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MEASURING THE ECONOMIC AND ACADEMIC IMPACT OF PHILANTHROPIC FUNDING: THE BREAST CANCER RESEARCH FOUNDATION

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Using survey data gathered from grantees of the nonprofit Breast Cancer Research Foundation (BCRF), we investigated the commercial and non-commercial impacts of their research funding. We found significant impact in both domains. Commercially, 19.5% of BCRF grantees filed patents, 35.9% had a project that has reached clinical development, and 12 companies have or will be spun off from existing projects, thus creating 127 new jobs. Non-commercially, 441 graduate students have been trained by 116 grantees, 767 postdoctoral fellows have been trained by 137 grantees, 66% of grantees have used funding for faculty salaries, 93% have achieved collaboration with other researchers, and 42.7% have enacted process improvements in research methodology. Econometric analysis identifies BCRF funding and associated process improvements as key factors associated with the likelihood to file patents. However, we also found that the involvement of more than one institution in a collaborative project had a negative impact on subsequent development. This may point to frictions introduced by multi-university interactions.

1 Introduction

The optimal amount of investment in biomedical research and development is frequently debated. Among such investments, cancer research with a focus on improved management, including cure, is one of the most active and capital intensive. Significant advances have been made in the field,

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as demonstrated by a significant decline in cancer deaths over the past quarter century. Nevertheless, the collection of diseases labeled *cancer* represents a major source of morbidity and mortality. In 2020, cancer claimed an estimated 606,520 lives in the United States alone, making it the second leading cause of death.

The effort to improve this situation involves intense competition for financial resources. However, the rewards are great for all stakeholders. According to Lakdawalla *et al.* (2010), average life expectancy in the United States has increased by four years across all cancer types, with an average willingness-to-pay of $322,000 for these survival gains. Life is, obviously, priceless, and cancer research and development has led to an estimated 23 million additional years of life in this population. In addition, $1.9 trillion of additional social value, or $82,000 per extra year of life is generated by this metric. Two principal financial stakeholders—the pharmaceutical industry and healthcare providers—capture between 5% and 19% of the value created.[1] Spending on breast cancer has the highest value-added, as breast cancer has the highest lifetime value of survival gains ($359,595) and the highest implied value of a life-year, on average $99,887 per patient.[2] In addition to profound humanitarian considerations, these high rates of return likely underlie the heavy flow of investment into breast cancer management research.

As the value of research and development in oncology has increased over time, however, so have the associated costs. DiMasi *et al.* (2003) report the cost of first-in-human (i.e., novel) drug trials over the period 1983 to 1994 was $802 million per approved drug (in 2000 dollars). For the later period of 1989 to 2002, Adams and Brantner (2006) estimate a higher cost: $868 million (in 2000 dollars). A subsequent study by DiMasi and Grabowski (2007), focused on large-molecule approved drugs first tested between 1990 and 2003, finds a cost of $1.2 billion (in 2005 dollars). Paul *et al.* (2010) find that new molecular entities launched in 2007 were developed at a cost of $1.8 billion (in 2008 dollars), while O'Hagan and Farkas (2009) estimate a cost of $2.2 billion (in 2009 dollars) for new molecular entities launched in 2009. The most recent study by DiMasi *et al.* (2016) puts the cost even higher, at $2.6 billion (in 2013 dollars), for drugs with initial human testing that occurred from 1995 to 2007.

However, an even more worrisome trend is the decline in the number of new drugs approved each year per billion dollars of research and development spending in the biopharmaceutical industry. This relationship was dubbed "Eroom's" Law—the reverse of Moore's law—by Scannell *et al.* (2012), and is displayed in Figure 1.[3]

Given these outsized costs and the declining relative productivity trend, a key factor in evaluating the allocation of research funding is the return on investment (ROI) of cancer research. Because the products of this research are inherently difficult to quantify, the academic literature has a variety of unconventional measures of ROI when evaluating funding decisions. Moreover, the recent focus on "impact investing" has created an entirely new set of metrics for measuring ROI, including the so-called "double bottom line" in which social impact is included in valuing the performance of financial investments.

This focus on the ROI of biomedical innovation serves as the motivation for our analysis of the research portfolio funded by the Breast Cancer Research Foundation (BCRF), a nonprofit foundation established in 1993 with the mission to end breast cancer by advancing the most promising biomedical research in this field. We do not rely on any theoretical model of the effects of funding, but instead examine the data directly. Investigating in

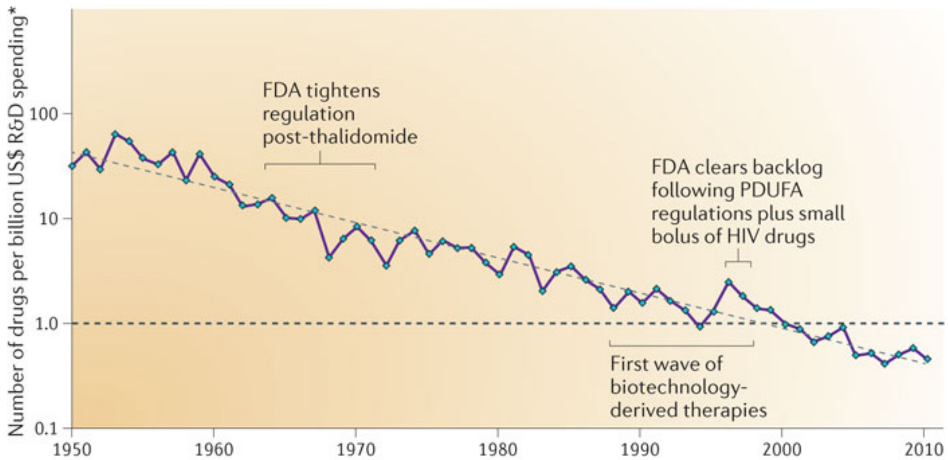

Figure 1 Eroom's Law: The number of new drugs approved each year per billion dollars of R&D spending in the biopharma industry.

Source: Scannell *et al.* (2012).

detail the outcomes of the BCRF-funded projects provides a snapshot of the creation of research value and the real ROI of funding for over two decades.

Using survey data gathered from grantees of BCRF, we investigated the commercial and non-commercial impacts of their research funding and document significant impact in both domains. Commercially, 19.5% of BCRF grantees filed patents, 35.9% had a project that reached clinical development, and 12 companies have or will be spun off from existing projects, thus creating at least 127 new jobs.

