Original Article

Catalyzing capital for Canada's life sciences industry

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Joseph Tucker
is an experienced biotechnology executive and investment industry insider with broad scientific expertise. Dr. Tucker currently holds simultaneous roles as an Adjunct Lecturer in the Masters of Biomedical Technology program at the University of Calgary (UofC) and as the Director of Biomedical Innovation at bphealth Innovation.

Justin Chakma
is an Innovation Consultant at the McLaughlin-Rotman Centre for Global Health and Business Analyst at bphealth Innovation.

Paul W.M. Fedak
is an active clinical cardiac surgeon, an experienced medical device innovator and translational scientist. Dr. Fedak currently serves as an independent research investigator at the University of Calgary, Director of Surgical Approaches to Heart Failure Programme at the Libin Cardiovascular Institute of Alberta, and the Founder and Executive Director of the Health Innovation and Research Commercialization Alliance.

Massimo Cimini
is an innovation consultant and Director of Strategy at bphealth. Dr. Cimini also serves as the administrative Director and Coordinator of the Health Innovation and Research Commercialization Alliance in Toronto, Canada.

ABSTRACT **Canada's biotech sector ranks within the top five globally, but its life sciences venture capital (VC) industry is among the worlds weakest. This makes for an interesting case study in understanding the disconnect between low levels of VC and a healthy innovation ecosystem in terms of R&D spending, skilled workforce and enterprise support. Three key provinces (Quebec, Ontario and British Columbia) that have taken significantly different approaches to attracting VC are large enough to attract as much government investment as whole emerging markets. The aim of this article is to present evidence from a Canadian natural economic experiment in order to evaluate the effectiveness of varying government policies in attracting VC investment, to illustrate how these policies need tailoring to individual sub-sectors of the life sciences sector, and to highlight potential policy mechanisms that may be applicable beyond Canada's borders. We employ VC returns on investment (ROI) and exit data as a proxy for our evaluation. Our results suggest that government biotechnology investment needs to be structured end-to-end from early to late stage in order to be successful, that prevalence of private and international VC flows is critical for generating market efficiency, and that there is an 'optimal' efficient amount of capital before ROI result in diminishing returns.**

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Correspondence: Massimo Cimini
bphealth Innovation, 84 Gerrard Street West, Toronto, Ontario,
Canada M5G1J5
E-mail: mcimini@bluepebble.ca

INTRODUCTION

Venture capital (VC) is widely considered one of the key ingredients to a healthy innovation system.[1] It is especially critical for the life sciences where significant amounts of capital are required and made illiquid for more than a decade because of the lengthy development and clinical trial process. Venture capitalists help to reduce risk for follow-on capital such as private equity and institutional investors through screening, due diligence and active monitoring of investments.[2]

Some key questions include: How can governments establish the right policies to attract VC for their life sciences sector? Should governments take an active role and direct the investment of funds themselves? Alternatively, should they take a passive role by attracting private-sector activity through tax breaks? What is the right policy mix?

While these questions are relevant to governments globally, they are particularly relevant to the Canadian life sciences industry. In July 2010, BIOTECanada reported that there were 668 biotechnology firms in Canada, with Toronto as the fourth largest center for life sciences research in the world.[3] Confirming this, Scientific American recently ranked Canada's biotechnology industry third (behind only the United States and Singapore) on the basis of R&D spending, enterprise support, availability of VC, workforce skill and entrepreneurship levels.[4]

Canada's life science innovation industry thus scores well against its international competitors in spite of its weak VC, which ranked lowest among the five indicators. Although Canadian VC-backed biotech firms directly employ 5000 employees, and generated sales of US$1.9 billion in 2007, the overall pool of VC has been shrinking disproportionately to market conditions.[5] Canada therefore makes an interesting case study for exploring this counter intuitive disconnect between low levels of VC and an apparently healthy innovation ecosystem, as measured by R&D spending, skilled workforce and enterprise support.

From this Canadian data we are able to examine the relative effectiveness of three types of VC funding: private independent, government-run and retail. Broadening our viewpoint to consider the larger context of government policy affords us the opportunity to postulate idealized strategies to improve VC ecosystem health, which may be applicable globally, and to make a specific policy proposal for Canada itself as well.

To reach its full economic potential and tap into its significant local R&D in the life sciences, every country, including Canada, must seek to develop the right policies and mechanisms to attract and retain VC. In this article, we employ the Canadian experience as a natural economic experiment in which many confounding variables such as wealth, education, political system, national tax treatment and culture are inherently held constant. We evaluate the effectiveness of different policies for attracting VC, discuss how these policies could be effectively tailored to individual sub-sectors of the life sciences sector, and conclude by proposing a policy model for VC based on the Canadian experience.

METHODS

We defined the life sciences industrial sector as encompassing both medical devices and biotechnology as standard in the life sciences commercialization literature. To identify and evaluate policies for attracting VC, as experienced in Canada, we undertook a combination of quantitative and qualitative data analysis that is described as follows:

Quantitative Analysis: Financial data, specifically exit data, funding level data and investment data, were extracted from Thomson Reuters VentureSource database (www.canadavc.com) for investments that had been classified as life sciences. We further separated these data into medical device and biotechnology investments. These individual data were then tabulated and analyzed to determine overall national-level investment trends, return on

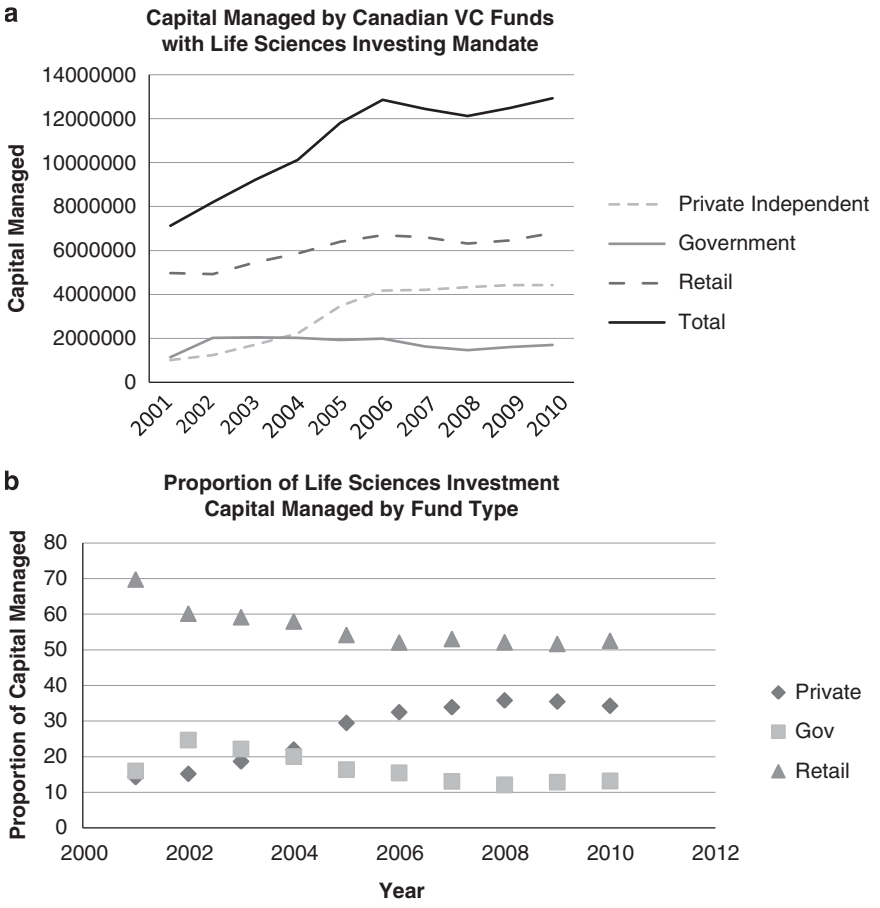

Figure 1: Government investment has been pivotal to the formation and organization of life sciences venture capital in Canada.

investment (ROI) by type of investor, and province and sub-sector type within the life sciences. Statistical software was employed to determine whether the results were significant.

