The role of government in the funding of clinical trials for the development of new therapeutics (drugs)

Over the period clinical trials have played a foundation in determining the safety and efficacy of a novel drug substance. The role of clinical trials cannot be overlooked. But, despite its valuable role, in the early stage, it occasionally comes with a high risk of failure and huge financial investments. Since private funding is often limited at this stage, government support plays a crucial role. In this essay, we dive into how government funding mitigates market risks in order to accelerate life-saving therapeutic innovations, ensure equal access to clinical trials, and address healthcare disparities.

Government Funding in Early-Stage Research:

One of the key roles of government funding in clinical trials is its ability to support early-stage research. Clinical trials often involve extensive testing, rigorous safety evaluations, and large-scale human trials to ensure efficacy and safety before a drug can be approved for widespread use, which requires approximately $1.3 billion and $2.6 billion, of which clinical trials account for approximately 60%.[1] The main reason for discouragement for any private company from investing in the early stage of the drug discovery and development process is that the probability of failure is about 90%.[2] So, the question is who fills this gap for the need for funding for clinical trials? Government agencies such as the National Institutes of Health (NIH), the Food and Drug Administration (FDA), and the National Sanitation Foundation (NSF) bridge this gap by providing crucial funding. Distinct examples of this role is the ground-breaking government-funded research during outbreaks such as Ebola[3] and COVID-19[4] for vaccines and treatments.

When private investors find it too risky to support drug research and development which involves high costs and risks typically in early-stage, the government plays the role in supporting such clinical trials.[5] For instance, the NIH's annual budget reached $45 billion in 2022 (Table s1 in supporting information), with a significant portion allocated to medical research, including clinical trials.[6]

Government initiative towards market failure:

The pharmaceutical industry tends to focus on drugs with high-profit potential, leaving rare diseases and global health issues underfunded and underserved. Government funding helps address this "*market failure*" by supporting treatment development for these neglected populations. The Orphan Drug Act (ODA) of 1983 is one example of how government intervention has addressed market failure. By offering incentives like tax credits and market exclusivity, ODA spurred the development of over 600 orphan drugs[7], which has contributed to a steady incline of orphan drug approvals over the years.[8,9]

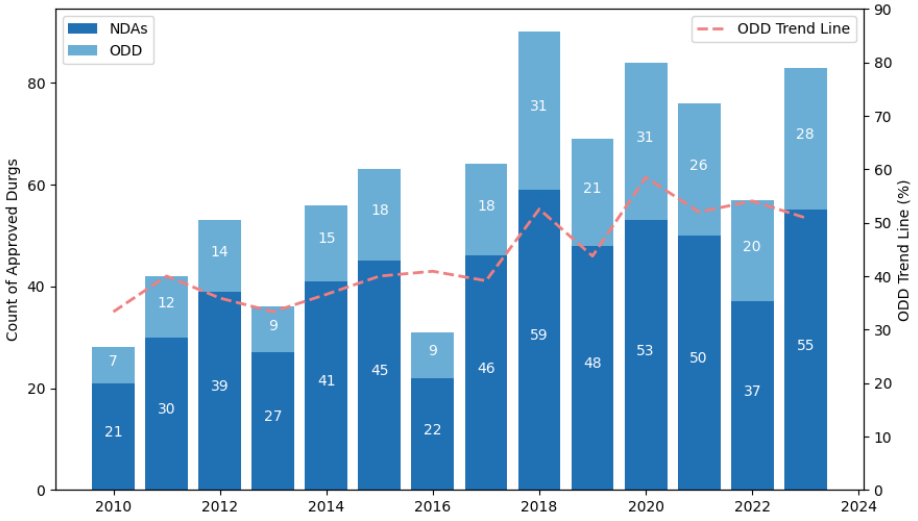
Nevertheless, the importance of government agency funding is crucial for the transformation of rare disease drug development. For instance, a study indicates that in 2022, the FDA's Orphan Product Grant Program allotted $38 million to support the development of treatments for rare diseases.[10] In 2023, $6.9 billion of NIH funding supported trials targeting rare diseases, enabling advancements that would not have been possible without public funding.[11] This commitment ensures that therapeutics are developed for conditions that may not have immediate financial returns but are critical for public health. FDA reported that 28 out of 51 approved drugs in the year 2023 are orphan drugs that treat rare diseases (Figure 1(a)). For example, an FDA-approved drug in October 2023 directly funded by the NIH is *vamorolone*, which was developed for Duchenne muscular dystrophy (DMD). This drug was created through a partnership between ReveraGen BioPharma and the NIH's National Center for Advancing Translational Sciences (NCATS) as part of the Therapeutics for Rare and Neglected Diseases (TRND) program.[12]

