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**VENTURE CAPITAL ACTIVITY
AND PERFORMANCE IN
HEALTHCARE AND MEDICAL
INNOVATION**

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Johns Hopkins Institute for Applied Economics,
Global Health, and Study of Business Enterprise



Venture Capital Activity and Performance in Healthcare and Medical Innovation

By Pythagoras Petratos

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About the Series

The Studies in Applied Economics series is under the general direction of Professor Steve H. Hanke, Co-Director of The Johns Hopkins Institute for Applied Economics, Global Health and the Study of Business Enterprise (hanke@jhu.edu).

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Summary

The U.S. is a global leader in life sciences and there is wide acceptance that venture capital currently constitutes the cornerstone of its innovation commercialization leadership. Healthcare is the second most important sector for Venture Capital (VC) investment and accounts for a large proportion of innovation, employment and welfare creation in the U.S. economy. This paper describes the innovation activity and performance of venture capital in healthcare. Using Thomson One's Private Equity module database for the period 1990-2014, we find that the performance of investment funds expressed by Return On Investment (ROI) measured by Internal Rate of Return, IRR) averages approximately 17%. Industry categories in life sciences present different behavior among them regarding returns, activity and exits. The benefits of venture capital and innovation in healthcare are attenuated by numerous barriers. We propose policy recommendations that could remove these hurdles in order to enhance venture capital activity and promote healthcare and medical innovation. These would mainly include tax reforms as well as financial regulations.

Acknowledgments

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Introduction

The United States is the global leader in life sciences¹. The U.S life sciences industry supports more than 7 million jobs, stimulates economic growth, and leads the world in venture capital (VC) investment². American research and development (R&D) accounts for approximately one third of the world total. Health related funding constitutes over half the non-defense federal R&D³ budget, and over the last two decades its increase has constituted the largest change in spending priorities. While the federal government is a major funder, most of the funding is provided by the private sector.⁴

The U.S. government has invested hundreds of billions in developing the medical sciences. Similarly, big pharmaceutical companies have invested amounts of equal magnitude in innovation that has advanced the life sciences industry. Venture capital investment in life sciences has become more important, not only because it can mobilize substantial resources from the private sector, but also due to the fact that it provides life sciences innovation with a valuable alternative to the traditional R&D of pharmaceutical companies. During the 1930s, 1940s and 1950s large vertically integrated companies led the chemo-therapeutic and biochemistry innovation transitions⁵. The most recent transition, which continues during the writing of this paper, is the biotechnology revolution. From the 1970s onwards small biotech companies led the way instead of the big companies, which developed alliances with these smaller innovative companies mainly financed by VC⁶.

By enabling and facilitating innovation, venture capital is an important element of both business and public sectors . The U.S also has a unique position in the venture capital industry. First of all, this is for historical reasons since the first modern venture capital firm was American Research and Development (ARD), established in Boston in 1946⁷. Today the U.S. venture capital market can be considered the most developed by far, and it accounts for more than two thirds of global VC activity. Health related technologies are the second most important sector for venture capital investment, after information technology industries, and constitute a large proportion of innovation in

the U.S. economy⁸. Information Technology also encompasses many applications for healthcare.⁹

Despite the importance of venture capital in healthcare, little academic attention has been paid to it. Thus, first of all, this paper describes the importance of venture capital to the economy and health related industries. We will also assess VC activity and how much value is created by analyzing the returns of funds invested in healthcare ventures. Finally, we briefly examine the regulatory framework and policies that are related to venture capital, and suggest ways of improving wealth generation.

The Importance of Venture Capital

‘Venture capital firms are professional, institutional managers of risk capital that enables and supports the most innovative and promising companies.’¹⁰ However, venture capitalists not only provide capital, they also typically play an active role in management areas such as strategic and operational planning, among other functions¹¹. Traditional forms of bank financing might not invest in new businesses due to the high level of risk. Venture capital fills this gap by funding high risk entrepreneurial projects that are expected to yield high returns.

While the purpose of the pioneer ARD venture capital firm was to add value to the companies that had been invested in, its founder George Doriot had a broader vision of financing ‘noble ideas’¹². The High Voltage Engineering Company, which developed X-Ray technology for the treatment of cancer, was the first investment based on ethical considerations that Doriot was encouraged to make, as it was not expected to make any money¹³. However, the High Voltage Engineering Company went public and yielded returns to its investors and health benefits to cancer patients.

Since the 19th century the word entrepreneur has been connected to value creation¹⁴. Social entrepreneurship provides socially valuable benefits and tends to be related to non-profit and not-for-profit activity¹⁵. Notable examples include: Mohammad Yunus, of the Grammen Bank, who provided microloans and therefore indirect benefits to

healthcare by reducing poverty; also initiatives such as OneWorld Health, the first non-profit pharmaceutical company to develop safe, effective, and affordable medicines for infectious diseases in the developing world¹⁶. Venture capital supports social entrepreneurship by providing capital, at times being highly philanthropic, and by sharing the guiding principles that led the VC industry for decades. This is done in numerous forms: such as investment by venture capital firms, (i.e. Benetech.org, Endeavour.org, etc.); venture philanthropic organizations' investment (i.e. Skoll and Swab Foundation, etc.); and funding by impact investors (i.e. Gray Ghost Ventures, Omidyar Network, etc.)¹⁷.

