An Analysis of Pharmaceutical Patent Evaluation Duration in Canada and the Role of R&D Intensity as an Indicator of Complexity

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Abstract

Patents have long been used to incentivize innovative activity. In the pharmaceutical sector, patents work well at encouraging innovation as firms incur years of research and development expenditures in exchange for a twenty-year monopoly over the production and sale of their drug products. While patents are of practical importance, allowing firms to realize their research investments, they are also of strategic importance because their evaluation duration can be used as indicators of the level of value and complexity of the protected product to competitors. In this paper, I analyse patent-specific factors of the examination duration of pharmaceutical patents in Canada using a sample collected from Health Canada's Patent Register. The results of my analysis indicate that higher research and development intensity in the three and four years leading up to the filing of a patent are associated with an increase in patent evaluation duration, likely because it indicates greater patent complexity. In contrast, patents that are used to protect multiple drugs are associated with a decrease in patent evaluation duration, largely because it indicates higher value patents.

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Contents

Introduction

Patenting an innovation is a lengthy process given that novelty, inventiveness, and usefulness must be established for a patent to be successful at the most basic level. However, firms whose innovations satisfy these criteria are rewarded with a monopoly for their innovation. For pharmaceutical firms, patents are considered to be a good means of incentivizing innovative behaviour because they induce research and development (R&D) while allowing for follow-on innovation ex-post (Gallini, 2017). Spurring innovation in the pharmaceutical sector is also a challenging process because it is often more complex than that for other industries. Pharmaceutical innovation frequently involves years of drug research and development to produce a single patentable product.

Whereas firms in other industries can take their innovation to market immediately after filing a patent, pharmaceutical companies must undergo several phases of clinical trials to prove both the efficacy and safety of their products before they can begin to manufacture and market them. In Canada, patent protection begins on the date of filing and extends 20 years from that date. However, a firm can only take legal action for all damages caused by infringement once their patent has been granted.[1] For any infringement that occurred before the patent has been granted, a firm may claim "reasonable compensation," but this action can only be taken once their patent has been issued. At the same time, pharmaceutical firms intending to take their drugs to market must undergo clinical trials consisting of three phases of testing. If successful,

[1] "A guide to patents" Canadian Intellectual Property Office, https://www.ic.gc.ca/eic/site/cipointernet-internetopic.nsf/eng/h_wr03652.html

Health Canada issues a Notice of Compliance (NOC) that allows the drug product to be manufactured and sold in Canada.[2]

Drug development is a costly process; estimates of US research and development firm out-of-pocket expenditures indicate that approximately $1.4 billion in 2013 dollars is spent on approved pharmaceutical compounds (DiMasi, Grabowski, & Hansen, 2016, pp. 26). Complicating the economics of pharmaceutical patents further, clinical trials are a lengthy process that induce firms to time the filing of their patents strategically. Patent applications are usually filed as late as possible to allow firms to protect their research interests and realise a longer period of profits afforded by market exclusivity (Humphreys, 2006). Despite this strategic timing, estimates for Canada indicate that it takes an average of seven years to obtain market approval, thus rendering the effective life – essentially the years of drug monopoly on the market – of a patented pharmaceutical product to about thirteen years if the firm files at the start of clinical trials.[3]

While the effective patent life is an important consideration for firms, the difference between the date on which a patent is filed and the date on which it is granted can be large and can lead to a wide range of consequences. For one, the evaluation duration, especially if it spills into the clinical trial phases, can open firms up to potential infringement and post-grant litigation that challenges the validity of their patents. The long wait time may also disincentivize innovation, which could result in further delays for important medicines, thus resulting in social costs in terms of less effective treatment (Regibeau & Rockett, 2010). Yet another consequence

[2] Office of the Parliamentary Budget Office "Patent Restoration and the Cost of Pharmaceuticals" pp. 7
[3] Ibid, pp. 40

is the signalling value of patent evaluation times: studies suggest that this is an important consideration for rival firms as it often conveys information on the value of the patent.[4]

In this paper, I explore the patent-specific characteristics of pharmaceutical patent examination duration for patents that have been granted in Canada between 1991 and 2016. Specifically, I identify a relationship between firm-level research and development intensity and patent evaluation time, measured in months, from a sample of patents filed in the Canadian Intellectual Property Office. Using evidence from reduced form empirical specifications, I also link my findings on the effect of R&D intensity on patent examination time to indicators of patent value and complexity.