Non-commercially, 441 graduate students have been trained by 116 grantees, 767 postdoctoral fellows have been trained by 137 grantees, 66% of grantees have used funding for faculty salaries, 93% have achieved collaboration with other researchers, and 42.7% have enacted process improvements in research methodology. Using econometric analysis on BCRF grantee data, we show that BCRF funding and associated process improvements are key factors associated with the likelihood to file patents. However, we also found that the involvement of more than one institution in a collaborative project had a negative impact on subsequent development. This may point to frictions introduced by multi-university interactions.

Although BCRF has a focus on breast cancer, some of the research extends to related cancer types. The framework developed in this paper can be applied by nonprofit and government research funding organizations that seek to optimize their impact on research. In addition, the factors that affect the outcomes of projects in academia funded by nonprofits may also affect the outcomes of projects in industry, since the conditions of the scientific process are similar, and the incentives for innovation are comparably strong.

2 Literature Review

Bisias *et al.* (2012) apply financial portfolio theory to data from the National Institutes of Health (NIH), which is the U.S. federal medical research agency and the largest investor in biomedical research worldwide. Using the impact on U.S. years of life lost (YLL) as a metric of ROI, and data on NIH funding appropriations for the period from 1965 to 2007, the authors estimate the set of optimal funding allocations across seven groups of disease-oriented NIH institutes that would provide the greatest expected ROI for a given level of risk. The findings suggest that improvements in expected ROI (89–119% vs. the present value) or reductions in risk (22–35% vs. the present value) are possible while holding risk or expected return constant, and that a 28–89% reduction in average YLL per unit of risk may be feasible. Given that YLL is not a perfect measure of disease burden, the results are not without controversy. Nevertheless, the analysis provides a concrete starting point for incorporating ROI into large-scale biomedical R&D funding allocations by the NIH and other funding organizations.

An additional approach to evaluating the return on biomedical R&D funding considers the short-term economic impact of funding decisions on labor productivity. As human capital accumulation is a significant driver of scientific discovery and development, labor productivity can be a metric for the effectiveness of funding allocation and ROI. Weinberg *et al.* (2014) analyze an extensive dataset of expenditure records for 2012 from nine major research universities in the Midwest. These universities received a total of about $7 billion in R&D funding from all sources in 2012 and of that amount, 56% was from federal agencies. As the type of scientific research conducted at these universities is representative of most other major research universities, this data provides a valuable insight into the outcomes of federally funded research activity.

Support from the NIH is substantial in biomedical research. The short-term labor productivity gained or lost by the people supported by R&D funds is an important measure of the ROI of NIH funding. Almost 40% of individuals on federally funded research projects are funded by the agency, in whole or in part. More than 50% of federally funded postdoctoral fellows use NIH grants in some way, but only 24% of graduate students and 22% of undergraduates. Because postdoctoral fellows are closest to completing their training, the consequences of funding cuts (or the benefits of funding increases) in a particular therapeutic area fall disproportionately on the future capacity for cutting-edge R&D in that area.

A metric for ROI specifically targeted for drug discovery is the number of new drug approvals. Given the consistently rising costs of drug development in the U.S., it is worth asking if drugs are being discovered more quickly, or whether there are other causes behind the higher costs of finding a cure.

Dorsey *et al.* (2009) attempt to answer this question. They estimate the overall biomedical research investment in the U.S. from both federal and industry sources and the number of drug approvals for the decade from 1995 until 2005, aggregating FDA approvals in eight therapeutic areas: cardiovascular, endocrine, gastrointestinal, genitourinary, HIV/AIDS, infectious disease excluding HIV, oncology, and respiratory. While financial support for biomedical research for the period increased across all therapeutic areas (between 43% and 369%), the figure for new drug approvals stayed flat or declined across therapeutic areas. Given an 8-year lag to allow for drug development, neither total funding nor industry funding was correlated with future drug approvals. The steep increase in R&D funds in this period failed to lead to a higher number of new drug approvals, despite the increase of funding across therapeutic areas and its alignment with disease burden.

Finally, a major reason to explore the outcomes of funding academic research, and to consider different metrics for determining its ROI, is the increasing commercialization of academic work.

Commercialization is the expected endgame of research within the biopharma industry. However, researchers in academia have started to experience pressure to commercialize their research to compete with industry and attract R&D funding and maintain a successful academic career (Caulfield and Ogbogu, 2015). The increased pressure to commercialize academic research will have both negative and positive effects, and at this point it is not possible to determine which ones will be dominant. However, it has the potential to lead to undesirable academic practices. These include not publishing negative results, not sharing findings that might speed the progress of other scientists, and avoiding research that is not commercially viable (e.g., basic research). Hence, should the trend for the commercialization of academic work continue, it would be advantageous to find incentives to proactively counteract the possible negative effects, including undesirable behavior among scientists. Simultaneously, we would need to optimize the potential for commercialization since commercialization is the proven way to make scientific discoveries help people. These goals will require close analysis of the outcomes of funded research.

3 The Breast Cancer Research Foundation

BCRF, founded in 1993, had raised and expended over half a billion dollars in breast cancer research at the time of our analysis. The foundation's stated mission is to further all aspects of breast cancer prevention, diagnosis, and management by providing "critical funding for cancer research worldwide to fuel advances in tumor biology, genetics, prevention, treatment, metastasis and survivorship" (Breast Cancer Research Foundation, n.d.). The focus on research is one of its main distinguishing characteristics and over 90% of funds raised are spent on research programs. BCRF has been awarded the highest grades for commitment, performance, and consistency by groups that monitor charities in the U.S. and worldwide.

Based on pharmaceutical spending, oncology is currently the third largest therapeutic area in the U.S. (after anti-diabetics and immunology), with $72 billion spent in 2020 (Statista, 2021a). Thanks to research on specific oncology therapies, the mortality rate from breast cancer in the U.S. has decreased from 31.9 per 100,000 people in 1950 to 19.7 per 100,000 as of 2018 (Statista, 2021b). Hence, considerable progress toward eradication of breast cancer has been accomplished, but it is also clear that much remains to be done.

BCRF has established itself as a leader among nonprofits that fund academic research on breast cancer. BCRF-funded researchers are in academia and other medical institutions and none of the funding goes directly into the commercial drug discovery pipeline. As stated on the foundation's website:

> In 2016-2017, BCRF will award $57 million in annual grants to more than 250 scientists from top universities and medical institutions around the globe. In addition, BCRF has established the Evelyn H. Lauder Founder's Fund, a multi-year international program dedicated to metastasis that is the first large-scale global effort to unravel the biology of metastasis, with more than $30 million earmarked to date. It is the largest privately funded project exclusively focused on metastasis in the world.