Venture capital has a protagonist role in promoting wealth through employment and economic growth. More than half the employment in life sciences is venture capital backed, and in medical devices this proportion reaches 83%¹⁸. More relevantly, there are 'multiplicative values' or simply 'multipliers' that indicate how much effect an economic activity in one sector has on another. The biopharmaceutical industry was found to have a multiplier of 6.7, meaning that one job in this industry generates an additional 6.7 times that, at the employment level, in other sectors of the U.S. economy¹⁹. Not only does it contribute to an increase in jobs but it also increases aggregate income²⁰. In addition, during technological transitions there is evidence that an 'entrepreneurship multiplier' broadens, deepens and extends the impact of innovations²¹. The same is likely to apply to VC in healthcare and further enhance innovation.

It is widely accepted that venture capital is an important factor for economic growth. Multipliers can apply in this case too, since \$ 1bn in medical R&D public investment can result in a sixfold increase in gains, and approximately a 0.048% increase in the U.S. GDP²². Companies backed by venture capital produced approximately \$ 3.1 trillion in revenue, from 1970 to 2010, for the U.S. economy. Significant tax from corporate revenues, as well as from income revenues, can be thus collected. Tax revenues can be used to increase healthcare funding. At the same time, a larger proportion of the population can afford health insurance and better quality healthcare due to higher

levels of employment and income. Increases in economic growth are essential in order to counterbalance the disproportionate rise of healthcare costs in relation to GDP²³.

An element that underpins much of the above analysis is that venture capital can enhance the rate of innovation. It could result in approximately three times more patents than traditional R&D²⁴. Another related issue is that small companies, which can be associated with venture capital, are more innovative than larger firms²⁵. This is particularly true in the biotechnology and medical devices sectors, since the R&D of large pharmaceutical companies has all but disappeared and is supplemented by smaller biotechnology firms²⁶. An increase rate of innovation would enhance economic activity, and thus increase employment, growth and value. Finally, innovations not only in life sciences but also in IT, financial technology and insurance could make healthcare more accessible and at the same time more cost effective²⁷.

Enabling Venture Capital and Innovation in Healthcare

The venture capital industry was a 'cottage industry' before the 1980s and its rapid development was attributed to two initiatives: a change in the Employee Retirement Income Security Act (ERISA); and in taxation, beginning with the Revenue Act of 1978.²⁸ More specifically, ERISA not only enacted the prudent man rule but most importantly, relaxed its stricter nature under common law²⁹. This enabled the active participation of institutional investors in VC, and is a principal factor in its rapid development due to the significant increase in funding.

Nevertheless, policy makers, regulators, and fund managers sometimes remain cautious. The prudent man rule, in contrast to its name, can be a constraint discouraging investment and not developing according to the modern portfolio theory³⁰. In addition, there is another layer of complexity to federal regulations arising from state laws. Some states and local governments adopt a combined approach, with the exception of the Employment Retirement Income Security Act (ERISA) and the common law version of prudent man standard, by applying quantitative limitations³¹.

It can be argued that quantitative limitations might create a quantitative 'rule of thumb' for fund managers, which could further restrict investment in alternative investments such as venture capital.

The prudent man rule and the ERISA enabled institutional investors to channel funds into venture capital. Tax policy and more particularly, changes in capital gains tax can provide incentives for individuals to invest in new ventures. It has been found that the introduction of a general capital gains tax has a negative impact on welfare by retarding entrepreneurship, through reduced support for VC³². There are two distinct effects; one stems from individual income tax, and the other from corporate capital gains taxation. It is supported that changes in the former have a greater impact on the effective tax burden of venture capitalists than changes in the latter³³.

Asymmetries between individual and corporate tax rates are important. When personal tax rates are higher than corporate tax, entrepreneurs have the incentive to reclassify their earnings as corporate, which could act in favor of entrepreneurial activity³⁴. Statistics on increases in income taxation indicate that it reduces investment by entrepreneurs³⁵. Similar research suggests that a substantial reduction in the marginal income tax rates of entrepreneurs not only increases the probability of job creation, but also promotes a rise in wages³⁶.