Qualitative Analysis: A comprehensive analysis of the literature was completed. We elected to use a combination of the case study and grounded research methods as the most appropriate to examine complex phenomena in context. We also analyzed background documents on the Canadian life sciences industry from the peer-reviewed literature and news reports; books published by innovation academics; and firm websites of life science VC funds in Canada.

RESULTS

Canada has a strong history of government involvement in life sciences VC (Figure 1)

We extracted year-by-year data on capital managed that was potentially available to the life sciences from 2001 to 2010. The data were further separated into three types of VC funds: private-independent funds, government-run funds and retail funds. Private-independent funds are traditional VC funds with a limited partnership structure. Examples of such funds in the life sciences include Genesys Capital (Toronto, Ontario) and Ventures West (Vancouver, British Columbia). Government-run funds are funds

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that have been endowed capital from the government budget directly, typically at the provincial level, primarily in order to promote local economic development. These include investing entities such as the Business Development Bank of Canada's (BDC) Venture Capital Fund (Montreal, Quebec). Finally, retail funds are funds that have been established by governments to draw on funds deposited by public investors in return of a tax-rebate of some form, in addition to a potential ROI. Examples include the recently defunct Vengrowth Asset Management (Toronto, Ontario).

Overall, levels of VC managed potentially available to Canadian life sciences companies appear to have more than doubled from 2001 to 2010, with strong correlation between the roughly 34 per cent increase capital managed by retail funds from 2001 to 2006, and a 410 per cent increase in capital managed by private-independent VC funds from 2001 to 2006. Potential government funding available has appeared stable from 2001 to 2010, which is indicative of the fixed budget allocated annually to entities such as the BDC. Total capital managed has also appeared to plateau from 2006 onwards. Overall, the proportion of total capital by private funds managed increased from 14 to 35 per cent, whereas the proportion of total capital managed by retail funds decreased from approximately 70 to 50 per cent.

Canadian life sciences VC investing is declining (Figure 2)

However, not all capital raised by VC funds with a mandate for life sciences investing is necessarily invested. We therefore tracked year-by-year investment activity for the life sciences on the basis of two metrics – total amount invested and the number of actual companies funded. The life sciences industry as a whole saw a significant decrease in overall investment levels from its peak in 2000, with the exception of 2007, which may have been because of the transient opening of an IPO window that saw some VCs exit their life sciences investments. Unlike overall investment levels, the number of deals being financed annually by VCs has decreased significantly from below the pre-2000 levels of roughly 100 deals per year to 30 deals per year, with continued decline in 2010. The average amount of capital invested per company appeared to increase significantly for life sciences investment overall from $2.6 million in 2001 to $7.4 million in 2010.

When we analyzed the data by medical devices and biotechnology sub-sectors, we found that these overall trends were correlated more closely with biotechnology, which was expected given that the vast majority of invested capital was going into biotechnology. The decline in overall levels of financing for biotechnology was comparatively not as severe – the overall levels of investment appeared stable, but was deployed to fewer biotechnology companies. This may reveal a recent shift in the focus of VC managers, from the typically smaller investments into new investees to larger follow-on investments into existing portfolio companies. This strategy can be often employed by venture investors during times of depressed financing conditions, in order to protect their existing investee companies from financial failure.

In contrast to biotechnology, medical device investment levels declined significantly from a peak of $127 million in 2001 to virtually $0 during 2009 in the depths of the financial crisis. Average levels of investment per medical device firm were relatively stable at around $2.5 million, regardless of the overall levels of funding with the exception of 2009, where the Thomson Reuters database recorded that no VC-backed medical device companies were funded.

Canadian provinces varied significantly in their total investment made and ROI (Table 1 and Figure 3)

To dissociate the impact of the individual policies implemented by each province, we analyzed the returns and probability of

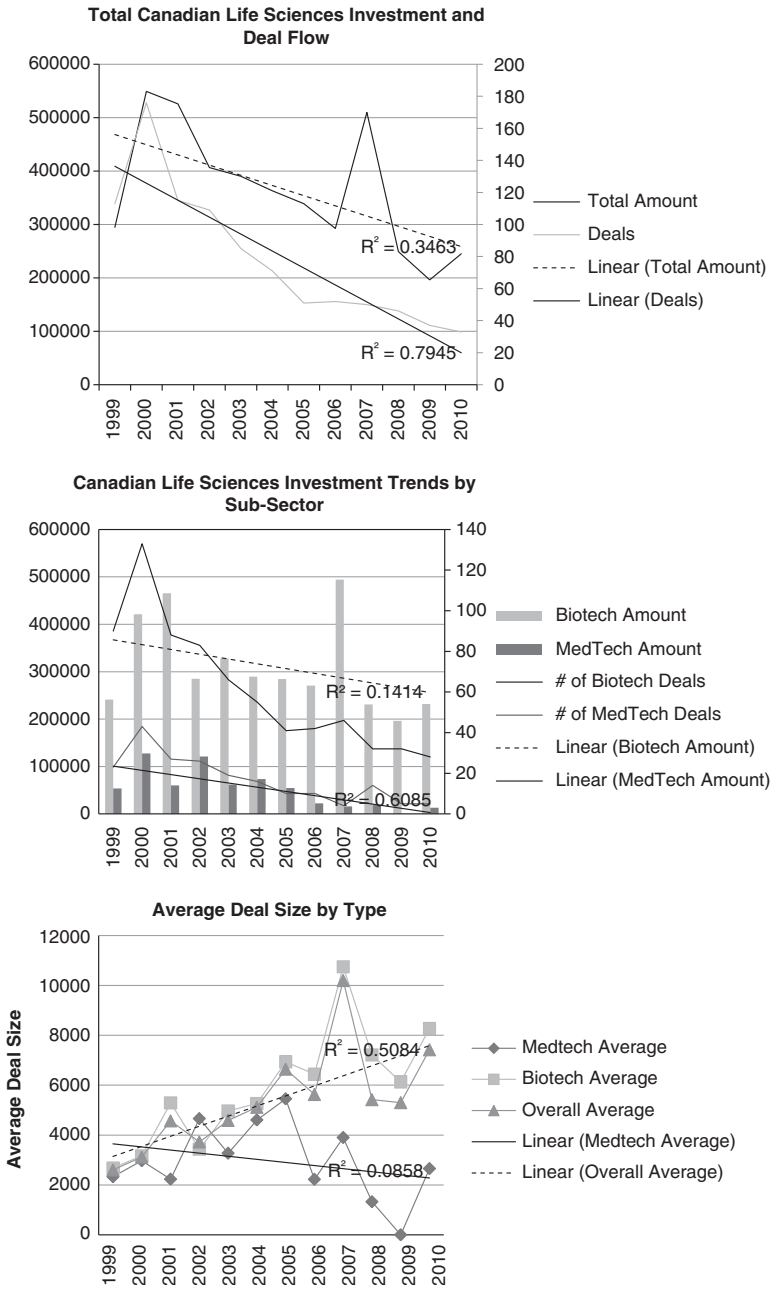

Figure 2: Venture capital investments into the life sciences have decreased significantly.

successful exit from investments exited over the last decade (likely, historical legacy investments from the earlier decade of 1990–2000 owing to the long investment timelines in the life sciences), as well as returns and probability of successful exit from investments actually made during the last decade. Owing to the lack of historical data from 1990 to 2000, we divided the total return on exits that occurred from 2000 to 2010 by the total amount of investment to determine the historical ROI despite the fact that some of these exits were on investments made from 1990 to 2000.