It should also be recognized that in an era in which molecular abnormalities underlying cancers are being discovered to cross organ-of-origin boundaries, progress against one type of cancer accelerates progress in other areas. Therefore, there is significant motivation to improve research management and operations as well as to collect and distribute more funds to support meritorious research. One result of this desire is the project described in this paper. BCRF was interested in enumerating the outputs from the projects it has funded since its inception, both commercial and non-commercial. This econometric research is intended to help clarify the magnitude of the foundation's impact by using different metrics for ROI. Furthermore, it may prove useful in informing decisions regarding policies to encourage investment in specific types of returns and in developing administrative structures to remove obstacles that might be hindering project outcomes.

4 Data and Methods

We designed two surveys to elicit information about all outcomes of the projects funded by BCRF through 2014. The first survey, "BCRF Economic Impact Study Survey," focused on commercial outcomes, and the second survey, "Non-Commercial Impact of BCRF Grants," on non-commercial outcomes. Both survey documents are included in the Appendix. All BCRF awardees, a total of 218, who were funded up to the 2014–2015 award year were asked to fill out both surveys online. Of note, some BCRF research involves sociologic, quality-of-life, and survivorship topics rather than projects likely to have commercial product implications. Our analysis has two parts. First, we identify ROI metrics that are of interest. Second, we analyze the results econometrically to determine the factors driving these ROIs and their implications for the future of BCRF. Table 1 provides a comprehensive list of the ROI metrics that we include in our analysis.

4.1 Non-commercial impact

Of the BCRF grantees surveyed, 72% completed the questions about the non-commercial impact of their BCRF-funded research. The ROI metrics used to determine the non-commercial impact of this funding include human capital in training, faculty payroll, collaboration with others, and improvements in research methodology.

Table 1 Non-commercial and commercial ROI metrics.

Non-commercial ROI metrics	Commercial ROI metrics
Number of graduate students supported	Number of patents filed
Number of postdocs supported	Clinical development phase reached
Number of faculty on payroll	Number of startups spun-off
Collaboration with other organizations/ researchers	Number of new jobs created
Improvements in research methodology	Venture capital attracted
Additional grant funding attracted	Intellectual property licensed

The impact on human capital in training is a significant metric for ROI from the societal point of view, as graduate students and postdoctoral fellows typically intend to move promptly into independent research positions. Based on this analysis, 441 graduate students were trained by 116 grantees, and 767 postdoctoral fellows were trained by 137 grantees. Most typically, a grantee will train one or two graduate students and two postdoctoral fellows on BCRF-funded research projects. Figures 2 and 3 give the full distribution of graduate students and postdocs who have been trained in the labs of BCRF-financed researchers.

Figure 2 shows that 41 grantees did not support graduate students. This is a high number and needs explanation. Typically, principal investigators that do not support graduate students are not affiliated with major teaching institutions. Our data shows that 68% of the grantees who did not support graduate students fall in that category.

The next metric for ROI is the impact on faculty payroll. BCRF funds may be used for research

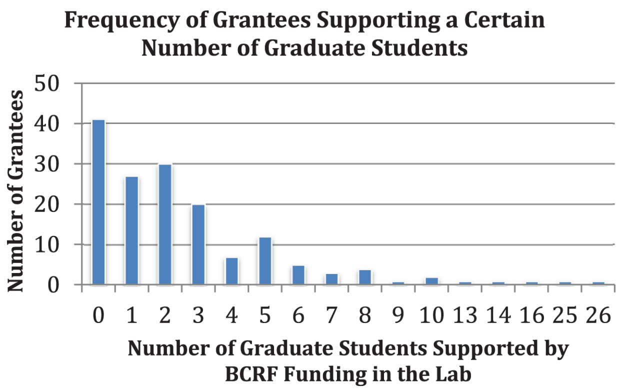

Figure 2 Frequency of grantees supporting a certain number of graduate students.

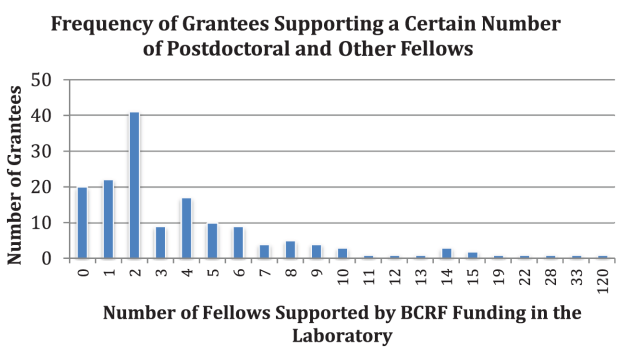

Figure 3 Frequency of grantees supporting a certain number of postdocs and fellows.

supplies, materials, and related costs, as well as for salary support for principal investigators and key research personnel. We found that 65% of grantees used funding for faculty salaries, as shown in Figure 4. This includes partially- and fully-paid salaries.

For the non-commercial impact of BCRF funding on the research process, we first consider the level of collaboration with others, and second, the presence of improvements in research methodology (e.g., reagent creation, process improvements, or validation assays). A large body of economic literature has shown that there are strong beneficial effects for the advancement of innovation when researchers collaborate, due to knowledge spillover. Figure 5 shows that 93% of BCRF grantees have collaborated with other organizations and researchers, suggesting a very high level of exchange of ideas within the breast cancer research community. BCRF funding has enabled new or expanded collaborations, including collaborations bridging clinical and basic research, collaborations with bioinformatics experts, international collaborations, collaborations for designing clinical trials, and collaborations extending research analysis into multiple tumor types, including ovarian, melanoma, prostate, colon, and lung cancers.

Improvements in research methodology lead to greater efficiency, which benefits current projects and any future research that uses similar techniques. We found that 42.7% of BCRF grantees enacted process improvements in their research methodology, as shown in Figure 6. For faster results, it may be optimal to encourage grantees to follow similar improvements as much as possible.

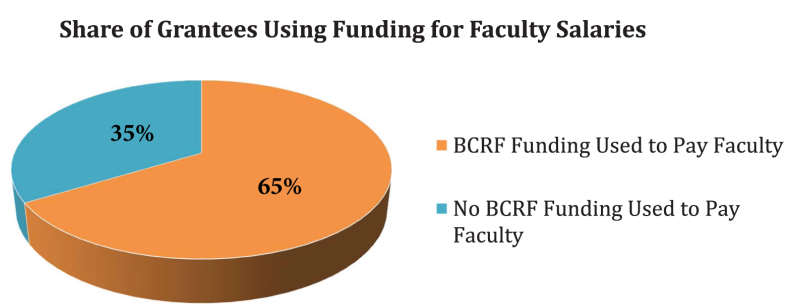

Figure 4 Share of grantees using funding for faculty salaries.