I find that an increase in R&D intensity in the three and five years prior to the filing of a patent is associated with an increase in patent evaluation time, indicating that R&D intensity prior the filing of a firm can be used as a signal of the complexity of patents. I also find that an increase in the number of drugs a patent protects is associated with a significant decrease in patent evaluation time, likely because it signals the value of a patent. Overall, these results are consistent with empirical specifications that identify the role of value and complexity in patents: complex innovations experience longer evaluation periods while valuable patents are processed more quickly.

The structure of this paper is as follows. The first section presents an overview of studies of the economics of patents and the consequences they carry for healthcare practice and policy, while also providing an overview of the literature covering the determinants of patent examination duration. The second section outlines the various sources used to construct the

[4] Regibeau and Rockett (2010) find that more important patents tend to be filed quicker. Similarly, Harhoff and Wagner (2009) find that patent examination durations at the European Patent Office can be used as a signal of value.

dataset that is at the core of this analysis. In the third section, I discuss the methodology used in my analysis, followed by a discussion of my results. Section five provides insights into the key limitations of my findings. Lastly, I conclude the paper with a brief overview of the key lessons learned from my analysis.

Perspectives from Empirical Research

Given the importance of medical innovation on healthcare practice and overall wellbeing, studies investigating the link between patents and research and development in the pharmaceutical sector have been numerous. Early work investigating the patent examination and duration for an arbitrary industry is largely theoretical. For example, work by Nordhaus (1969) and Scherer (1972) take a theoretic approach to the economics of patents and find that an increase in patent life incentivizes firms to carry out cost reducing R&D. Incorporating welfare economics into their approach, they also find that patent durations should be longer for firms that are able to achieve cost reducing R&D for novel inventions. Building off these findings, more recent work on this topic focuses on a broader definition of 'optimal level' of intellectual property rights, usually denoted in terms of the breadth or duration of patents that impact innovative activity, firm monopoly power, and social welfare. While my study identifies patent-specific determinants of evaluation duration for pharmaceuticals, it is still important to review some of the consequences of the patent duration on public health outcomes in order to motivate discussion.

Traditional Approaches to Pharmaceutical Patents: Patent Duration

Studies that have analysed patent duration tend to look at policy changes that increase the amount of time a patent guarantees a firm monopoly power over a drug. Cockburn, Lanjouw, and Schankerman (2016) look at the role of policy changes, including those that affect patent length,

on the diffusion of new drug innovations. Using a sample of 76 countries with varying patent lengths prior to the implementation of TRIPS in 1995[5], the authors find that longer patent periods, defined as those spanning more than seventeen years, significantly increase the rate of diffusion of drugs in both high- and low-income countries. Patent duration also matters for drug prices, as they find that longer patent length is associated with increased prices, highlighting the inherent trade-off between the incentive to innovate and the monopoly power created by pharmaceutical patents.

Similarly, Grootendorst and Di Matteo (2007) look at the effect of patent policy change in the form of Bill C-22 on pharmaceutical research in Canada and find that increased patent length is associated with more drug research and greater drug expenditures incurred by provincial governments.[6] The authors analyse the effect of Bill C-22 on pharmaceutical research and development (R&D) using R&D expenditure in the motor vehicles and parts sector as a proxy for the counterfactual research activity that would have occurred in the absence of the policy change. They find that the increase in patent duration led to a $4.6 billion dollar increase in R&D spending between 1988 and 2002. Like Cockburn et al. (2016), they also note that the longer duration led to increases in drug spending. However, taking a cost-benefit approach to analysing the public health outcomes of the weakening and subsequent elimination of compulsory drug licensing, they find that research gains attributed to an increase in patent duration outweigh increases in associated drug costs.

[5] TRIPS (Trade-Related Aspects of Intellectual Property Rights agreement) harmonized pharmaceutical patent rights, including the length of a patent, setting the standard at 20 years of coverage with no exception for pharmaceutical patents.

[6] Implemented in 1993, Bill C-22 eliminated compulsory licensing in Canada by granting a panentee seven years of market exclusivity following federal drug approval, thereby increasing the length of guaranteed monopoly afforded by patents by reducing generic competition (Grootendorst and Di Matteo, 2007, pp.66).

Patent – Specific Determinants of Patent Evaluation Time

A large body of research studies the outcomes of policy changes that increase patent duration but relatively little empirical work focuses on patent evaluation duration and its implications. Harhoff and Wagner (2009) approach this area by analyzing the application characteristics of a random sample of patents filed at the European Patent Office between 1982 and 1998. Using data on patent renewals as an indicator of the value of granted patents, they employ an accelerated failure time model and find that valuable patents are granted significantly faster compared to less frequently renewed patents. Furthermore, the authors use the number of patent references and claims as an indicator of complexity and they find that an increase in both measures is associated with longer patent pendency times. Relevant for my study, Harhoff and Wagner (2009) also find that more complex technology sectors, like biotechnology and telecommunications, experience significantly longer patent evaluation duration relative to industries like printing.