Table 1: Relative performance by ROI and exit probability percentage in major Canadian provinces

Province	*Total investment (millions)*	*Total deals*	*Recent ROI*	*Historical ROI*	*Recent exit (%)*	*Historical exit (%)*
Biotechnology						
Quebec	−1710	329	24.166	43.438	3.647	7.9
Ontario	812	167	27.76	46.215	7.186	14.97
British Columbia	943	131	15.05	51.733	3.05	8.39
Alberta	157	48	14.59	34.98	2	8.33
Medical Devices						
Quebec	279	75	27.3494	54.79	2.666	8
Ontario	192	65	40.708	68.23	4.615	7.69
British Columbia	49	15	0	14.94	0	7.14

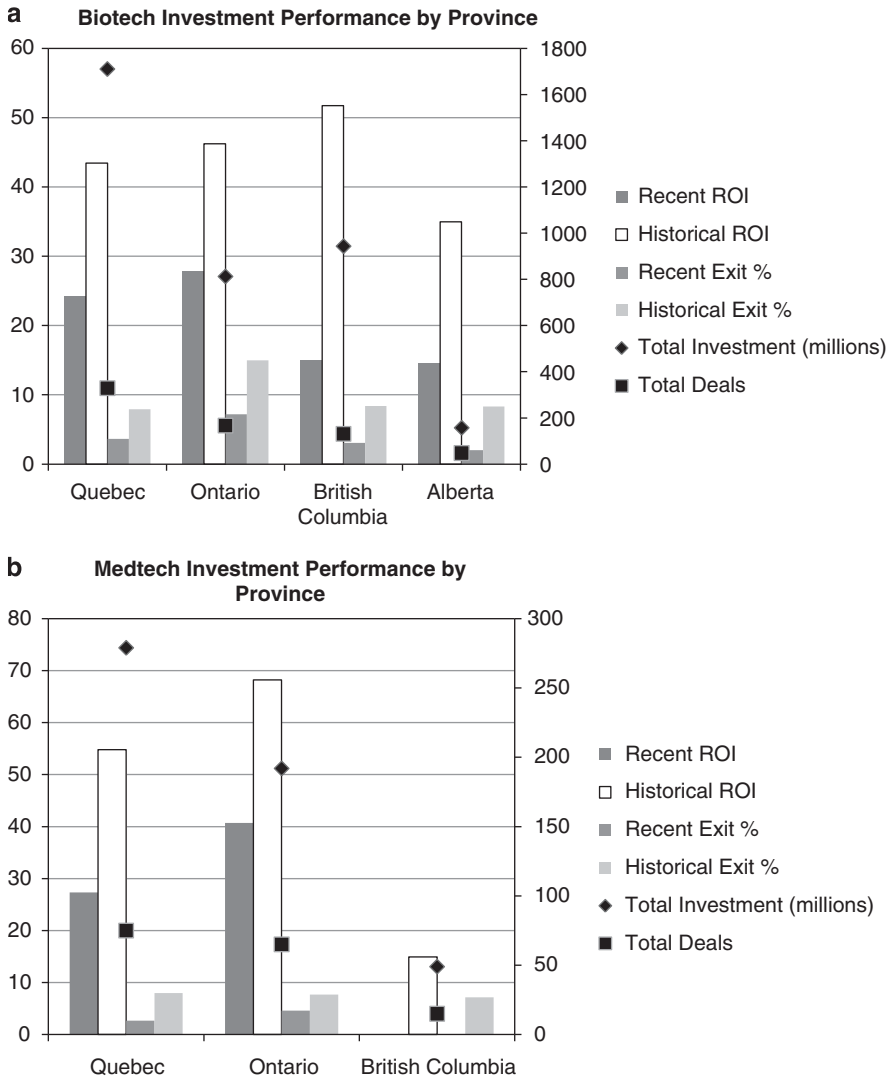

Figure 3: Financial performance varies province by province and by sub-sector within the life sciences.

This provided an approximate lower bound on the expected ROI of biotechnology and medical device investments for each province because the total amount of investment capital deployed from 2000 to 2010 was significantly greater than that from 1990 to 2000, when the Canadian VC industry was nascent. We also divided the total return on exits that occurred from 2000 to 2010, but whose date of investment was between 2000 and 2010, by the total amount of investment from 2000 to 2010 in each province, to see how each province was faring thus far on its most recent set of VC investments as opposed to its legacy investments.

To determine the likelihood of an exit, we divided the total number of exits that occurred from 2000 to 2010 by the total number of deals financed by venture capitalists from 2000 to 2010. This generated a historical exit percentage. However, as described earlier, not all these exits made between 2000 and 2010 were from investments made from 2000 to 2010. Thus, we generated another metric by dividing the total number of exits that occurred from 2000 to 2010, whose date of investment was also between 2000 and 2010, by the total number of deals made from 2000 to 2010, in order to evaluate the recent likelihood of making a successful exit.

Only Quebec, Ontario, British Columbia and Alberta had sufficient levels of data for the biotechnology analysis, therefore other provinces were omitted from our review. Alberta was furthermore excluded from the medical device analysis due to a lack of sufficient deal flow. The data reveal that Quebec has deployed the greatest amount of capital – more than double any other province for both medical devices and biotechnology – over $1.7 billion for biotechnology and $279 million for medical devices, in the last decade. However, its historical rates of return have not been optimal for biotechnology, with both British Columbia and Ontario outpacing Quebec on historical ROI, whereas more recent ROI do reveal a greater level of competitiveness for Quebec.

For medical devices, Quebec and Ontario were by far the Canadian leaders in terms of both historical and recent ROI. British Columbia has not had any recent ROI, which may be confounded by the small total amount of investment. Interestingly, medical devices had a higher historical and recent ROI than biotechnology investments for those provinces with sufficient deal volume (Ontario and Quebec), but the probability of successful exit was lower for both recent and historical transactions for medical devices – roughly 30–50 per cent lower for medical devices.

Private-independent venture investors provided superior ROI (Figure 4)

To dissociate the differential impact that each type of investor had on the expected ROI, we used metrics such as historical ROI to provide a lower bound on expected ROI for the current generation (from 2000 to 2010) of investments, and used recent ROI to quantify their performance. Both metrics are defined as described in Figure 3 of section 'Results'. In short, recent ROIs excluded returns from exits that occurred from 2000 to 2010 that were not a result of investments made from 2000 to 2010. Similarly, we determined recent exit and historical exit probabilities with exits made from investments from 1990 to 2000 vintage excluded from the calculation for recent exit probability.