Public Health Benefits of Government-Funded Trials:

Government funding of clinical trials is crucial during public health crises, where rapid development and dissemination of therapeutics are essential. For example, during the COVID-19 pandemic, the U.S. government played a pivotal role in accelerating the development of vaccines through initiatives like "Operation Warp Speed" and invested over $10 billion in funding pharmaceutical companies, the government fast-tracked clinical trials set the highest achievement in medical history.[13,14] The trend of notable government-funded projects has been given in Table s1.

Beyond the emergencies, government-funded trials focus on diseases concerning disproportionately affected vulnerable populations. Government-funded clinical trials to advance treatments for diseases like HIV/AIDS, tuberculosis, and malaria—illnesses that primarily affect lower-income countries, shows commitment towards prioritizing public health objectives over profit.[15,16] This is where government-funded trials differ from private-sector trials, which are mostly driven by the market potential over public health concerns.

(a)



(b)

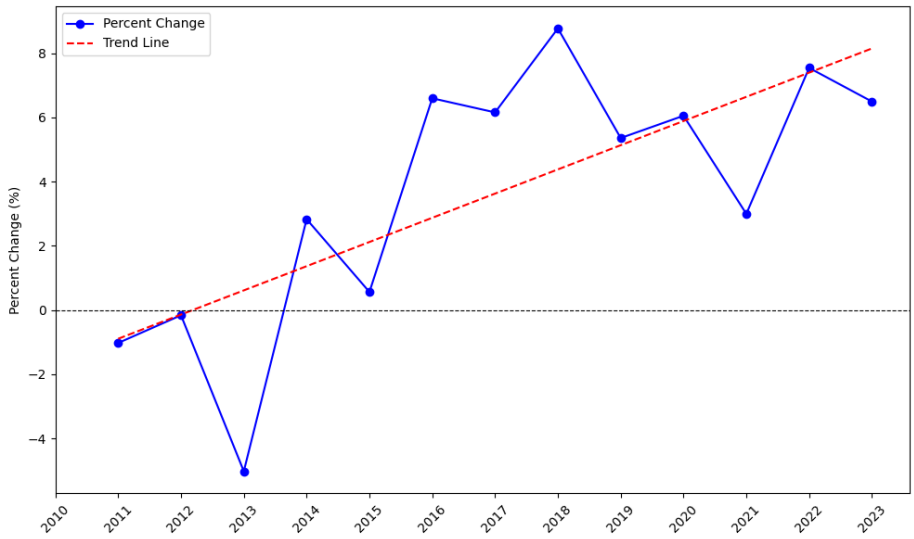


Figure 1: (a) FDA Annual Counts of Total New Drug Approvals (NDAs) and Orphan Designated Drugs (ODDs) (b) Percent Change in NIH Budget Over the Years

Ensuring Access and Equity in Therapeutic Development:

Another significant argument for government funding is that it ensures equitable access to new API. The pharmaceutical industry prioritizes research and development in areas with high potential returns, often targeting chronic diseases like cancer and diabetes that are more common in wealthier populations, which can increase health disparities. In contrast, government agencies like the NIH and FDA focus on diseases that are less profitable but have a bigger impact on global health.

Government intervention is helping to address these disparities by funding clinical trials for drugs that serve underserved populations. Figure 1(a) depicts the annual increase in the proportion of ODD among total NDAs from 2010 to 2023, highlighting the success of government intervention in addressing conditions neglected by private industry. By providing the financial support needed to study rare diseases, the government ensures that all patients, regardless of the rarity of their condition, have access to life-saving treatments.