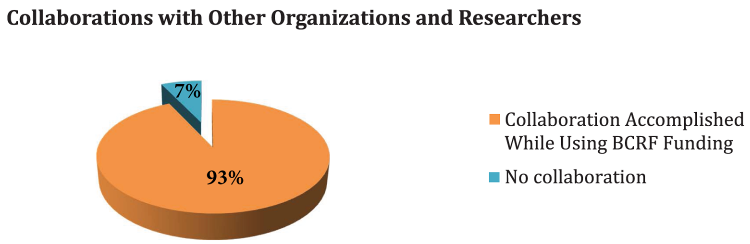

Figure 5 Proportion of BCRF grantees with collaborations with other organizations and researchers.

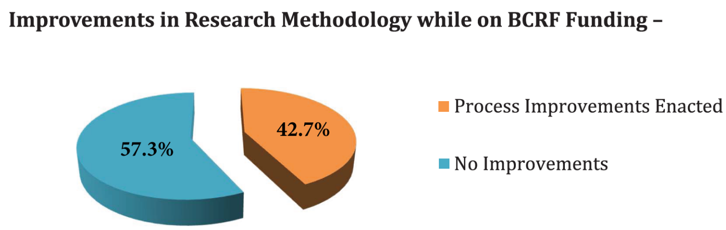

Figure 6 Proportion of BCRF grantees who have enacted process improvements in their research.

4.2 Commercial impact

Of the BCRF grantees surveyed, 59% completed the questions about the commercial impact of their BCRF-funded research. As mentioned above, many BCRF-funded projects are not expected to have potential commercial implications. For ROI metrics that measure this impact, we consider the share of grantees that filed for a patent, the share of grantees whose projects have reached clinical development, and the number of companies and jobs created because of a BCRF-financed project.

Filing a patent is frequently considered a major step in commercializing academic research. We find that 19.5% of respondents have so far filed a patent, as shown in Figure 7. Although this number may seem low, a large part of BCRF's research portfolio is focused on basic science. Such projects rarely lead to patentable results out of the laboratory. On the other hand, it might be worth encouraging patents by providing researchers with easy access to attorneys. Patents give a sense of ownership of one's discovery and serve as a bridge between academia and the pharmaceutical industry. Figure 8 shows the

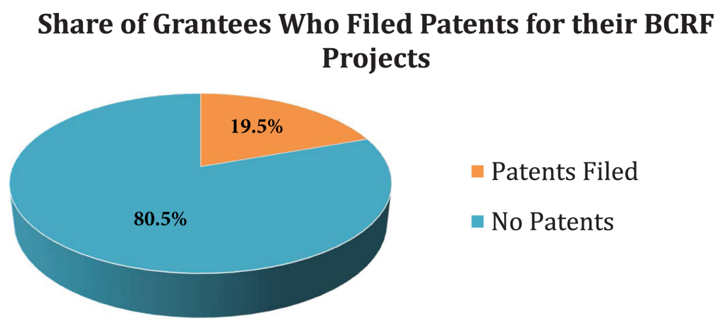

Figure 7 Share of BCRF grantees who have filed at least one patent for their BCRF-funded work.

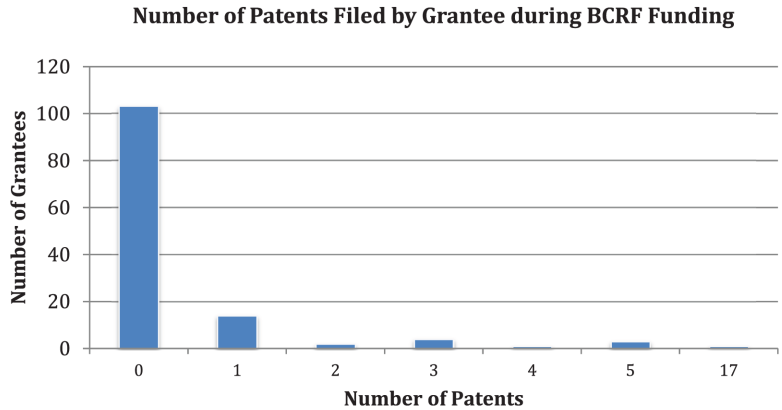

Figure 8 Distribution of the number of patents filed by grantee during BCRF funding.

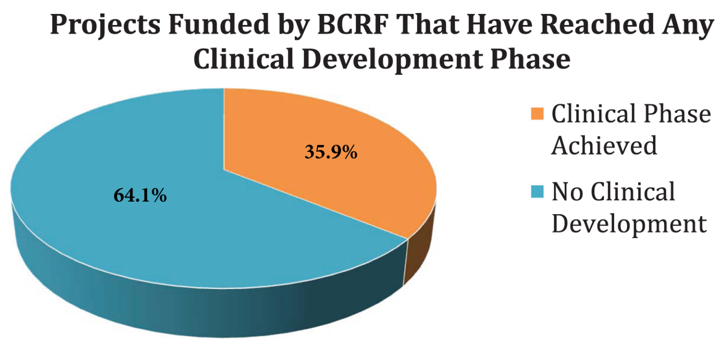

Figure 9 Portion of BCRF grantees with a project that has reached clinical development.

distribution of the number of patents filed, with one patent per researcher being the most common non-zero outcome.

The next ROI metric is the share of grantees whose project has reached the commercial pipeline: 35.9%, as shown in Figure 9. Practically speaking, this metric may be a better measure of commercialization than the number of patents, since in the biomedical industry, usually only easily applied research will reach clinical development. Since the mission of BCRF is to find an actual cure, however, it is important to explore the factors affecting all commercial outcomes. We do this in the second phase of our analysis.

Finally, we evaluated the effectiveness of BCRF-funded research by the startup activity of the grantees. As shown in Table 2, nine companies have been formed and 127 new jobs created because of BCRF funding, with an additional three startups reported as in progress and an additional 12 investigators who started companies prior to BCRF funding. In addition, $140 million in capital funding has been raised to launch the companies. This is a substantial impact, as the

Table 2 Company formation by BCRF grantees.

Status of company formation	Number of companies	Number of jobs created
No company	104	N/A
New companies spun off	9	127
In progress	3	New jobs in progress
Company started before BCRF funding received	12	N/A

number of reported new jobs is more than half the number of grantees.

5 Econometric Analysis

A key purpose of our study is to determine the effects of funding on research outcomes so as to draw policy-relevant conclusions. We identified five significant research outcomes from the available data, four of them commercial (filing patents, licensing IP, reaching a clinical development phase, and receiving outside capital for a company started from BCRF-funded work) and one non-commercial (obtaining additional non-BCRF grant funding).

Based on this analysis, the key factors associated with research outcomes are: the amount of BCRF funding, the number of graduate students and postdocs supported by BCRF funding, the presence of collaboration with other researchers, the support of faculty payroll by BCRF funding, the initiation of process improvements in the project, and whether the principal investigator supported graduate students. Unless the explanatory variables are binary, we use their natural-log values to capture nonlinearities.