Taxation is highly complex and there is a plethora of ways with which it can affect VC in healthcare. There are two additional key issues. Carried interest is a form of compensation paid to partners of a private investment and venture capital fund, which is based on profits. It partially functions as an incentive mechanism for better performance. Recent suggestions to change carried interest could have effects similar to changes in personal and corporate taxation. This is because the incentive structure could also change and discourage superior performance and activity in VC. Taxation of life sciences products is another major concern. It has been argued that an increase in excise taxes is hard to justify, it reduces the revenues of companies and thus it could threaten the dominant position of the U.S in the production of medical devices.^{37,38}

Another major category of initiatives is related to the government's active encouragement to finance small businesses. In 1958, Congress passed the Small Business Investment Company Act. It finances small enterprises through Small Business Investment Companies (SBICs) that tend to act as venture capitalists. However, in the past there were noticeable differences from VC firms, such as a lack of industry expertise, and problems resulting from the use of debt and government guarantees³⁹. Nevertheless, the evidence on government sponsored venture capital (GVC) in general, suggests that a modest amount of government support, but not too much, seems to improve the performance of small businesses⁴⁰.

Data and Methods

The main database used for the analysis is Thomson ONE. It includes the private equity analysis, previously known as VentureXpert programme. We extracted various types of venture capital information using Private Equity Screening and Analysis software. The main dataset is based on the Venture Economics Industry Code (VEIC), which classifies funds and firms according to specific industries. In order to capture the broad field of life sciences we selected various industrial categories and sub categories. The two principal categories that embody life sciences are Biotechnology and Pharmacology (4000), and Medical/Health Related (5000). The former has seven key subcategories and the latter five. We analyzed these subcategories since the purpose of this study is to measure not only the performance of industrial categories, the 'interindustry' effects, but also to study the subcategories, the 'intra industry' aspects.

Since we are interested in the United States' health affairs and policy, the sample includes venture capital activity in the U.S. The dataset comprises quarterly data for the 25 year period, from January 1990 to December 2014, consisting of approximately 17,000 new firm formations. Before 1990, activity in the biotechnology sector was moderate and there were significant issues with the availability and reliability of data. Similar studies use the same starting point⁴¹. Events such as the Dot-Com bubble and the 2007-9

financial crisis, which are very important from the perspective of performance and public policy, are included. Although we should acknowledge the importance of previous periods and waves of innovation in healthcare, possibly affecting subsequent venture capital activity, the pre 1990s VC data present many limitations⁴².

Venture Capital Activity in Health Related Industries

Employment The first objective is to analyze data that can illustrate and validate some of the arguments presented above. We present a number of companies with large capitalization and workforces that were the result of life science financing by venture capital (Table 1). They are a representation of both value and employment generated by venture capital activity. The 20 biggest life sciences enterprises financed by VC in the U.S. account for 858,457 jobs. We focus on employment for numerous reasons. Employment is always a sensitive policy issue, since it plays fundamental roles in the economy and public opinion.

Job creation in health related industries has substantial multiplier effects as discussed earlier. It is thus responsible for the generation of significant employment in other sectors of the economy. But what is of immense interest, is the significant growth of employment among health related companies. Medtronic Inc., for example, grew from 1,287 employees in its initial public offering (IPO) in 1978, to approximately 49,000 in 2014. In addition, it displayed a sustainable growth, and in 2000 it had 21,490 employees, in 2006 36,000, and eventually 85,000 in 2013⁴³. This is an indication that the growth of innovative technology product life science companies can continue at relatively high rates after firm exit and produce significant value. Reinvesting in innovation is a strategy that can achieve sustainable growth. Thus, numerous mature life science corporations fund Corporate Venture Capital (CVC) or acquire with Mergers and Acquisitions (M&A) smaller venture backed firms.

There is another crucial implication for public policy. Employment in health related industries remained comparatively stable or even increased during the financial crises

of 2000 and 2008, and thereafter. This might be due to the fact that demand for healthcare can be regarded pretty immune to economic shocks. In that sense, supporting life sciences and health related industries can be considered critical for economic stability and in particular, employment. This fact is amplified by the multiplier effect on other industries.

Table 1 - Employment and Value

Company name	Number of employees	Capitalization (USD Millions)	Sales (USD Millions)
Abbott Laboratories	69000	63366	21819
Actavis, Inc.	19200	65180	N/A
AHS Medical Holdings LLC	11000	N/A	962.1
Alere Inc	17600	3284	2981
Beverly Enterprises, Inc.	34300	N/A	1,723.40
Centennial Healthcare Corp	10000	N/A	656.8
Community Health Systems	87000	6432	15414
Crothall Services Group, Inc.	19000	N/A	502.4
Dentsply International, Inc.	11800	6486	2953
Envision Healthcare Corp	12562	6245	4030
HealthSouth Corp	13900	3367	2303
Hercules Holding Ii LLC	199000	N/A	18424.8
Humana Inc	52000	19655	44440
IASIS Healthcare Corp	12395	N/A	903.5
Medtronic Inc	49000	64384	17195
National Healthcare Corp	11500	806	830
Quintiles Transnational Corp	27000	7038	5224
Regency Health Services	15000	N/A	932.3
Select Medical Corp	31200	1586	3004
UnitedHealth Group Inc	156000	84162	126019
Total	858457	331991	270317.3