Private-independent investors showed a significantly higher ROI than either retail or government investors. The effect was even more marked for foreign VC investors (investing in the Canadian life science sectors) who achieved ROI almost double that of the Canadian government, retail or private-VC investors. Conversely, the participation of retail VC investors appeared to have a negative impact on the recent ROI for biotechnology. The probability of exit did not differ significantly among the different types of investors regardless of the type of investment, although once again,

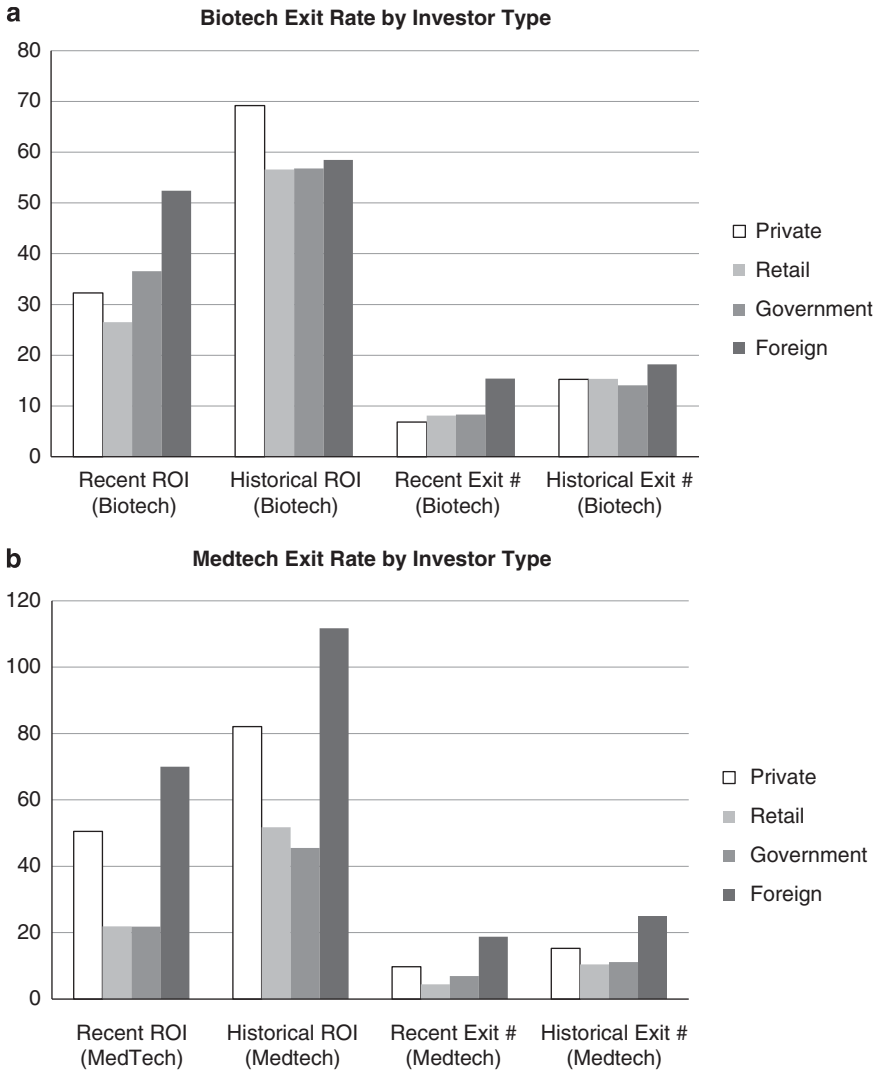

Figure 4: Financial performance by type of investor and sub-sector of life sciences industry.

having a foreign VC investor appeared to significantly increase the probability of a superior ROI.

For medical devices, the difference between private-sector/foreign investors and government/retail investors was even more significant than those for biotechnology – with ROI of 2.4- and 3.3-fold, respectively. Interestingly, the ROI achieved by foreign VCs from medical device exits was the only positive ROI in the entire data set – foreign VC investors actually received a positive ROI of an additional 11.7 cents for every dollar they put in from 2000 to 2010. Similarly, probability of a successful exit in terms of both historical exit percentage and recent exit percentage was also significantly greater for private-sector/foreign VC investors compared with government/retail investors. Private-sector and foreign VC investors were 1.4- and 2.7-fold more likely to exit than were government VC investors, respectively, whereas they were 2.2- and 4.2-fold more likely to exit than were retail VC investors, respectively (both comparisons made in terms of recent exit probabilities).

Canadian provinces employ differing VC strategies

Quebec (centralized government approach)
Within Canada, Quebec has the highest absolute amounts of capital deployment in both medical devices and biotechnology with approximately double the amount invested by any other province. Quebec offers not only significantly generous tax credits for the life sciences industry, but also significant capital deployment. Similar to Ontario and British Columbia, Quebec has an early-stage government-financed VC fund (Innovatech Quebec – www.innovatechquebec.com/) that invests from R&D to Series A to the first round of financing, up to a maximum of $5 million per firm. Financial instruments vary from participating shares, convertible debentures or non-convertible debt from a company.

Unlike the other provinces, tax policy for the early-stage technology businesses is coordinated by a single financial and economic development institution – Investissement Quebec (www.investquebec.com/en/). Solutions range from the Small and Medium Business Financial Program, which allows eligible firms to receive loans or loan guarantees for almost all project related expenditures, to the Fiscal Measures Program, which grants biotechnology firms beneficial tax treatment if they operate in regional centers identified by the Quebec Government. Finally, the Regional Economic Intervention Fund within Investissement Quebec helps firms obtain equity or quasi-equity financing. The organization also provides firms with access to a team of professionals that can aid the firms in building strategic alliances with international partners, accessing the right financing solutions across provincial government departments and establishing the appropriate business locations.

Late-stage financing comes from the Société générale de financement (SGF) du Québec (www.sgfqc.com/en/index.htm), which is industrial and financial holding corporation of the Quebec government. In 2007, SGF's investment portfolio totaled nearly $2.5 billion. SGF aims to act as a catalyst in the industry by helping companies to attain the critical mass they need to penetrate international markets. Using its financial muscle, SGF can structure business consolidation, mergers and partnerships among life science firms.

In the life sciences industry, SGF offers financing in the form of equity investment, with a minimum $5 million investment, a 20–49 per cent stake and an investment horizon of 5–8 years. Besides the financing opportunities presented by SGF, it also boasts an in-depth knowledge of the laws, procedures and key players in its targeted industries, extensive deal-making experience, a vast network of contacts both within Quebec and globally, and extensive knowledge to assist partners with financial, commercial and technical analysis, project implementation and business management.

What do the raw numbers say about this centralized approach? In absolute terms, Quebec has achieved the highest number of deals, but its ROI has not been as capital-efficient as British Columbia for biotechnology (43.438 per cent versus 51.733 per cent in terms of historical ROI) or Ontario for medical devices (54.79 per cent versus 68.23 per cent) (Figure 3a and b). In addition, the probability of exit for its investments has also been inferior to Ontario in terms of both biotechnology exit probability (3.647 per cent versus 7.186 per cent) and medical device exit probability (4.615 per cent) (Figure 4a and b). In short, Quebec takes a more shots on goal approach with a high level of subsidization and capital-intensity. Nevertheless, by sheer brute force, Quebec has established a strong presence in both medical devices and biotechnology. This approach is probably not employable for many jurisdictions, internationally or within Canada, owing to the high capital requirements and diminishing returns on that capital.

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Ontario (decentralized government approach)

In contrast to Quebec, Ontario takes a much more decentralized and passive approach to innovation – relying more on private-sector dollars for funding, and focusing more on passive policy and softer enterprise support services. Since 1 July 2010, there has been no capital tax on businesses operating in Ontario, and the marginal effective tax rate on new capital investments will fall to 18.6 per cent, dropping further to 16.2 per cent by 2018. When tax credits are factored in, $100 in R&D expenditures can be reduced to an effective cost of less than $44 and less than $37 for small businesses. New corporations that commercialize intellectual property developed by Canadian universities, college or research institutions can take advantage of the Ontario Tax Exemption for Commercialization (OTEC). OTEC refunds provincial income tax and corporate minimum tax for each of a corporation's first 10 taxation years.