In a similar vein, Regibeau and Rockett (2010) employ both a theoretical and empirical approach to outline the relationship between patent value and examination duration at various stages of a technology cycle, which begins when a "fundamentally new technology route is explored" (Regibeau & Rockett, 2010, pp. 223). In their model, the authors focus on the behaviour of the filing party and distinguish between good patents, which comply with the standards set for acceptable patents, and bad patents - ones that do not conform to novelty and non-obviousness. For their empirical results, the authors use data on patents for genetically modified crops between 1983 and 1999. For their measure of importance, the authors create an index of scope, where a larger scope relates to patents that do not restrict their claims to a particular plant or trait, thus indicating greater importance. Overall, Regibeau and Rockett (2010) find that patents filed near

the beginning of a new technology life cycle experience longer delays in granting, largely because patent examiners need more time to investigate the new technology. Over time, delays tend to decrease. They also find that after controlling for technology life cycle, patents that are more important have shorter evaluation times.

Liegsalz and Wagner (2011) study the effect of patent and inventor characteristics on examination duration for patents filed at the State Intellectual Property Office of China. Using data spanning 1991 to 2002 provided by the European Patent Office, they specify a hazard function that measures the failure rate of patents as a function of several patent characteristics. The authors find that the applicant's country of origin matters, as patents filed by Chinese applicants tend to experience shorter examination times and longer patent duration. They also find that revealed technology advantage areas – or technologies in which a country preforms well relative to other countries – experienced shorter patent examination times and subsequently, increased patent duration.

While the aforementioned papers look into the patent and inventor specific characteristics that impact patent evaluation duration, they do not look into firm-level R&D spending as a proxy for the research intensity that goes into a patent, as well as an indicator of patent complexity.

Data

The main issue in analyzing Canadian pharmaceutical patents is that a comprehensive database containing information on the attributes and inputs of patents is not available. As such, the empirical analysis in this paper relies on data collected from a variety of sources and compiled into one dataset. Specifically, I use Health Canada's *Patent Register* and *Drug Product Database*, as well as the Patented Medicines Price Review Board's (PMPRB) annual reports and the

Canadian Intellectual Property Office's (CIPO) *Patent Database* to collect and hand-match the information provided for a given patent to that patent's identifier. The following section outlines the specific data sources used and summarizes the variables of interest.

The set of pharmaceutical patents analysed in this research are collected from Health Canada's patent register, which is compiled by the Therapeutic Products Directorate (TPD) as required by the Patented Medicines Notice of Compliance Regulations. As an administrative database, the register is intended for use by pharmaceutical companies conducting research when citing prior art in their patents. The register, which is updated daily and available to the public through Health Canada's website, contains information pertaining to patents that have been submitted for addition to the register. This information includes the patented medicinal ingredient or process and the drugs in which they are used, denoted by drug information numbers (DIN). Pertinent to this study, the Patent Register also contains information such as the file date, grant date, and expiration date of submitted patents, as well as the service company that filed them. As of May 7, 2019, the register contained 2,223 unique patents.

The Patent Register is a useful source of information when looking at pharmaceutical patents filed in Canada. However, a few limitations were encountered when compiling the data needed for this study. Since the Patent Register identifies the service company that filed a patent and not the owner or assignee of the patent, companies that employed a law firm to submit a patent were not identified in the Register. To obtain this information, I searched the CIPO electronic Patent Database for patents with a law firm was listed as the service company, using their patent identification number to match these patents to the innovating firm. The owner of the patent was

then identified and manually linked to the corresponding patent in the patent register.[7] To ensure that this process was conducted accurately, the file date and grant date of the patent in the CIPO database were also used to confirm that the correct patent owner was matched to its corresponding patent in the Patent Register.

Another limitation of the Patent Register is that it exists in three separate files: one that identifies the patented drug by DIN and its various attributes, one that identifies a patented medicinal ingredient or process and its service company, and one that identifies submission certificates. Because this study requires information such as the therapeutic class of the drug that a patent is used in, the drug file and service company file needed to be merged. To do this, I relied on the drug identifier, which provides no information in and of itself, but was common to both files. This identifier was used to hand match a DIN to a patent in order to collect further information, such as the main active ingredient of drug and whether it is intended for human or veterinary use.