Our dataset combines responses from the commercial and non-commercial surveys. Only 119 grantees of the foundation filled out both surveys, which further reduces the size of the dataset. Since all five outcomes are binary variables, probit and logit are the most suitable regression techniques. Similar results in both typically act as validation that the analysis is well formulated. Preliminary data exploration showed three highly correlated variables: the amount of BCRF funding, the number of graduate students supported, and the number of postdocs supported. The pairwise correlations of the variables range from 39% to 59%. This result makes intuitive sense, as the amount of funding largely determines the number of graduate students and postdocs that can be hired by a grantee.

We estimated three specifications of each type—logit and probit—while varying only the three proxies identified above. This gives us six regressions for each research outcome. Finally, we identified all statistically significant variables according to the value of their z-statistic, which must exceed 1.65 for significance at the 10% level, and 1.96 for significance at the 5% level. Because the logit and probit results are practically identical, we report only the logit results here and provide the probit results in the Appendix. The R^2's of all specifications are small, but this is not surprising given our small sample sizes. Some specifications are run with as few as 81 observations as there are missing values for some variables. The sample sizes for each specification have been provided in the tables with results.

5.1 Impact on filing patents

As shown in Table 3, the initiation of process improvements, the amount of funding, and its proxy, and the number of postdoctoral fellows supported have a positive impact on whether patents will be filed. These variables, highlighted in bold, are statistically significant for all three specifications of the regression equations. This is consistent with the innovation dynamics of industry. The more money and human resources that are invested in R&D projects, the likelier they are to develop significant new discoveries, and the likelier is the researcher to claim ownership by filing patents. In a commercial setting, this is done to secure commercial success for drug discovery efforts, which require a lengthy time commitment and a large financial investment. Nonprofit research organizations and academic institutions are not exempt from this dynamic, as their reputation and ability to attract philanthropic donors

Table 3 Factors that impact likelihood of filing patents. Statistically significant variables are bolded.

	Logit specifications		
Variable	Coefficient (z-statistic)	Coefficient (z-statistic)	Coefficient (z-statistic)
Ln(Funding)	**0.78 (2.01)**		
Ln(Grad. students)		0.09 (0.27)	
Ln(Postdocs)			**0.96 (2.85)**
Collaboration	0	0	0
Faculty on payroll	0.33 (0.58)	0.52 (0.82)	0.58 (0.96)
Process improvements	**1.87 (3.27)**	**1.96 (3.11)**	**1.58 (2.66)**
Support for grad. students	0.65 (0.99)	0	0.39 (0.58)
Number of observations	111	81	101
R^2	17.55%	13.87%	19.78%

and talent are determined by the impact of their scientific discoveries.

At the same time, process improvements in the laboratory serve as an indication that a principal investigator is committed to the latest innovations in their specialty. This channel could have a significant positive impact on filing patents, as innovation builds on innovation. The econometric analysis suggests that to be the case.

5.2 *Impact on licensing intellectual property*

It is unexpected that only one factor in our data—the number of postdocs—has an influence on licensing intellectual property. No other factor is statistically significant in any of the specifications, as presented in Table 4. A brief thought experiment, however, can shed light on this result. Licensing intellectual property is a complex activity that involves legal, commercial, and administrative entities. Research in the laboratory is only the first link in a longer chain leading to actual licensing. The academic research laboratory is removed by at least three degrees of separation from industry. The ultimate outcome will depend on the other three links, as they are in charge of bringing scientific discoveries to commercial applications. From this point of

Table 4 Factors that impact licensing intellectual property. Statistically significant variables are bolded.

	Logit specifications		
Variable	Coefficient (z-statistic)	Coefficient (z-statistic)	Coefficient (z-statistic)
Ln(Funding)		0.36 (0.99)	
Ln(Grad. students)			0.49 (1.21)
Ln(Postdocs)	**0.58 (1.68)**		
Collaboration	0	0.01 (0.01)	−0.03 (−0.02)
Faculty on payroll	1.20 (1.61)	0.92 (1.32)	1.61 (1.47)
Process improvements	0.41 (0.68)	0.90 (1.58)	0.42 (0.63)
Support for grad. students	−0.97 (−1.47)	−0.45 (−0.73)	0
Number of observations	101	119	87
R^2	8.28%	6.08%	7.38%

Table 5 Factors impacting the likelihood of reaching clinical development. Statistically significant variables are bolded.

	Logit specifications		
Variable	Coefficient (z-statistic)	Coefficient (z-statistic)	Coefficient (z-statistic)
Ln(Funding)	0.40 (1.48)		
Ln(Grad. students)		−0.42 (−1.32)	
Ln(Postdocs)			0.26 (0.98)
Collaboration	**−2.23 (−2.47)**	**−1.84 (−1.97)**	**−2.5 (−2.13)**
Faculty on payroll	−0.43 (−0.97)	−0.54 (−1.02)	−0.44 (−0.97)
Process improvements	−0.09 (−0.22)	−0.09 (−0.19)	0.08 (0.18)
Support for grad. students	**−1.30 (−2.88)**	0	**−0.88 (−1.78)**
Number of observations	119	87	106
R^2	10.12%	5.95%	7.38%

view—a simplified but realistic version of the complexities of successfully licensing intellectual property—it is not surprising that only one of our independent variables has a significant impact on its likelihood.

5.3 *Impact on the project's likelihood to reach a clinical development stage*

Another unexpected result concerns the likelihood of a project funded by BCRF to reach clinical development. The only two factors that appear to be statistically significant are the presence of collaboration with other researchers throughout the project duration and whether the principal investigator supported graduate students. In all specifications, collaboration has a negative impact on the likelihood of reaching clinical development and graduate-student support has a negative impact in two specifications as shown in Table 5. This result is surprising because published scientific research is almost always the product of several researchers. In addition, supporting graduate students provides additional human resources to move research projects forward. We performed several robustness checks to ensure that we were not misinterpreting the data.[4]

Our econometric analysis, however, is confirmed by the direct experience and observations of senior management at BCRF and researchers at academic institutions receiving BCRF funding. When two or more laboratories start collaborating across institutions, the administrative complexity to overcome on the path to clinical development is so great that it often slows down the process substantially, even if the laboratories are in close physical proximity. One possible solution to this problem may be the creation of a corporate structure that would eliminate the burden of bureaucracy among research institutions. This would be a highly beneficial development, as the goal of BCRF-funded collaboration is to advance promising research into clinical development and ultimately, to patients.

Regarding the negative impact of providing support for graduate students, the result is less surprising when we consider what this variable represents. Graduate students are researchers in training and their presence implies that both

Table 6 Factors impacting ability to attract venture capital funding.