Additionally, government-funded clinical trials are often conducted in public hospitals and universities, which tend to include more diverse populations, ensuring that drugs are effective across various demographic groups. For instance, a study found that 64% of NIH-funded trials enrolled women and minority groups, compared to only 36% of industry-funded trials. Where government agencies are enrolling more diverse populations (women and minorities) in clinical trials, industry and federal agencies still must ensure that the enrolment is fair and equitable.[17,18] This diversity is essential for ensuring that drugs are safe and effective for all segments of the population, reducing healthcare disparities, and promoting more equitable health outcomes. Government involvement also ensures that the results of publicly funded trials are disseminated in open-access formats, contributing to the broader scientific knowledge base and preventing redundant studies.[19]

Economic Benefits of Government-Funded Clinical Trials:

In addition to public health benefits, government funding for clinical trials also generates significant economic advantages. By sharing the financial burden of early-stage research, government funding reduces the cost of drug development for private companies, potentially leading to lower drug prices once therapeutics reach the market, and can also lead to significant cost savings for public health systems. For instance, the importance of therapeutics in managing COVID-19 effective treatments has decreased the severity of the disease, thus reducing the need for intensive care, hospitalization, and the burden on healthcare infrastructure.[20]

The average return on investment (ROI) for research funded by the National Institutes of Health (NIH) in 2022 resulted in approximately $2.64 in economic activity for every dollar invested. The ROI for every $100 million of NIH-supported research funding is 498%, which can be utilized in further research and development.[21] Furthermore, the government is significantly funding the universities and pharmaceutical companies, which has a huge indirect impact on job creation in all the nations. As a result, government funding not only benefits public health but also contributes to the overall economic well-being of society.

Limitations in Public Funding:

While government funding for clinical trials offers numerous advantages, it is not without limitations. Public funding is often constrained by budgetary limitations, which can result in underfunding for certain research areas or delays in the approval and completion of clinical trials.[22] Funding from the NIH to universities or research institutions frequently involves substantial indirect cost reimbursements, which can limit the amount available for direct research costs.[23] The NIH budget for research funding (Figure 1(b)) as well as in clinical trials (Table s1) have been growing over the years. However, numerous studies indicate that public funding tends to offer fewer potential benefits for clinical trials compared to private funding.[16] While government financing of R&D has decreased from 44.2% in 1981 to 28.3% in 2013, industry funding has risen from 51.6% to 60.8% during the same period.[24]

Nevertheless, the government is potentially making efforts to improve current challenges in clinical trials. For instance, revising existing laws or introducing new legislation that explicitly addresses the reimbursement

challenges faced by patients and healthcare providers involved in clinical trials. By addressing the gaps left by private industry, the government ensures that public health remains a priority and that innovations in medicine are accessible to all. Further improvements in the budgets can be seamless with the use of budget tools in order to ensure the efficiency and fair transparency of the trial budget.[22]

Conclusion:

Government funding for clinical trials is essential for advancing drug development, ensuring equitable access, and protecting public health, especially in areas where private investment is limited. By prioritizing diseases that lack immediate commercial incentives and addressing healthcare inequities, government support facilitates therapeutic advancements that may not be financially viable for private entities. While budget limitations pose challenges, the economic and public health benefits of government-funded trials highlight the importance of continued public investment in clinical research.

Supplementary materials:

Supplementary material associated with this essay can be found in the online version at https://github.com/AriSa365/essay_gov_ct.com/blob/Data-Science/supp_info_govt_ct.pdf

References:

1. DiMasi JA, Grabowski HG, Hansen RW. Innovation in the pharmaceutical industry: new estimates of R&D costs. *Journal of health economics*. 2016;47:20-33.
2. Hay M, Thomas DW, Craighead JL, Economides C, Rosenthal J. Clinical development success rates for investigational drugs. *Nature biotechnology*. 2014;32(1):40-51.
3. Kiszewski AE, Cleary EG, Jackson MJ, Ledley FD. NIH funding for vaccine readiness before the COVID-19 pandemic. *Vaccine*. 2021;39(17):2458-2466.
4. Balaguru L, Dun C, Meyer A, et al. NIH funding of COVID-19 research in 2020: a cross-sectional study. *BMJ open*. 2022;12(5):e059041.
5. Reddy P, Singh M. The Impact of Research and Development Investments on Drug Development Outcomes and Health Improvements. *International Journal of Responsible Artificial Intelligence*. 2023;13(12):1-10.
6. National Institutes of Health (NIH) Budget and Spending. Accessed October 27, 2024. https://www.nih.gov/about-nih/what-we-do/budget
7. Shulman SR, Bienz-Tadmor B, Seo PS, DiMasi JA. Implementation of the orphan drug act: 1983-1991. *Food & Drug LJ*. 1992;47:363.
8. Brown DG, Wobst HJ. Analysis of orphan designation status for FDA approved drugs, and case studies in oncology, neuroscience and metabolic diseases. *Bioorganic & Medicinal Chemistry*. 2023;80:117170.
9. Fermaglich LJ, Miller KL. A comprehensive study of the rare diseases and conditions targeted by orphan drug designations and approvals over the forty years of the Orphan Drug Act. *Orphanet Journal of Rare Diseases*. 2023;18(1):163.
10. Rubin R. New funding for research into rare diseases treatments. *JAMA*. 2022;328(19):1898-1899.
11. Health NIo. *Estimates of Funding for Various Research, Condition, and Disease Categories (RCDC)*. May 14 ed. NIH Research Portfolio Online Reporting Tools (RePORT); 2024.
12. Disorders NIoN, Stroke. NINDS Small Business Funding Leads to New Therapy for Duchenne Muscular Dystrophy. 2024. https://www.ninds.nih.gov/news-events/news/highlights-announcements/ninds-small-business-funding-leads-new-therapy-duchenne-muscular-dystrophy
13. Tewarson H, Greene K, Fraser MR. State strategies for addressing barriers during the early US COVID-19 vaccination campaign. American Public Health Association; 2021. p. 1073-1077.
14. Ho RJ. Warp-speed Covid-19 vaccine development: beneficiaries of maturation in biopharmaceutical technologies and public-private partnerships. *Journal of pharmaceutical sciences*. 2021;110(2):615-618.
15. Fu W, Chou S-Y, Wang L-S. NIH Grant Expansion, Ancestral Diversity, and Scientific Collaborations in Genomics Research. *Available at SSRN 4499917*. 2023;

16. Zhang J, Yuan Y. Industry-funded clinical trials: Beneficial or harmful? : Taylor & Francis; 2015. p. 109-112.
17. Flores LE, Frontera WR, Andrasik MP, et al. Assessment of the inclusion of racial/ethnic minority, female, and older individuals in vaccine clinical trials. *JAMA Network Open*. 2021;4(2):e2037640-e2037640.
18. Health NIo. Research Investment and Scientific Resources (RISR). Updated 2024-10-27. Accessed October 27, 2024. https://report.nih.gov/RISR/
19. Suber P. Ensuring open access for publicly funded research. British Medical Journal Publishing Group; 2012.
20. Cutler DM, Summers LH. The COVID-19 pandemic and the $16 trillion virus. *Jama*. 2020;324(15):1495-1496.
21. Health NIo. *Direct Economic Contributions*. Updated March 30, 2023 ed. National Institutes of Health; 2023.
22. Nevens H, Harrison J, Vrijens F, et al. Budgeting of non-commercial clinical trials: development of a budget tool by a public funding agency. *Trials*. 2019;20:1-10.
23. Office USGA. *National Institutes of Health Research: Impact of Indirect Cost Rate Setting on Biomedical Research at Universities*. Government Document. 2013:Accessed October 27, 2024. https://www.gao.gov/pdf/product/658087
24. Archibugi D, Filippetti A. The retreat of public research and its adverse consequences on innovation. *Technological Forecasting and Social Change*. 2018;127:97-111.