The last limitation encountered in constructing this dataset was the problem of missing data. Because of the changing nature of the patent submission form used to create the register, several fields for a given record could be empty, resulting in missing data (Health Canada, 2018). The therapeutic class of drug was one such field that was empty for most drugs, but also integral to this study. To overcome this limitation, I restricted the sample to drugs intended for human use and used the DIN corresponding to each patent to search Health Canada's Drug Product Database.

[7] Firm names in the CIPO database differed (albeit subtly) from firm names listed in the PMPRB annual reports. In these cases, I gave both firms one common name. There were some instances where firms merged in a given year, but PMPRB R&D expenditure to sales revenue ratios were reported for the individual firms while patents were filed by the merged firm. In these cases, I applied the R&D expenditure ratio of the firm in which the headquarters were kept. For example, with the merger of the Swedish firm Astra and the British firm Zeneca in 1999, the headquarters were located in London, England. Therefore, I applied Zeneca's R&D expenditure to sales revenue ratio to patents filed by AstraZeneca until post-merger R&D ratios were reported to the PMPRB.

I then obtained the anatomical therapeutic class (ATC) from the drug database record and hand matched it to the patent in the patent database. To ensure accuracy, I verified that the active ingredient and drug company owner in both the Patent Register and Drug Product Database were the same.

Established by the World Health Organization, the ATC classification system provides information on the attributes of a drug, including the organ systems affected, the active ingredients contained, and dosage (World Health Organization, 2018). For the purposes of this paper, the main anatomical/pharmacological group, or first level, is used to categorize the class of drug.[8] Because of the varying extent to which certain therapeutic classes were represented in the resulting sample of patents (for example, there were 184 patents for active ingredients used in drugs affecting the alimentary tract and metabolism, and 2 for antiparasitic products), I grouped therapeutic classes further, resulting in a sample with eight combined anatomical/pharmacological categories.

Table 1: Summary Statistics

R&D/sales	Summary Statistics				Quantiles					
	N	Mean	S.D.	Kurtosis	Min	0.25	Mdn	0.75	0.9	Max
File year	954	10.74	11.56	31.891	0	6.1	9.1	12	17.0	115
One-year prior	916	11.51	15.77	56.406	0	6.1	8.9	12.1	19.0	172.9
Two- years prior	777	11.62	13.9	41.076	0	6.3	9.3	12.5	21.0	172.9
Three – years prior	803	11.27	12.45	30.399	0	6.7	9.1	11.9	20.9	115
Four – years prior	729	11.81	13.52	28.817	0	6.7	9.1	12.2	21.7	115
Five – years prior	658	12.94	15.33	34.34	0	7.1	9.6	12.5	23.2	172.9
Patent evaluation duration	971	97	36.81	3.44	13	72	95	117.5	143.5	232.5

Note: Not all patents have an R&D expenditure to sales revenue ratio in every leg length.

[8] Note that not all drugs have an ATC code. These drugs were omitted from the sample.

As a means of estimating the effect of R&D expenditure on the amount of time it takes for a filed patent to be granted, data on the R&D-to-sales revenue ratios were collected from the PMPRB annual reports.[9] While patent-specific R&D expenditures alone would be optimal in this study, in its absence, the incorporation of sales revenues in the denominator of the R&D estimate allows for control for scale of firm size. With the annual reports, the PMPRB data was manually entered and hand matched to patents based on the year in which the patent was filed and the name of the patent owning firm. The decision to match on file year and then estimate the five-year lagged R&D effects was made in order to evaluate the effect of contemporaneous R&D relative to that which led up to the patent being filed. Because R&D expenditure – to – sales revenue is only available by firm and year (rather than drug or molecule and year), it is difficult to estimate the optimal R&D lag that, on average, results in a patent. As a result, matching the R&D ratio to a patent based on file year provides a chronological point of reference.

The PMPRB R&D expenditure – to – sales revenue data are collected under the Patent Act, which requires pharmaceutical firms patenting in Canada to report their total gross revenues from the sales of all medicines, as well as their R&D expenditures in Canada (PMPRB, 2017). Firms that do not sell patented medications in a given year are not required to provide the agency with their R&D and sales revenue data. As such, the estimated R&D to sales revenue figures do not necessarily cover all pharmaceutical research in Canada in a given year. Note that the PMPRB classifies R&D expenditure as non-capital expenses on research, including but not limited to those related to wages and salaries, direct materials, contractors, and factory overhead (PMPRB, 2017).

[9] PMPRB annual reports for 2017 – 2003 are publicly available. Annual reports for years 2002 - 1991 were requested and the R&D-to-sales revenue ratios were manually entered.