	Logit specifications		
Variable	Coefficient (z-statistic)	Coefficient (z-statistic)	Coefficient (z-statistic)
Ln(Funding)	0.23 (0.48)		
Ln(Grad. students)		−0.08(−0.17)	
Ln(Postdocs)			0.23 (0.53)
Collaboration	0	0	0
Faculty on payroll	1.47 (1.35)	1.32 (1.20)	1.51 (1.38)
Process improvements	0.53 (0.74)	0.86 (1.11)	0.37 (0.50)
Support for grad. students	1.03 (0.95)	0	0.72 (0.64)
Number of observations	111	81	101
R^2	7.44%	5.57%	6.53%

the principal investigator and the institution are engaged in teaching and mentoring as well as research. These additional activities inevitably reduce the resources that could otherwise be dedicated to the commercialization of scientific research. Of course, pedagogy and mentorship are important investments in future productivity and innovation, and our metrics do not capture the impact of this investment.

5.4 *Impact on the ability to attract venture capital*

Attracting venture capital is often an indicator of the viability of biomedical research, where it can have a significant impact on advancing discoveries to benefit patients. This is, in fact, the primary return to philanthropic donors. However, we find that the ability to attract venture capital for BCRF-funded projects is not dependent on any factors in our data. As shown in Table 6, none of the independent variables is statistically significant. Much like licensing intellectual property, attracting venture capital is a complex process that involves multiple parties, and producing high-quality research is only the first step. It should come as little surprise that what happens in the laboratory has no effect on receiving venture capital.

5.5 *Impact on ability to obtain additional grant funding*

Although the nonprofit community plays a major role in the funding of academic biomedical research, no single agency or foundation can fully support an investigator's research program. Indeed, it is critical that an investigator secures support from several sources for any one project. This is considered not only a measure of success for the researcher and their institution, but also a valuable form of ROI in its own right, in terms of advancing a nonprofit's mission. Table 7 shows that for BCRF grantees, the amount of grant funding and its two proxies, the number of graduate students and the number of postdocs, have a positive impact on this outcome in all specifications, while faculty support and process improvements only occasionally have a significant impact. The amount of funding and the number of trainees or faculty it supports appear to be a signal of a researcher's success: the larger the figure, the stronger the conviction that the funded project will generate substantial results. In addition, the grant amount from BCRF is a stamp of approval

Table 7 Factors impacting likelihood of obtaining additional grant funding. Statistically significant variables are bolded.

	Logit specifications		
Variable	Coefficient (*z*-statistic)	Coefficient (*z*-statistic)	Coefficient (*z*-statistic)
Ln(Funding)	**0.98 (3.38)**		
Ln(Grad. students)		**0.95 (2.47)**	
Ln(Postdocs)			**1.36 (3.46)**
Collaboration	−0.94 (−0.97)	−0.37 (−0.32)	−0.87 (−0.7)
Faculty on payroll	0.66 (1.39)	0.73 (1.31)	**1.16 (2.20)**
Process improvements	**0.81 (1.75)**	0.63 (1.18)	0.34 (0.67)
Support for grad. students	0.27 (0.57)	0	0.10 (0.18)
Number of observations	119	87	106
R^2	13.73%	10.77%	17.51%

for a researcher, as BCRF is known to be very selective in its funding process.

6 Conclusion

Nonprofit research-funding organizations such as BCRF are crucial in supporting the biomedical research that is essential to optimizing health outcomes in oncology. Nevertheless, there is a paucity of econometric research regarding the impact of these funding efforts. Such research is essential to improving the ability of organizations to accomplish their socially valuable missions, as well as in assessing the impact of impact investments.

The biomedical research process is a complex multidimensional endeavor that cannot be fully explored by just one study with a small dataset. However, the use of both commercial and non-commercial survey data sheds light on the factors that drive key outcomes from BCRF-funded projects: the likelihood of filing patents, out-licensing intellectual property, reaching clinical development, and obtaining additional grants. While these factors vary according to each outcome, understanding them better will help formulate forward-thinking outcome-enhancing policies.

The returns achieved by BCRF investment shown here are manifold. These include positive outcomes for the grantees, scientific research in general, society, and the economy. The non-commercial ROI of BCRF funding is evident in the high numbers of graduate students, post-doctoral fellows, and faculty that it supports. In economic terms, this translates into developing human capital for future socially beneficial research endeavors. Its non-commercial impact is also seen in the strong levels of collaboration with other researchers, which leads to knowledge diffusion and the generation of innovative ideas. It is also important in initiating process improvements that eventually transform research methodologies. Meanwhile, the commercial ROI of BCRF funding is clear from the substantial number of patents filed by the grantees, the high number of projects reaching clinical development, and the creation of new companies and jobs from the projects funded by BCRF.

Our results may be especially useful for informing directions for further research. Our findings are consistent with a recent study by Huang *et al.* (2021) documenting the large impact of the portfolio of life sciences patents at the Massachusetts Institute of Technology, and we hope that other nonprofit organizations will conduct similar studies and share their learnings. More sophisticated and detailed data are needed before we can develop quantitative models and methods to optimize the funding decisions of nonprofit organizations. From a policy perspective, it makes sense for the leaders of BCRF and like organizations to nurture the factors that will have the most positive effect on the scientific community and on society. While there is no simple recipe for success, we hope that the framework and results of this article can serve as a starting point in measuring the impact of breast cancer research and other forms of biomedical innovation.

Appendix

Table A.1 Factors that impact likelihood of filing patents. Statistically significant variables are bolded.

	Probit specifications		
Variable	Coefficient (z-statistic)	Coefficient (z-statistic)	Coefficient (z-statistic)
Ln(Funding)	**0.60 (3.48)**		
Ln(Grad. students)		**0.58 (2.60)**	
Ln(Postdocs)			**0.77 (3.63)**
Collaboration	−0.57 (−1.01)	−0.24 (−0.36)	−0.51 (−0.71)
Faculty on payroll	0.40 (1.40)	0.44 (1.30)	**0.65 (2.12)**
Process improvements	**0.50 (1.83)**	0.38 (1.21)	0.23 (0.79)
Support for grad. students	0.15 (0.53)	0	0.02 (0.05)
Number of observations	119	87	106
R^2	13.94%	11.21%	17.23%

Table A.2 Factors that impact licensing intellectual property. Statistically significant variables are bolded.