Nevertheless, Ontario itself has begun to create investment pools for seed capital including: (a) Ontario Emerging Technologies Fund (www.mri.gov.on.ca/english/programs/oetf/program.asp), valued at $250 million in matching funding with qualified VC funds and private-sector investors, (b) The Ontario Venture Capital Fund (www.ovcf.com/), which is valued at $205 million and (c) MaRS Investment Accelerator Fund (www.marsdd.com/aboutmars/partners/iaf/), which is a $29 million fund that provides firms with early-stage financial support and management expertise to make these businesses more attractive to follow-on investors. Similar networks focused on medical devices such as the Health Technology Exchange (www.htx.ca) have also been created to provide early-stage scientists, engineers and entrepreneurs with funding, market research and intelligence. Unlike Quebec, however, none of these organizations are explicitly linked together to support the life sciences industry.

These initial investments have led to successful partnerships including a joint venture between Johnson & Johnson and MaRS Innovation (www.marsinnovation.com), which is an organization established by multiple research institutes with first right of refusal on intellectual property in Toronto, and $30 million to establish proof of concept and make technologies attractive to investors.[6] With multiple organizations involved with wide-ranging mandates, one challenge for Ontario will be to avoid duplicating efforts, and ensure that resources are efficiently deployed while minimizing the bureaucratic blockage that can come with public organizations.

The superior ROI experienced for medical devices in Ontario compared with the rest of Canada suggests that it is a potential hot-spot, and thus would be well advised to consider pouring more resources into promoting this area (Figure 3b). It may be that a less centralized approach to innovation is more beneficial to medical devices, although less beneficial for drug discovery as reflected by Quebec's superior performance compared with other provinces for drug discovery.

British Columbia (decentralized private-sector approach)

British Columbia appears to be the province closest to achieving a private-sector driven VC industry to support the life sciences. In 2009, the British Columbia government announced the British Columbia Renaissance Capital Fund, a $90 million VC fund targeted toward the life sciences (www.bcrcf.ca/BCRCF/Pages/Default.aspx). Rather than assigning local government bureaucrats to manage the fund, British Columbia took the unique approach of having the capital overseen by a team of top-tier private-VC fund managers.

The money is focused on early-stage firms, and is structured to be deployed over a period of up to 5 years. It reallocates a portion of the existing BC Immigrant Investor Fund established in 2001 under the federal

government's Immigrant Investor Program. The Renaissance fund managers are Arch Venture Partners, VantagePoint Venture Partners, Kearny Venture Partners, Walden Capital, Ventures West and Celtic House Venture Partners. Collectively, they have more than $2.3 billion in capital under management.[7]

Richard Glickman, founder of Aspreva Pharmaceuticals, a Victoria life sciences company that was sold in 2007 to Swiss health care company Galenica for $915 million, described the strategy 'as a powerful opportunity for local and external venture groups to work together to bring wider attention to British Columbia'. 'Through the significant resources of the six managers, the BC Renaissance Capital Fund is an ingenious way to get larger funds to look at B.C. as an attractive place to invest'.[8] Local venture capitalists are able to partner with non-local investors, so that 'even with limited amounts of cash, their [local venture capitalists'] money acts as leverage, and more important, they can keep an eye on these firms, providing information to foreign investors'.[9]

The data suggests that British Columbia appears to have struck an effective balance between achieving a critical mass of capital, and not allocating excess amounts of capital in an inefficient fashion. This region appears to have established itself as a biotechnology powerhouse with the highest historical ROI compared with the other provinces, with the biomedical devices still an emerging work in progress, with no deals exited so far and financing activity for medical technology only 20 per cent that of Ontario (Figure 4a and b).

Customizing VC for medical devices and biotechnology

Although attracting private-sector VC in the right amounts is a laudable goal, there are more nuances to the life sciences than simply having the right amount of capital. There are significant differences between medical device and biotechnology innovation. Medical device innovation is much more user-intensive, and predictable in some ways, when compared with biotechnology innovation. One would hypothesize that medical device investments would have a lower ROI given the lower level of risk, and would also be more easy to find given the lower technical and financial barriers to innovation.

In contrast to this expectation, our results suggest that medical device investments offer a superior ROI compared with biotechnology, even when adjusted for the significantly higher risk that biotechnology maintains owing to its greater capital and time requirements (Figure 3b). Medical device investments actually provided investors in the Canadian life sciences industry an overall net positive ROI. Ironically, venture investment has been significantly lower for medical device investment, disproportionate to the superior ROI (Figure 2a and b). They were, however, significantly less successful when measured in terms of the proportion of exits achieved compared with the number of deals (Figure 4b).

DISCUSSION

Poor ROI from retail investors

Given the aggregate negative ROI on the entire sector as a whole (Figure 3), perhaps it is not that surprising that VC investment into Canadian life sciences has been declining. The question arises, 'why have the ROI been so poor?'

One explanation may be that too much capital was invested into the life sciences sector, which consequently led to inferior investment opportunities being funded. The government may have distorted the market by introducing retail funds that encouraged public citizens to invest in the life sciences. Such retail funds were mandated to deploy a certain percentage of capital every year, and fund manager incentives were subsequently misaligned with actual performance on investments.

The retail initiative appeared to have succeeded in attracting matching independent private VC with total capital managed more than quadrupling from 2000 to 2005. However, the actual number of investments made has returned to relatively lower pre-2000 levels that existed before the enormous 'New Economy' influx of capital that was further potentiated by various government tax credit policies from 2000 to 2005 (Figure 2a and b). In combination with increased risk adversity owing to the poor exit environment for VCs, the larger VC fund size by itself may have forced VCs to wait to make larger investments in order to yield satisfactory returns, as reflected in the increase in average biotech investment from $2.6 million to $7.4 million per company (Figure 2c).

Our results corroborate previous observations, as retail investors have a net negative impact on ROI even when compared with government investors, which in this study was used as a control group. Presumably, retail and government investors would intuitively appear to have similar levels of quality control (for example, not being as discriminating as private-independent VCs), yet recent ROI figures shows an almost 10 per cent superior ROI by government over retail VC investors for biotechnology (Figure 4a).

These poor returns could potentially be explained by the inability of bureaucrats to provide the necessary support and due diligence, as well as the lack of incentives in compensation structures. Matchmaking bureaucrats are not likely to know much about the people seeking funding, and do not bring the experience of business founders who are often involved in start-ups on a daily basis. However, government funds suffer the same type of problems – therefore, a more likely explanation is simply that too much capital was allocated in a capital-inefficient fashion through retail funds. Similarly, other analyses report that subsidized venture capitalists in retail funds with misaligned incentives can crowd out other private investment, and provide less effective mentoring, even when adjusting for the higher quality threshold for investment.[10]

The failures of labor-sponsored retail funds have contributed to the global perception of the Canadian VC industry as mediocre. Furthermore, a survey of over 500 general partners of VC firms around the world by Deloitte & Touche found that 40 per cent of US investors singled out Canada as having the least favorable treatment of investors, and they noted the dismally low returns for Canadian venture capitalists.[11] International capital flow is critical to the long-term growth of the sector, especially for Series C and D financing for clinical trials in humans for biotechnology companies.