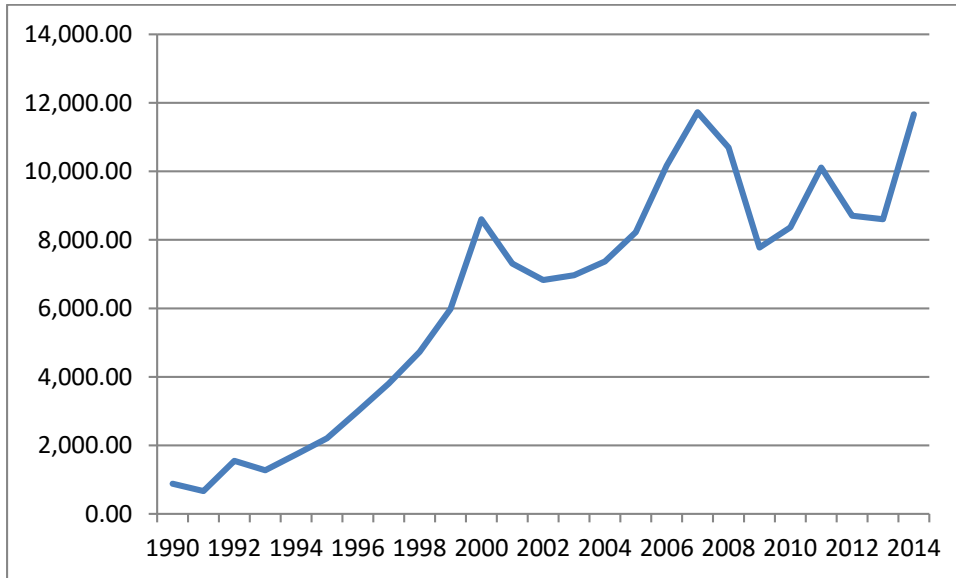
Wealth Creation The most important aspect of health related industries funded by VC is their sizable value. Table 1 shows the size and value of the 20 largest venture capital backed life science companies in the United States in 2014. These sale figures, which account for approximately 1.6 per cent of U.S. Gross Domestic Product (GDP), demonstrate the substantial demand for innovative health related products. The value of this representative market is close to 2 per cent of GDP. This excludes the valuation of some companies that are privately owned and for which there is no available data.

The multiplier effect applies in this case, and significant value is created in other sectors of U.S. industry. Of course, it should be emphasized that although these corporations reflect a large proportion of the VC funded companies, there are many more large corporations, and smaller ones, that significantly generate value for the U.S. economy and its healthcare system.

Deal Activity and Funding Capital Employment and value creation is associated with VC activity in the establishment and funding of entrepreneurial ventures. In general, both the number of life sciences deals, and the funding capital per deal (average equity per deal) are steadily increasing. Both sets of figures, deals and average capital invested, fell during the Dot-Com bubble and the 2007-9 financial crisis. There are two important observations related to this. The first is the rapid growth of VC equity investment activity during the 1990s, which grew from \$ 880 million to approximately 10 times this figure during the 2000 technology peak. Even if we exclude figures for 2000 and 2001, years of extraordinary activity, there is an increasing linear trend up to 2007 (US\$ 11.726 billion).

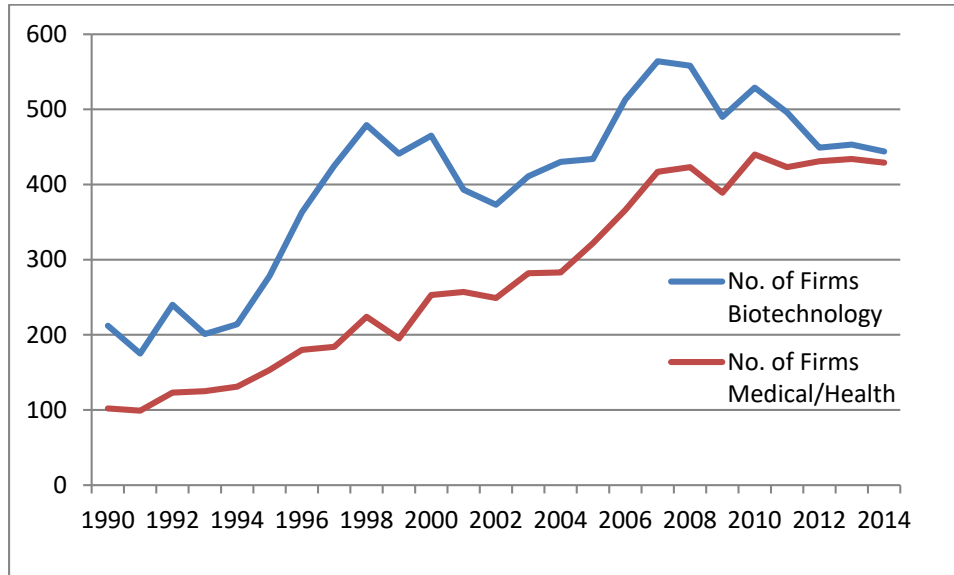
Nevertheless, this does not seem to be the case for the 2007-2009 financial turmoil. While the Great Recession officially ended in June 2009⁴⁴, it seems to have been more profound, and recovery to pre-crisis levels appears to have been more sluggish (see Exhibit 1). This poses important policy questions regarding the effectiveness of public policy responses to the crisis and to healthcare in particular. Nevertheless, at the end of 2014 VC investment in equity had almost reached the 2007 maximum.