	Probit specifications		
Variable	Coefficient (z-statistic)	Coefficient (z-statistic)	Coefficient (z-statistic)
Ln(Funding)		0.19 (0.96)	
Ln(Grad. students)			0.27 (1.18)
Ln(Postdocs)	0.32 (1.62)		
Collaboration	0	0.05 (0.08)	0
Faculty on payroll	**0.68 (1.70)**	0.54 (1.45)	0.83 (1.59)
Process improvements	0.21 (0.62)	0.50 (1.62)	0.23 (0.63)
Support for grad. students	−0.52 (−1.40)	−0.23 (−0.67)	0
Number of observations	101	119	87
R^2	8.28%	6.23%	7.44%

Table A.3 Factors impacting the likelihood of reaching clinical development. Statistically significant variables are bolded.

	Probit specifications		
Variable	Coefficient (z-statistic)	Coefficient (z-statistic)	Coefficient (z-statistic)
Ln(Funding)	0.23 (1.50)		
Ln(Grad. students)		−0.25 (−1.32)	
Ln(Postdocs)			0.16 (0.99)
Collaboration	**−1.39 (−2.54)**	**−1.11 (−2.00)**	**−1.54 (−2.26)**
Faculty on payroll	−0.27 (−1.04)	−0.31 (−0.98)	−0.28 (−1.00)
Process improvements	−0.06 (−0.25)	−0.06 (−0.21)	0.05 (0.17)
Support for grad. students	**−0.80 (−2.90)**	0	**−0.54 (−1.77)**
Number of observations	119	87	106
R^2	10.14%	5.93%	7.41%

Table A.4 Factors impacting ability to attract venture capital funding. Statistically significant variables are bolded.

	Probit specifications		
Variable	Coefficient (z-statistic)	Coefficient (z-statistic)	Coefficient (z-statistic)
Ln(Funding)	0.13 (0.54)		
Ln(Grad. students)		−0.05 (−0.21)	
Ln(Postdocs)			0.12 (0.54)
Collaboration	0	0	0
Faculty on payroll	0.74 (1.48)	0.68 (1.30)	0.75 (1.52)
Process Improvements	0.27 (0.72)	0.47 (1.16)	0.18 (0.48)
Support for grad. students	0.49 (0.99)	0	0.35 (0.67)
Number of observations	111	81	101
R^2	7.64%	5.79%	6.64%

Table A.5 Factors impacting likelihood of obtaining additional grant funding. Statistically significant variables are bolded.

	Probit specifications		
Variable	Coefficient (z-statistic)	Coefficient (z-statistic)	Coefficient (z-statistic)
Ln(Funding)	**0.60 (3.48)**		
Ln(Grad. students)		**0.58 (2.60)**	
Ln(Postdocs)			**0.77 (3.63)**
Collaboration	−0.57 (−1.01)	−0.24 (−0.36)	−0.51 (−0.71)
Faculty on payroll	0.40 (1.40)	0.44 (1.30)	**0.65 (2.12)**
Process improvements	**0.50 (1.83)**	0.38 (1.21)	0.23 (0.79)
Support for grad. students	0.15 (0.53)	0	0.02 (0.05)
Number of observations	119	87	106
R^2	13.94%	11.21%	17.23%

Commercial Impact Survey

BCRF Economic Impact Study Survey

Grantee Name: [PREFILLED NAME]

1. BCRF records show your funding began in [PREFILLED YEAR]. Is this correct?

   a. If incorrect, please indicate the correct year: ___________.

2. BCRF records show your cumulative amount of grant funding received from BCRF is [PREFILLED DOLLAR AMOUNT]. Does this match your institutional records?

   a. If not, please indicate the cumulative amount of grant funding that your records indicate: ___________.

3. Please provide example(s) of funded project(s) and stage at which BCRF funding was received, e.g., animal models, toxicology, medicinal chemistry, clinical trials, drug discovery, etc.

   Project 1:
   Project 2 (if applicable):
   Project 3 (if applicable):
   Project 4 (if applicable):
   Project 5 (if applicable):
   Project 6 (if applicable):

4. For the projects funded by BCRF, have you filed any patents? Yes No

   If yes, when?
   How many patents have you filed?
   What is the current status of your patent filing(s)?

   (i) Pending review
   (ii) Rejected
   (iii) Approved
   (iv) Other (please describe)

5. Have you licensed any of the IP that has resulted from the work funded by BCRF?
   Yes No In process

   a. If yes, what type of license?

      (i) Commercialization (ii) Additional Research (iii) Other (please describe)

6. Has a company been created around the work funded by BCRF?
   Yes No In process Not applicable

   a. If yes, please indicate the number of full-time equivalent employees: _________

7. Has the company that was created around the work funded by BCRF received any venture capital or other investment funding?
   Yes No In process

   a. Please indicate the pre-money valuation prior to your most recent round of funding in $USD, if applicable: ___________.
   b. Last round of funding (Series A, B, etc.), if applicable: ___________.
   c. Please indicate the amount of capital raised during that round: ___________.

8. Has the project reached clinical development phases? Yes No

   a. If yes, what is the current status, e.g., animal models, medicinal chemistry, toxicology, phase 1–3, NDA, etc.?

9. Please describe any other steps you've taken to commercialize the project:

Non-Commercial Impact Survey

Non-Commercial Impact of BCRF Grants

1. Grantee Name: [PREFILLED NAME]
2. BCRF records show your funding began in [YEAR]. Is this correct?

   a. If not, please indicate the correct year

3. BCRF records show your cumulative amount of grant funding received from BCRF is [FUNDING AMOUNT].
    a. Does this match your institutional records?
    b. If not, please indicate the cumulative amount of grant funding that your record indicate.
4. What is/are the primary objective(s) of your BCRF-funded research?

We have included below a number of non-commercial ways in which BCRF grant funding could make an impact. For any that may be relevant for your research, please provide as much objective documentation as possible. Anecdotes are helpful, but quantitative evidence will be more useful for the purposes of citation and publication of our study.

Impact on Ability to Obtain Other Additional Grant Funding

1. Has BCRF grant funding enabled other additional grant funding awards?
    a. If yes, how much have you received and who is/are the funding source(s)?[Fields for grant #, granting institution, dollar amount]
2. Other ways? [open-ended Q]

Impact on Patient Lives

1. How has the research funded by BCRF impacted patient lives?
    a. Please provide objective evidence, e.g., published research or reports, clinical statistics, etc.
2. If your BCRF-funded research has not yet reached patients, what steps are required to do so?
3. Other ways? [open-ended Q]

Impact on Education

1. Number of graduate students involved in BCRF-funded research
2. Number of postdocs involved in BCRF-funded research
3. Other ways? [open-ended Q]

Collaborations with Other Organizations and Researchers

1. Has BCRF funding enabled new relationships with organizations or researchers that may not have been otherwise possible?
    a. What has been the product of such collaborations (e.g., research publications, additional research projects, etc.)?
2. Other ways? [open-ended Q]

Job Creation and the Impact on the Local Economy

1. Number of new jobs created to support BCRF-funded research (e.g., administrative staff positions and/or technical staff positions)
2. Has the BCRF grant funding been used to support faculty payroll?
    a. If so, how many faculty total?
3. Other ways? [open-ended Q]

Process Improvements

1. Has any of your BCRF grant funding been used to enhance or improve the drug development process in general?
    (a) If yes, how so?