The success of the United States in terms of ROI may well be reflected in the structure of the VC industry. The Canadian Venture Capital Association reported in 2007 that private-independent funds represented only 19 per cent of the total number of VC funds, whereas in the United States over 77 per cent of the total number of funds are privately run and independent.[5] It is difficult to imagine that such a significant structural difference might not play any role in the difference in ROI that was revealed in this study when comparing private sector with government or retail financing.

In Canada, there has been an overall increase in the amount of private-sector-backed life sciences VC funding, but the continued availability of significant government and labor-sponsored funding in absolute terms may be contributing to significant inefficiencies in the allocation of capital. In order to have a healthy life science industry, each country must find a way to move toward more private, independent VC funding.

National-level initiatives are showing modest success

Part of the solution may be to attract more foreign VC investment. Our results suggest

that foreign VC investors achieve overwhelmingly superior ROI and probability of successful exit when compared with all types of Canadian investors including private independent, government and retail VC funds. While their superior ROI may be because of foreign VCs cherry-picking the top Canadian start-ups after local investors have taken the greatest, initial risk, foreign VCs do benefit from several clear advantages such as having access to much larger pools of capital, greater experience and expertise, a direct market entry into the United States and Europe and also from receiving more attention from potential acquirers such as multinationals.

It is interesting to note that an increase in VC investment, particularly foreign investment, into Canadian life sciences start-ups has occurred in the last three quarters of 2010 (Figure 2b). While this may be confounded by the economic recovery following the tightening of VC purse-strings during 2009, the marked increase in foreign investment may in fact be, at least in part, a function of the government's recent repeal of Section 116 of the Canadian Income Tax Code in the 2010 budget in Q1 2010.[12] Earlier, when US VC firms had wanted to exit start-ups, they had to pay 25 per cent tax on their gains or file cumbersome paperwork to get an exemption, and also are required to file Canadian tax returns.[13] The North American Venture Capital Association reported that these procedures lead to protracted wait times of up to 4–8 months to obtain clearance certificates with 25 per cent of the gross sale proceeds withheld by the buyer of the VC-backed company until the clearance certification is granted.[14]

In Canada, the hurdles erected by legislation not only reduce attraction from badly needed international capital flow from foreign, primarily American, venture capitalists, but may also result in the loss to Canada of biotech firms that especially need large infusions of capital. The most straightforward solution to the funding problem has been to move the firms to the United States as soon as they are large enough to attract cross-border interest. As a result of such decisions, the life sciences industry loses talent, fails to increase the performance of those who stay, and ironically, ends up losing tax revenues it might otherwise have had.

Although the repeal of Section 116 was a necessary step for Canada, it is unlikely to be sufficient in and of itself to attract significantly more foreign investors. More local, early-stage private-sector-backed VC funding is probably required, as well as organizations and initiatives that can aid foreign investors in sourcing prospective investments. Without strong pools of smart domestic capital, Canadian VCs report that the United States will cherry-pick investments during the later stages. This occurs when Canadian VCs lack Series C and D capabilities, and are forced to exit their positions earlier than they otherwise would have, leading to lower achieved ROI.[15]

In Canada, while attempts have been made to develop local capital markets for prospective exits such as the TSX Venture, only seven qualified life sciences transactions have been completed in the last 5 years. The apparent lack of retail investor appetite for such offerings may be because of the low ranges of eligible capital and the infrequency and uncertainty of funding associated with small public equity offerings that make them imperfectly matched for the long time lines and high levels of fundraising associated with life sciences start-ups.

The lack of domestic VC has also implied that too many firms were competing for too little capital, and Canadian VCs have been criticized for spreading their investments too thin (although now the opposite problem may be the case for private-independent funds). This may have historically made it difficult for international VCs to identify good opportunities in an environment where both superior and inferior opportunities were being funded.

Typically, a US biotechnology firm can attract 3.5 times the investment that a Canadian firm can. The lack of capital also prevents Canadian biotech firms from overcoming the paucity of top executives in the life sciences industry, as many are drawn to the superior funding environment in the United States.

'When Canadian firms are compared with US companies, (lack of executive talent) is a definite hurdle', notes one prominent venture capitalist that we spoke to. 'We have recruited CEOs from the United States (that is, New York, Boston), and we get them in on the ground here to build teams around them. When it comes to closing B round financing, which may take $20–40 million, the company has a much better chance to attract the required capital'.

Consider the experience of New York-based OrbiMed Health care Fund Management, one of the world's largest health care funds with over $7.5 billion under management. It made the single largest investment in Canadian biotechnology in Montreal-based Enobia Pharma, which develops therapies for genetic bone disorders. It partnered with CTI Life Sciences Fund LP of Montreal, the Fonds de solidarite FTQ and Desjardins Venture Capital, and UK-based Lothian Partners, for a total of $90.1 million in invested capital.[16]

OrbiMed also invested $21.5 million into ARIUS Research, a Toronto-based company focused on developing personalized cancer therapy through antibodies. Roche acquired ARIUS barely 2 years later in 2008. Another prominent Canadian biotechnology, NeurAxon, received $32 million in financing in 2007 from OrbiMed and Delphi Ventures, both US-based firms, but without Canadian funds as lead lenders. In 2009, an additional $8.75 million was raised by NeurAxon from OrbiMed. Clearly, top-tier international VCs are interested in Canada – they just need help finding the right investments through early-stage co-investors supported by the right government innovation policies.

Local VC success, in Canada at least, depends on international capital flow, which ironically requires first the creation of larger domestic capital pools to attract it.

Canadian provincial experiments in innovation suggest capital-efficient model

While the ultimate goal may be to have a greater private sector presence in VC, Canadian governments still have a critical role to play in the interim. Both provincial and federal governments have made significant investment in publicly funded R&D occurring at hospitals and universities, as well as providing tax credits to promote R&D in the private sector. According to the Organization for Economic Co-Operation and Development, every dollar invested in R&D yields 18.7 cents in tax breaks in Canada, versus just 6.6 cents in the United States.[17] In 2010, $135 million was announced for expanding the National Research Council Canada's regional innovation cluster programs, launching a Small and Medium Enterprise Innovation Commercialization Program with $40 million and streamlining compliance associated with the taxation of cross-border activity by removing Section 116 of the Canadian Income Tax Code.[18]

Such indirect methods of attracting the local pools of VC are important, but have been insufficient in creating the desired effect. Although direct policy interventions such as publicly run government-sponsored labor funds have historically been failures, better structured public money can be a boon to creating a self-sustaining private-VC industry in the life sciences, and moreover increasing the percentage of local Canadian funds in the long run. The varying experiences of Canada's provincial innovation policies, as well as their ROI can help to guide this long-term policy strategy.

In our data set, Ontario appears to have the most potential in terms of medical device

Table 2: Comparing the different approaches to life sciences VC policy

Province	*Centralization*	*Medical devices*			*Biotechnology*		
		Investment intensity	*ROI efficiency*	*Exit efficiency*	*Investment intensity*	*ROI efficiency*	*Exit efficiency*
Ontario	Medium	Medium	High	High	Medium	Medium	High
Quebec	High	High	Medium	Medium	High	Medium	Medium
British Columbia	Low	Medium	Low	Low	Medium	High	Medium

Overall scores	*Medical devices*	*Biotechnology*
#1	Ontario	Quebec
#2	Quebec	British Columbia
#3	British Columbia	Ontario

opportunities, while Quebec's centralized approach to drug discovery makes it the overall leader for biotechnology investment, which makes sense given the high capital requirements, and much longer timeframes required to coordinate efforts (Table 2). However, Quebec's approach is also the least efficient in terms of exit opportunities and ROI among the provinces. In contrast, Ontario's decentralized approach has largely resulted in a failure to attract a strong cluster of biotechnology companies when compared with British Columbia and Quebec. It appears that Ontario has neither created effective policies for attracting private-sector VC nor offered sufficiently significant subsidization through its own financial muscle the way Quebec did in order to brute force the creation of a local biotechnology sector.