Exhibit 1 - Total Investment in Equity (US\$ millions)



We will further investigate the activity of the two main categories: Biotechnology and Pharmacology; and Medical/Health related industries. The total number of deals in these two categories, for the period of 1990 to 2014, amounts to 6,914 and 10,030 new companies respectively. While the number of deals is consistently lower in biotechnology and pharmacology innovations, the average investment per deal is consistently higher on average than medical/health related investments (US\$ 7.13 to 6.22 million). Correlation between the number of deals in the two categories stands at around 0.85. Although Biotechnology has now regained the new firm creation activity that was lost in the last financial crisis (see Exhibit 2), this has not happened for medical/health related innovations. This suggests that public policies had a different impact on the two industrial sectors. In addition, while investment has recovered to its 2007 maximum level, the total number of new firms has not made a similar recovery. This means that there is also higher average investment per new firm.

Exhibit 2 - Number of New Firms



It has been supported that broader economic trends appear to affect venture capital activity⁴⁵. In that sense it would be useful to further investigate how macroeconomic actors and especially changes in GDP might influence venture capital activity. Above, we examined two main activities, the deals and firm formation of VC backed companies, and total funding. It is useful then to examine them from a broader economic trend, that of business cycle perspective. Related literature has controlled for changes in GDP and accordingly, we will do so by using the Hodrick-Prescott filter⁴⁶. We observe that venture capital in healthcare seems to be procyclical. This is confirmed in other empirical research⁴⁷.

Exhibit 3 - Total Equity Investment (1990-2014)

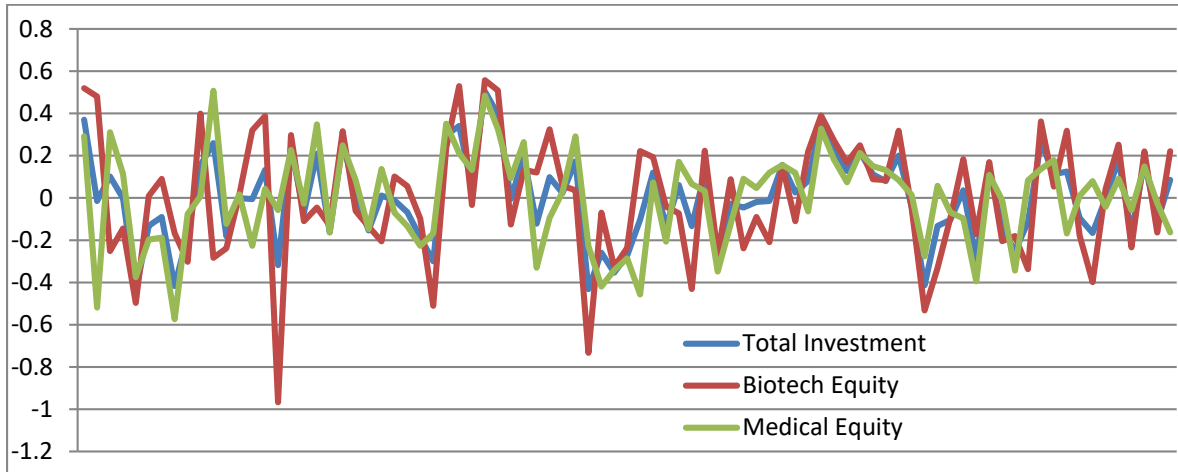
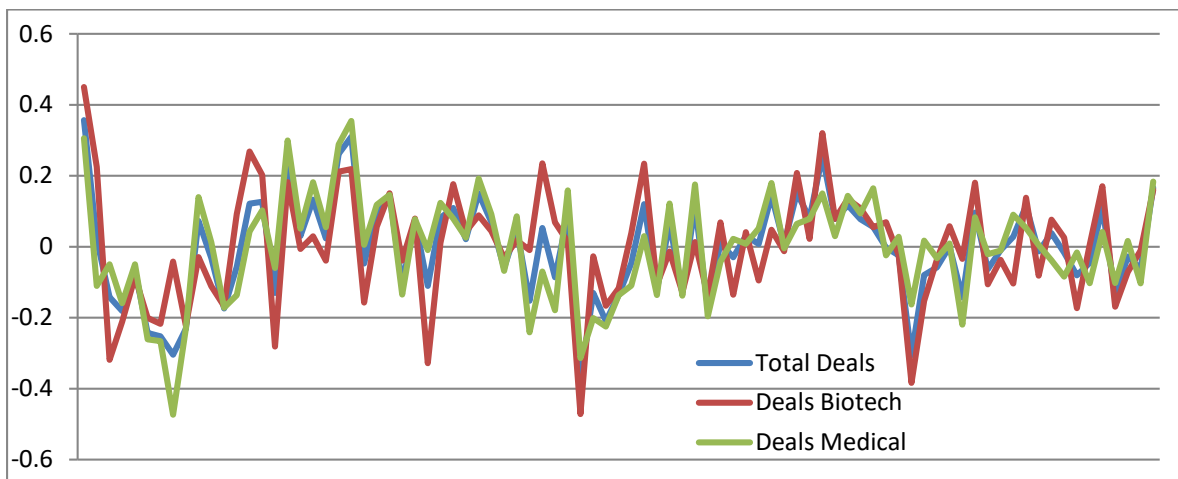