Other

1. In what other ways has your BCRF-funded research made an impact?

Notes

[1] The pharma and healthcare providers' range of social surplus is estimated by Lakdawalla *et al.* (2010, pp. 339–342). The authors estimate separately the aggregate consumer and producer surpluses arising from gains in cancer survival in the 1988–2000 period. For the same period, the aggregate cost of R&D on cancer treatments is aggregated and subtracted from the sum of both surpluses. The range of producer surplus is estimated as the share of total profits from the total aggregate surplus for the period. The range is rather large as the authors account for the wide variability in profit margins across healthcare producers—for example, big pharma companies typically report high margins, while healthcare facilities such as small hospitals have fairly low profit margins. The authors ensure their estimates are consistent with the data in the healthcare economics literature.

[2] The value of a life-year is estimated by Lakdawalla *et al.* (2010). The value of a life-year is estimated by dividing the total social surplus by the total number of additional life-years due to the increased life expectancy created from gains in cancer survival for the 1988–2000 period. The authors use sophisticated economics frameworks to find estimates that are consistent with the healthcare economics data.

[3] However, Ringel *et al.* (2020) report some promising new evidence that we may finally be reversing Eroom's Law.

[4] We applied the winsorization technique by using the deviance residual. Observations with a deviance residual more than 2 may indicate lack of fit. For each of the six specifications, we performed sensitivity analysis at three levels. First, we exclude the observations with residuals higher than 2 and rerun the specification. Second, we lower the threshold to remove observations with residuals of 1.95 and higher and rerun. Finally, we remove observations with residuals of 1.9 and higher and rerun. In all the reruns, the "collaboration with other researchers" and "support for graduate students" independent binary variables stay negative and statistically significant

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Conflicts of Interest Disclosures

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DV reports no conflicts. LN is the founding scientific director of BCRF, and MH was chief mission officer of BCRF at the time of writing. LN and MH report no other conflicts.

AL reports personal investments in private biotech companies, biotech venture capital funds, and mutual funds, and is a co-founder and partner of QLS Advisors, a healthcare analytics and consulting company. He is also an advisor to BrightEdge Ventures, Thales, and an advisor to and investor in several biotech companies and biotech VC funds. He is a director of Atomwise, BridgeBio Pharma, Roivant Sciences, and Annual Reviews; chairman emeritus and senior advisor to AlphaSimplex Group; a member of the Board of Overseers at Beth Israel Deaconess Medical Center; and a member of the NIH's National Center for Advancing Translational Sciences Advisory Council and Cures Acceleration Network Review Board. A more detailed disclosure statement is available at https://alo.mit.edu/.

References

Adams, C. P. and Brantner, V. V. (2006). "Estimating the Cost of New Drug Development: Is It Really $802 Million?" *Health Affairs* **25**(2), 420–428.

Bisias, D., Lo, A. W., and Watkins, J. F. (2012). "Estimating the NIH Efficient Frontier," *PLoS One* **7**, e34569.

Breast Cancer Research Foundation (n.d.). Available online: https://www.bcrf.org. Accessed on March 14, 2018.

Caulfield, T. and Ogbogu, U. (2015). "The Commercialization of University-Based Research: Balancing Risks and Benefits," *BMC Medical Ethics* **16**, 70.

DiMasi, J. A., Hansen, R. W., and Grabowski, H. G. (2003). "The Price of Innovation: New Estimates of Drug Development Costs," *Journal of Health Economics* **22**(2), 151–185.

DiMasi, J. A. and Grabowski, H. G. (2007). "The Cost of Biopharmaceutical R&D: Is Biotech Different?" *Managerial and Decision Economics* **28**(4–5), 469–479.

DiMasi, J. A., Grabowski, H. G., and Hansen, R. W. (2016). "Innovation in the Pharmaceutical Industry: New Estimates of R&D Costs," *Journal of Health Economics* **47**, 20–33.

Dorsey, E. R., Thompson, J. P., Carrasco, M., de Roulet, J., Vitticore, P., Nicholson, S., Johnston, S. C., Holloway, R. G., and Moses, H. (2009). "Financing of U.S. Biomedical Research and New Drug Approvals Across Therapeutic Areas," **4**(9), e7015.

Huang, S., Siah, K., Vasileva, D., Chen, S., Nelsen, L., and Lo, A. (2021). "Life Sciences Intellectual Property Licensing at the Massachusetts Institute of Technology," *Nature Biotechnology* **39**, 293–301.

Lakdawalla, D. N., Sun, E. C., Jena, A. B., Reyes, C. M., Goldman, D. P., and Philipson, T. J. (2010). "An Economic Evaluation of the War on Cancer," *Journal of Health Economics* **29**(3), 333–346.

O'Hagan, P. and Farkas, C. (2009). "Bringing Pharma R&D Back to Health," Available online: https://www.bain.com/insights/bringing-pharma-r-and-d-back-to-health/. Accessed on March 14, 2018.

Paul, S. M., Mytelka, D. S., Dunwiddie, C. T., Persinger, C. C., Munos, B. H., Lindborg, S. R., and Schacht, A. L. (2010). *Nature Reviews Drug Discovery* **9**, 203–214.

Ringel, M. S., Scannell, J. W., Baedeker, M., and Schulze, U. (2020). "Breaking Eroom's Law," *Nature Reviews Drug Discovery* **19**, 833–834.

Scannell, J. W., Blanckley, A., Boldon, H., and Warrington, B. (2012). "Diagnosing the Decline in Pharmaceutical R&D Efficiency," *Nature Reviews Drug Discovery* **11**, 191–200.

Statista (2021a). Leading 10 U.S. Therapy Areas Based on Drug Spending in 2020. Available online: https://www.statista.com/statistics/238698/us-health-spending-leading-areas/. Accessed on December 13, 2021.

Statista (2021b). Deaths by Breast Cancer in the U.S. from 1950–2018, Available online: https://www.statista.com/statistics/184615/deaths-by-breast-cancer-in-the-us-since-1950/. Accessed on December 13, 2021.

Weinberg, B. A., Owen-Smith, J., Rosen, R. F., Schwarz, L., Allen, B. M., Weiss, R. E., and Lane, J. (2014). "Science Funding and Short-Term Economic Activity," **344**(6179), 41–43.

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