Despite its decentralized approach, Ontario was able to succeed quite well in the medical devices area, which may be reflective of its critical mass of physicians – Ontario has more university-based physicians than any other province – a resource that could be tapped into even further. Ontario's success may also be because of the nature of medical device discovery, which is more serendipitous and spontaneous than the more structured nature of drug discovery. In contrast, British Columbia's medical device sector is still nascent and under development, while Quebec has managed to foster some success simply by throwing enough capital at the problem. Alberta did not register for medical devices at all, indicating it has yet to reach a critical mass.

Interestingly, our data suggests that reaching a critical mass of capital (however limited our data set) for a biotechnology cluster requires slightly less than $1 billion CAN annually in investment, whereas reaching a critical mass of capital for a medical devices cluster only requires about $200 million CAN annually in investment. It will be interesting to see at what point capital deployment efficiencies begin to level off – for example, what is the ideal amount of capital that yields the maximal ROI and exit likelihood efficiency (Figure 3a)?

The most efficient way of deploying capital appears to be through mostly private-sector funding. Among government-based funders, a decentralized approach appeared to be more efficient despite the higher transactional costs and overheads associated with multiple funding agencies. There appeared to be a minimum amount of capital required for investment in a region in order for there to be a relatively efficient ROI for venture capitalists. This agrees with earlier studies describing the synergies that develop for identifying and supporting investments through life sciences cluster development. However, there also appears to be a maximum amount of capital, presumably relative to the availability of superior investment opportunities present, before diminishing, and then negative returns on

biotechnology investments are achieved, as poorer investments are funded.

Opportunities exist for medical device investment

Within the medical device investment sector, dichotomy of fewer exits and greater overall return may have negatively and inappropriately influenced the willingness of investors to allocate capital to this area. Part of the reason for the discrepancy may also rest with the lack of an entrepreneurial culture among physicians. Unlike biotechnology, which relies on relative-standalone industrialized processes (for example, assays, optimization and so on) that can be outsourced to third parties as far afield as China and India, medical device innovation is intimately tied to physician involvement. One study reported that over 20 per cent of the 26 000 medical device patents granted from 1990 to 1996 were filed by physician inventors.[19] Moreover, these patents tended to have a disproportionate clinical impact compared with those that were filed by non-clinicians – in particular, physician-driven innovations draw more heavily on scientific knowledge than corporate patents, better anticipated technological trends and create patents that are cited more frequently and more broadly than corporate patents. As an example, over 90 per cent of the biomedical device firm Medtronic's top selling medical products originated from physicians according to the Boston-based Center for Integration and Medicine and Innovative Technology.

Creating programs similar to Stanford University's BioDesign Initiative (innovation .stanford.edu/bdn/index.jsp) may be a solution to the disproportionately smaller investments in medical devices.[20] The process centers on teams that integrate medical residents, biomedical engineers and an individual with intellectual property or business experience, places them into a clinic to identify clinical needs for which they then proceed to develop a product that will form the basis for a business plan and a start-up. The global results have been stunning with the creation of several FDA-approved medical devices that have treated over 10 000 patients. Although the primary application of the methodology has been in surgical disciplines, the approach is being experimented with for regenerative medicine and biomedical imaging at some medical schools. Linking these incubator-like initiatives with VC funds similar to what New Enterprise Associates, one of the world's largest VC funds, has done with ExploraMed in Palo Alto, California could be potentially fruitful for Ontario, which we have identified as a potential biomedical device hot-spot based on ROI and exit probability.

Clearly, there are significant investment opportunities that have been overlooked in the medical device space. While there has been significant focus on biotechnology, medical device investments may help to cross-subsidize the significant losses in biotechnology, and create a better diversified environment for venture investors in the Canadian life sciences industry. More initiatives to involve physicians in user-driven innovation, government initiatives to support medical device specific innovation, and early-stage venture funding that actively seeks to cultivate and grow medical device firms are required.

CONCLUSIONS

Therefore, what policies and learning can be derived from the Canadian experience that may be generalizable to other countries that are trying to improve their VC ecosystem?

Conclusion #1: More of the right type of funding is needed – private-sector funding – owing to the poor historical returns from both government- and labor-sponsored capital. Labor-sponsored funds should not be employed, whereas multiple government funding agencies may be merged into a one-stop shop as in Quebec, to benefit from economies of scale. It may also be possible

to increase the probability of biotechnology companies to succeed, in particular in Canada, by providing funding all the way through Series C and D and by having a significant base of capital to leverage against international investors. This would in turn hopefully lead to the attraction and establishment of a critical mass of private-sector funding. The disparate experiences of the United States and Canada suggest that transitioning to a system of mostly private-sector funding will be critical to restoring healthy and stable rates of return for venture investors.

Conclusion #2: British Columbia points the way to the most efficient policy for allocating capital, maintaining relatively minimal government involvement and encouraging the creation of a critical mass of independent private-sector VC industry. Ignoring political considerations, Quebec demonstrates an extremely inefficient approach, while Alberta has yet to reach a critical mass. Nevertheless, Quebec illustrates that it is possible to generate a reasonable critical mass of life sciences industry activity and ROI by simply throwing enough money at the problem. This, however, is not necessarily the most capital-efficient way of fostering critical mass development.

With regard to Canada itself, efficient and effective policy means that Quebec must streamline its investments and Alberta must step them up. Ontario has largely failed in terms of both structuring the right kind of government VC funding and creating conditions that are conducive to private-sector VC innovation. On the government side, Ontario could benefit from following the lead of British Columbia in promoting the growth of private-sector VC through the establishment of public–private funds managed by private-independent investors, or by following the example of Quebec in structuring government-based funds that provide end-to-end support of investments. Specifically for medical devices, Ontario needs to better integrate funding with the physician-led innovation in order to increase the probability of a successful exit occurring. It is worth noting that our results and conclusions contrast with current global trends in this arena.

Policy proposal 1: An efficient and effective strategy to improve a VC ecosystem

We propose either the hybrid private–public fund structure that British Columbia has taken or the fund of funds approach that Quebec has taken, and posit Burrill Canada and Quebec's Teralys Capital as respective points in case, for these emerging classes of funds. Burrill has proposed a $200 million fund, to be capitalized from joint public- and private-venture funding, but managed by private-sector investors and targeted at Canadian life sciences investment.[21] The model has been successfully employed by governments in South Korea and Malaysia. Teralys Capital is a recently announced fund of funds in Quebec that closed in June 2009 with over $700 million in capital commitments. This fund will make investments as a limited partner into private-sector and government-based VC funds. Both of these fund structures would benefit from decentralized, sector-specific government agencies, with the smaller scale of fund enabling smaller levels of investment, which helps to provide much needed early-stage financing. Although some commentators have argued that more funding is badly needed for the VC industry – and suggest the creation of government-sponsored fund of fund programs, retail VC programs and VC tax credits – the results of our analysis suggest that more retail VC money will probably be ineffective, and it is unclear whether more local VC is actually needed for biotechnology investments.[22]

Policy proposal 2: For Canada, a public–private VC fund targeted at medical devices

Medical devices offer a significant investment opportunity that has been overlooked and

Box 1: A Venture Capital Policy Proposal for Ontario, Quebec and British Columbia

The medical device industry in Ontario requires roughly US$100 million more in investment every year in order to reach its potential. This US$100 million needs to be attracted through a combination of increased capital deployment from the government through the right structure (either a public–private fund, or a fund of funds) and incentives, or the creation of direct incubators or physician training programs linked to rapidly available early-stage financing for proof of concept. Given the spillover effects and matching private-sector capital, roughly US$40 million annually for direct funding, and US$10 million for the creation of incubators and physician innovation programs could be sufficient. Given that medical devices are the only life sciences investment class that maintained a positive ROI during the recent market downturn, the Ontario government would be prudent to take advantage of this opportunity.