Exhibit 4 - Number of Companies (1990-2014)



Exits Venture capitalists entering a deal envision a profitable exit. A large number of companies financed by venture capital become bankrupt due to the high levels of risk in entrepreneurial innovation. However, a few companies manage to exit through Mergers and Acquisitions (M&A) or Initial Public Offering (IPO). Venture capital investors have the incentive to exit a deal not only profitably, but also quickly, in order to maximize the returns. We find that there are interindustry and intra industry variations regarding the survival rate (i.e. how many companies managed to exit profitably) and how long it took to exit.

Table 2

Industrial Category	Deals	IPOs	M&A	Time
Human Biotechnology (4100)	530	312	151	5.28
Agricultural/Animal Biotechnology (4200)	30	12	6	7.57
Industrial Biotechnology (4300)	33	27	17	5.72
Biotech Related Research & Production Equipment (4500)	58	19	19	5.69
Biotech Related Research & Other Services (4600)	51	19	14	5.76
Biotechnology and Pharmacology (4000) Total	702	389	207	5.46
Medical Diagnostics (5100)	161	65	48	5.46
Medical Therapeutics (5200)	354	130	131	5.55
Medical/Health Products (5300)	151	54	49	5.05
Medical Health Services (5400)	211	57	52	6.42
Pharmaceuticals (5500)	215	87	79	5.45
Medical/Health Related (5000) Total	1092	393	359	5.61
Other Exits	9	4	3	5.87
Total exits	1803	756	569	5.56

Table 2 displays the number of M&A and IPOs in the healthcare sector during the period 1990-2014. In total there are 1803 exits of which most were IPOs (58%). In all of the industrial categories IPO is the prevalent method for exit, while in some categories M&A activity is equally important. While the total weighted average time for exit is approximately 5.56 years, there are significant deviations in some categories, such as Agricultural/Animal Biotechnology, 7.57 years, but most notably Medical Health services companies, with 6.42 years. This is interesting from a public policy perspective since it means that innovation in some industrial healthcare segments could lag behind others.

Financial Performance

The value that corporations generate is defined by their Returns On Investment (ROI). The literature on venture capital performance indicates that the most common and standard return measure used by academics and practitioners respectively, is the Internal Rate of Return (IRR)⁴⁸. The best IRR estimate is the 'since inception', because all

the cash flows and recent valuations are included⁴⁹. Therefore we use data since inception for the years 1990-2013, when VentureXpert database was discontinued. In addition, the pooled IRR method is applied, because it can capture timing and scale by pooling the cash flows of all funds and it is similar to the methods used by many investors⁵⁰. Finally, the data returns are net of management fees, partnership expenses and carried interest. We present fund performances for the two main categories, Biotechnology and Pharmacology and Medical/Health Related industries and then we combine them in order to observe the overall venture capital fund performance in healthcare.

The growth of the venture capital market is absolutely remarkable, from a total of US \$ 1.267 billion in 1990 to 40.623 billion in 2013. Funds investing in Medical and Health Related industries present double the activity of those investing in biotechnology. The number of funds (144 to 77) and also the total capitalization of the sample funds (US \$ 26.941 and 13.681 billion) was doubled by 2013. It is disproportionate to the number of start-ups and exits in each category. In the beginning of the 1990s the number of funds and also the capitalization of the two categories were very similar. However, in the mid 1990s and especially in 1995, this doubling effect became apparent. This is an interesting finding since it displays that experienced fund managers prefer to invest more in Medical/Health industries than in Biotechnology. It is subject to further examination, since the cumulative returns of Biotechnology (19.17%) are higher than those of Medical and Health Related innovations (16%). Returns are associated with risk. Therefore, a potential explanation might be that investors' risk preferences lean towards Medical/Health related start-ups rather than more risky Biotechnology. In general, funds investing in life sciences have returns of approximately 17.00%. This is a relatively high return in relation to traditional R&D returns in healthcare⁵¹.

