Dozens of scientists supported by NIH have received Nobel Prizes for their groundbreaking achievements. NIH consistently attracts and educates the best scientists of the biomedical field. As of 2024, 174 researchers, either from NIH or supported by NIH, have received or shared 104 Nobel Prizes. 214 researchers, who are either extramural, intramural researchers or institutional award recipients, received the Lasker Award, also known as "America's Nobel." The Lasker Award recognizes the contributions of scientists, physicians, and public servants who have made significant advances in the understanding, diagnosis, treatment, cure, and prevention of human disease.[73]

NIH has well-established research training and career development programs for early career researchers and health professionals. For example, recent college graduates can have opportunities for research training in basic, translational, or clinical research at NIH. This program also supports students with diverse backgrounds to have a career in research and health care.[74] NIH's postdoctoral training program further provides excellent research training for future scientists and scientific leaders with recent doctoral degrees. Our earlier article found that over 1,700 former NCI fellows or employees trained by NCI are current or former employees of the 20 biggest pharmaceutical companies.[75] If we examine the whole NIH for this purpose, we will estimate that this number would exceed 2,000.

(10) Taking Initiative Steps to Share Data with the Research Community to be Used in Secondary Research Purposes

NIH has a mission to share publicly-funded research results with the research community and the public to accelerate biomedical research, validate research outcomes, and provide access to datasets for secondary research purposes. NHGRI, one of 27 NIH institutes, completed the human genome sequence in April 2003. NHGRI gives an opportunity for scientists around the world to access a database that facilitates and accelerates biomedical research. Another example is The Database of Genotypes and Phenotypes (dbGaP), an NIH-sponsored data repository. The dbGaP was established in 2006 to archive, curate, and distribute data generated from millions of study participants and samples, and trillions of phenotypes. This database provides data, including individual-level molecular and phenotype data, analysis results, medical images, and general information about the study, including research protocols and questionnaires.[76]

(11) Having a Mission to Create Public Health Awareness to Prevent Cancer via Health Information Initiatives

One of NIH's great missions is to share research findings and the most recent updated health information with the public. This helps the public build better health habits, gain knowledge of health-related topics, and be aware of early disease symptoms, which is crucial for wellness, including social,

70 Allison, M., "NCATS launches drug repurposing program (2012)," *Nature Publishing Group U.S. New York.*

71 Cheng, S.K., M.S. Dietrich, and D.M. Dilts, "A sense of urgency: evaluating the link between clinical trial development time and the accrual performance of cancer therapy evaluation program (NCI-CTEP) sponsored studies." *Clinical Cancer Research, 2010.* 16(22): p. 5557-5563.

72 Massett, H.A. *et al.,* "Transforming the early drug development paradigm at the National Cancer Institute: the formation of NCI's experimental therapeutics clinical trials network (ETCTN)." *Clinical Cancer Research, 2019.* 25(23): p. 6925-6931.

73 Scientific Breakthroughs. https://www.nih.gov/about-nih/impact-nih-research/revolutionizing-science/scientific-breakthroughs.

74 NIH Research Training and Career Development Programs. https://researchtraining.nih.gov/

75 Uygur, B., S. Ferguson, and M. Pollack, "Hiding in plain sight: surprising pharma and biotech connections to NIH's national cancer institute." *Journal of Commercial Biotechnology, 2022.* 27(2): p. 5.

76 Tryka, K.A. *et al.,* "NCBI's Database of Genotypes and Phenotypes: dbGaP." *Nucleic Acids Research, 2014.* 42(D1): p. D975-D979.

emotional, physical, and disease and environmental wellness. NIH's health information related to wellness also contributes to cancer prevention.[77]

4. Conclusion

Everything starts with an idea, like a seed. You then need to nourish it with all your effort to see it grow into a big tree as a shade for a warm summer or watch its little blooms transform into fruits. The innovations in cancer therapeutics are much the same. They all start with an idea. If they are lucky enough to find a place like NIH, they can grow and become a cure for a disease. All these transformations from the seed into a fruitful tree or transforming an idea into a cure require a community and an ecosystem with resources and active effort.

In this study, we aimed for two purposes:

1. Uncovering the contributions of NIH in the cancer drug development landscape
2. Demonstrating the role of technology transfer as an important catalyst at every step of cancer drug development

As we have described, cancer drug development requires a tremendous amount of time, funding, and excellent expertise. In Figure 16, 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 practical application and on to the bedside for a patient's health. ■

NIH Health Information:
https://www.nih.gov/health-information

77 Kreps, G.L., "The central role of relevant health information for promoting cancer prevention and control." *Medical Research Archives, 2023.* 11(2).