Quebec has significant capital available for deployment, but could benefit from incubators/physician-innovation programs that more efficiently deploy that capital into the medical devices. Although its centralized large-scale capital deployment has worked relatively well for biotechnology, capital alone is not sufficient for success in the medical device arena given the iterative development process. British Columbia has comparatively little activity in the medical device space, and needs to also create similar institutions and funding mechanisms if it aspires to build a medical device cluster to complement its strength in biotechnology.

which could be effectively developed and promoted by government agencies, particularly by involving physicians through innovation initiatives and the creation of incubators linked directly to private-sector capital. In Canada, Ontario is a potential hot-spot for medical device innovation, which has been, until recently, largely ignored by VC investors. Extrapolating from the results that Quebec has achieved, and the larger critical mass of biomedical engineering talent present in Ontario, the province could significantly benefit from the addition of at least another $100 million in investment annually specifically targeted to medical device innovation, and which would not be expected to dilute its overall ROI or exit efficiency. We propose such a policy mechanism for attracting VC for biomedical devices (Box 1).

Within Canada, the federal and provincial governments have invested substantial amounts in supporting R&D, both in academia through direct funding and in industry through tax credits, and there are large benefits available from the commercialization of this research. Globally, the VC industry is a critical part of the ecosystem that takes research from the laboratory to commercial products, and if the VC industry is not healthy, the potential benefits will be lost. Building a strong and innovative technology-based economy, in Canada or around the world, requires a strong VC industry.

REFERENCES

1. Ackerly, D.C., Valverde, A.M., Diener, L.W., Dossary, K.L. and Schulman, K.A. (2008) Fueling innovation in medical devices (and beyond): Venture capital in healthcare. *Health Affairs* 28(1): w68–w75.
2. Gompers, P. and Lerner, J. (2004) *The Venture Capital Cycle*, 2nd edn. Cambridge, MA: The MIT Press.
3. BIOTECanada. (2010) Punching above its weight. *Biotech Canada Insights*, http://www.biotech.ca/en/media-centre/insights-magazine/past-issues.aspx, accessed 18 January 2011.
4. Friedman, Y. and May, M. (2010) Worldview: A global biotechnology perspective. *Scientific American*, http://www.saworldview.com/article/the-top-5, accessed 2 January 2011.
5. Canadian Venture Capital Association. (2009) Why venture capital is essential to the Canadian economy: The impact of venture capital on the Canadian economy. 15 January, http://www.cvca.ca/files/downloads/cvca_2008_vc_economic_impact_single.pdf, accessed 12 January 2011.
6. MaRS Innovation. (2010) MaRS innovation establishes co-managed fund to advance transformative healthcare technologies. 7 August, http://www.marsinnovation.com/wordpress/wp-content/uploads/2010/08/MI-JnJ-Press-Release-CLEAN-August-7-2010-FINAL.pdf, accessed 4 January 2011.
7. Canadian Venture Capital Association. (2008) New L.P. funds. (January–June), Fall, http://www.cvca.ca/files/Downloads/CV83_LowResForWeb.pdf, accessed 9 January 2011.
8. Ministry of Economic Development. (2008) B.C. launches $90M venture capital fund. 18 April, http://www2.news.gov.bc.ca/news_releases_2005-2009/2008ECD0020-000563.htm, accessed 8 January 2011.
9. Salazar, M. and Holbrook, A. (2004) In Search of Impact and Outcome Indicators Based on

Vancouver Biotechnology Cluster Studies. Montreal, Quebec. Presented at the Colloquium on Measuring the Impacts of Science, 17–18 June.

10. Brander, J., Du, Q. and Hellmann, T. (2010) The effects of government-sponsored venture capital: International evidence. 9 June, http://sites.kauffman.org/efic/conference/BranderDuHellmannJune9th2010.pdf, accessed 15 January 2011.
11. Deloitte & Touche and Canadian Venture Capital Association. (2007) Global trends in venture capital survey. 5 December, http://www.deloitte.com/assets/Dcom-Canada/Local%20Assets/Documents/ca_en_TMT_VC_2007survey_dec2007(1).pdf, accessed 17 January 2011.
12. Deloitte & Touche. (2010) Change in tax law sends strong signal that Canada is 'open for business'. 4 March, http://www.deloitte.com/view/en_CA/ca/pressroom/ca-pressreleases-en/press-release/2629cd49b8a27210VgnVCM200000bb42f00aRCRD.htm, accessed 17 January 2011.
13. Brenner, R. and Brenner, G.A. (2010) Venture capital in Canada: Lessons for building (or restoring) national wealth. *Journal of Applied Corporate Finance* 22(1): 86–98.
14. Hurwitz, S.A. and Marett, L.J. (2007) How to navigate Canada's Byzantine tax rules. *Thomson Reuter Venture Capital Journal*, Issue 4.
15. Ho, D. (2007) Breakfast with dealmakers – The Canadian VC panel. *BioFinance Newsletter* 3, http://www.biofinance.ca/documents/BF%20Newsletter%20Volume%203.pdf, accessed January 18 2011.
16. Melnitzer, J. (2010) Lawyers, U.S. firms filling Canada's biotechnology void. *Law Times*, 14 January, http://www.lawtimesnews.com/201006147036/Headline-News/Lawyers-US-firms-filling-Canadas-biotech-void, accessed 18 January 2011.
17. Mack, G.S. (2005) Canada's alternative biotech scene is an Island apart. *Nature Biotechnology*, 14 July, http://www.nature.com/bioent/bioenews/072005/full/bioent872.html, accessed 18 January 2011.
18. National Research Council of Canada. (2010) Minister goodyear announces investment in research and innovation in communities across Canada. 24 June, http://www.nrc-cnrc.gc.ca/eng/news/nrc/2010/06/24/cluster-stjohns.html, accessed 19 January 2011.
19. Chatterji, A.K., Fabrizio, K.R., Mitchell, W. and Schulman, K.A. (2008) Physician-industry cooperation in the medical device industry. *Health Affairs* 27(6): 1532–1543.
20. Chakma, J. (2009) Back to first principles: We need more physician innovators, not more physician scientists. *Nature* 460(7256): 769.
21. Saskatchewan Regional Economic Development Authority. (2010) Burrill and company announces plans for Burill Canada Fund. 30 August, http://www.sreda.com/en/pages/235/news_details.html?id=100, accessed 5 January 2011.
22. Deloitte & Touche. (2010) Canadian VC industry's decline intensifies. 7 September, http://www.deloitte.com/view/en_CA/ca/pressroom/ca-pressreleases-en/3ceacc2478aea210VgnVCM1000001a56f00aRCRD.htm, accessed 6 January 2011.