Exhibit 5 - Number of Funds

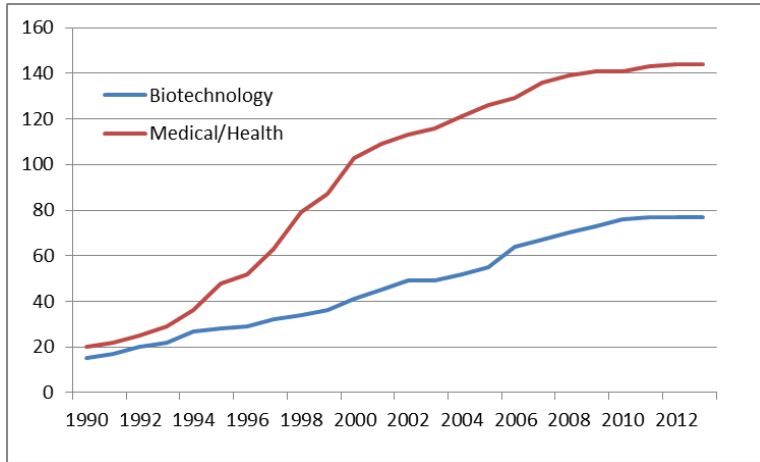


Exhibit 6 - Total Capitalization of Funds

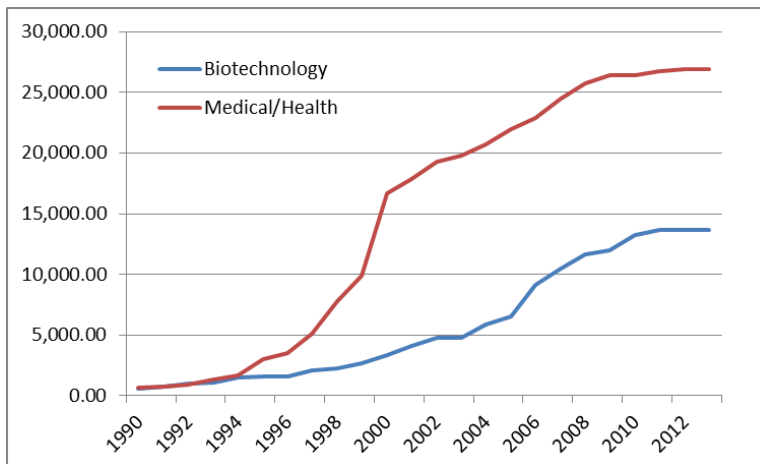
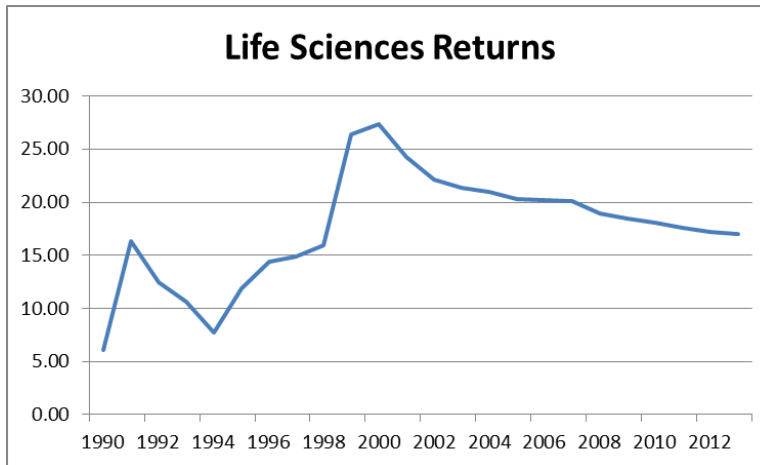


Exhibit 7 - Returns - Cumulative Pooled IRR



Discussion

The United States remains the global leader in life sciences. Our analyses suggest that medical related entrepreneurship financed by venture capital generates substantial wealth, employment and economic growth. These important factors for the U.S. economy are further boosted by relatively high growth in comparison to other industrial sectors. It is reflected in the high returns of VC backed ventures. High returns also mean that there is significant demand for such innovative products and services. Innovations could fulfill the demand for cost reduction, or improvement in the quality of treatments, or both. While healthcare expenditure, as part of the GDP, is increasing, and is projected to possibly rise further, more cost cutting innovations are essential⁵². There are some suggestions that technology could increase costs, although this is subject to much uncertainty⁵³. At the same time it is unethical to discourage better quality treatments. This fuels a long and rather heated debate on healthcare and further empirical evidence would be useful. Certainly, an important question for future research would be how VC activity influences rising medical costs and cost effectiveness. What is really needed is an effective incentive and a pricing mechanism that encourages innovation and efficiency, as measured by cost-benefit analysis.

Despite the contribution of VC backed life science entrepreneurial innovation that brings benefits to consumers and positive effects to economic factors and GDP growth, U.S. life science innovation can be considered to be under threat. The 2007-2009 pre-crisis levels of entrepreneurial activity have not fully recovered, but there are upward trends. The U.S. relative leadership power can be considered to be in decline, as other countries invest more in venture capital and innovation⁵⁴. What is most worrying, is will returns and innovation activity continue to be sustainable in venture capital financed entrepreneurship? There are numerous barriers to entrepreneurship in healthcare that prevent venture capital from growing⁵⁵. We have discussed the profound impact of regulation on the venture capital industry, and following on from this we will discuss some policies that could facilitate entrepreneurial activity.

Policies and Regulation

ERISA had a catalytic effect in enabling venture capital. The venture capital industry was allowed to attract investment and grew massively. Although many restrictions were removed, they remain in some states. Some versions of the 'prudent man' rule could discourage venture capital activity and should therefore be amended. The 2007-2009 financial crisis has not only affected venture capital activity but also financial regulation. New regulations have been enacted and the financial system is evolving. Regulators should be careful to avoid creating unintended barriers to the inflow of capital, and generating transaction costs for the venture capital industry. This would prevent entrepreneurs from raising capital, especially at a time when activity is rather low.

Recent examples include provisions in the Dodd Frank Act that could affect angel capital investing and impose further costs⁵⁶. The Volcker Rule could also influence the functions of venture capital firms, with negative consequences⁵⁷. Finally, crowdfunding regulation should be simple and avoid costly processes such as lengthy registrations and further delays. It should establish a transparent property right and ownership framework, and avert restrictions on raising capital. The Jumpstart Our Business Startups (JOBS) Act, which regulates crowdfunding, is certainly a step in the right direction. It removes barriers to funding new and emerging growth companies. However, additional relaxation of some rules, such as quantitative and time limits, could also prove beneficial⁵⁸.

The second most important incentive for venture capital innovation, which was previously discussed, is taxation. The general conclusions were that lower tax rates could enhance innovation activity, increase returns and employment levels and improve performance. In that sense, excise taxes can be deemed inappropriate, because they decrease revenues and returns, and could endanger performance. Comparatively high taxation could encourage venture capital outflow to other countries and persuade

life science companies to relocate their operations and invest abroad. Even though tax rate reduction is difficult to balance and reach political consensus on, corporate and individual tax exemptions, credits, and deductions could be useful incentive mechanisms for venture capital investors, especially regarding life sciences.

Three specific forms of tax incentives could have positive impacts on innovation. R&D tax credits is one of them. In the U.S they were introduced in the Economic Recovery Act of 1981 and were continuously renewed but never constituted permanent legislation. The American Research and Competitiveness Act of 2014 (H.R. 4438) is trying to enact R&D tax incentives. The second form can be related to intangible assets. The passing of 'The Patent Box' in the UK can serve as a useful paradigm. Lower corporation, and other taxes, can apply to profits earned from patenting and innovations. This could significantly incentivize innovation and commercialization and be complementary to other R&D incentives. A third policy option is to apply additional tax incentives to life science industries, such as progressive tax credits and more allowances (i.e. education of personnel, health insurance, etc.).

Nevertheless, it is critical to have a holistic approach to regulation, since innovation policies can be interdependent. The life sciences industry features a variety of regulations. An illustrative example is the patenting of pharmaceutical products, which can be associated with R&D and patent tax incentives. This can accordingly be linked to the Federal Drug Administration (FDA) approval process and the product life cycle time and returns⁵⁹. In that sense, incentives should be structured consistently with other regulatory frameworks and factors, such as time and pricing, in order to maximize innovation activity and returns. If there is uncertainty regarding pricing controls, or general changes to regulation, companies could shift their attention to larger markets and short term projects with lower risk⁶⁰. An appropriate approach to differential pricing could facilitate competition and make drugs and other products more affordable to consumers⁶¹.

It has been argued that healthcare policies and the recent Affordable Care Act could have both positive and negative effects on innovation⁶². But what is crucial to the

legislative process and the interpretation and implementation of laws, is their complexity. Healthcare policies should present simplicity, transparency and clarity in a coherent manner, avoiding conflicts of laws and confusion in general. 'The R&E tax credit ...is a good example of a how even a simple public policy idea that has bipartisan support can emerge from Congress both greatly complicated and weakened in its effects.'⁶³

Appropriate regulation is essential in order to enable and enhance entrepreneurial activity. It could be simplified and integrate various legislative pieces in a consistent manner in order to avoid inefficiencies. It should contain effective incentives to encourage entrepreneurial activity, value added and better returns. It is argued that technology in healthcare has been 'sustainably' applied in almost every case⁶⁴, and that regulatory barriers are one of the main reasons for this. As healthcare costs and medical expenditure increase, the need for more innovation to increase efficiency and productivity is becoming more imperative. New business models and 'disruptive' innovation can deliver more affordable, accessible and better quality healthcare. In that sense, 'disruptive regulation', the regulation enabling disruptive innovations could generate the incentive structures needed to encourage more innovative activity, better performance, and wealth creation.

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