Once all information was matched, merged, and complied into one dataset, I restricted the sample to patents that were granted having been filed between 1991 and 2016. The sample also covers drugs intended for human use only and classified under the ATC system. Because of the extent of missing data in the Patent Register, I also removed patents for which there was no file date, grant date, or service company listed. In total, the dataset includes 971 patents with R&D expenditure to sales revenue ratios for at least one period.

Table 2: Summary of Variables

Variable	Source	Description
Patent evaluation duration	Health Canada's Patent Register	Number of months between a patent's file date and grant date.
R&D expenditure to sales revenue	Patented Medicines Price Review Board (PMPRB) Annual Reports	Ratio of a firm's research and development expenditure to sales revenue. Used as an indicator of R&D intensity, it is attributed to a patent based on the patent's file year. Note that lag lengths are taken relative to the file year.
Drugs per patent	Health Canada's Patent Register	The number of drugs covered by a patent - counts the number of DINs listed in the Patent Register that are associated with a given patent.
Number of patents filed by firm	Health Canada's Patent Register	The number of patents a firm filed in a given year. Note that this count only includes patents that were eventually granted.
Total number of patents filed	Health Canada's Patent Register	The number of patents in the Patent Register that were filed in a given year. Note that this count only includes patents that were eventually granted.
Firm	Health Canada's Drug Product Database and CIPO Patent Database	Fixed effect representing the firms filing patents that were later granted.
Anatomical Therapeutic Class	Drug Product Database	Universal indicator of drug type. The first level, or pharmacological group, is used in this paper. ATC categories are grouped in this paper.
Year filed	Health Canada's Patent Register	Fixed effect variable representing the patent file year.

Methodology and Results

To investigate how research and development intensity, measured as the share of R&D expenditures to sales revenue, affects patent evaluation duration, I estimate all specifications by ordinary least squares. To control for effects that are common across all patents, yet may affect their duration, year fixed effects are included in all regressions. Therapeutic class and firm fixed effects are also included. Standard errors are clustered at the firm and year level. My main specification takes the following form, where *i* is the patent, *j* is the filing firm, *k* is the drug, *t* is the file year, and *m* is the number of years prior to the file year (also referred to as lag lengths):

$$\begin{aligned} PATLAG_{ijkt} = {} & \beta_0 + \beta_1(RDexpenditure - to - sales - revenue\ ratio)_{jt-m} \\ & + \beta_2(drugs\ per\ patent)_{ij} + \beta_3(patents\ filed)_{jt} + \beta_4(total\ patents\ filed)_t \\ & + \beta_5(grouped\ ATC)_k + \beta_6(file\ year)_i + \beta_7(firm)_i + \varepsilon_{ijkt} \end{aligned}$$

Eq (1)

While the results provide insights into the relationship between R&D and patent duration, it is important to keep in mind that this analysis only includes information on the characteristics of patents that have been granted.

Optimal Lag Length

Pharmaceutical research is often a long process, resulting in years of research and development spending that may lead to the eventual filing of a patent. As such, an optimal model specification that estimates the effect of R&D on patent duration would include patent – specific estimates of R&D expenditures; that is to say, the resources employed specific to a particular filed patent. Because this type of data is unavailable, I use firm-specific estimates of R&D intensity to estimate their effect on patent evaluation time. However, these data give rise to an important issue: what year of R& matters most for a firm's patent evaluation time?

Because each patent is unique and varies in complexity and value, variation likely exists in determining the optimal lag structure for different drugs. Addressing this issue is complicated by the fact that R&D ratios by firm are highly correlated over time, indicating that multiple lag lengths should not be included in the same regression.[10] Economic theory suggests that research and development expenditures occurring in the discovery and preclinical stage of drug development matter most for that patent (Abrantes-Metz et al, 2004, pp.6). The R&D expenditure to sales revenue data I use in this paper works well with the theory as it encompasses firm-level spending on the drug discovery, as well as resources spent on pre-clinical trials. I look at the effect of R&D intensity occuring in the file year of a patent (i.e. the contemporaneous effect), as well as R&D intensity that occurred up to five years prior to the filing of a patent.[11] To select the optimal lag length, I minimize the Bayesian Information Criterion (BIC).[12] The results show little variation across lag lengths, suggesting that there is no strong statistical argument for the use of any particular lag length.

Results and Discussion

The results of the estimation of equation (1), which are presented in Table 3, indicate that for two to five years prior to the year in which the patent was filed, an increase in R&D intensity leads to an increase in patent evaluation duration. Of particular interest are the effects of the three- and four-year R&D intensity lag that are significant at the 99 percent level. These results indicate that a one percentage point increase in the share of R&D expenditure to sales revenue three years

[10] The correlation between the R&D ratios of each lag length range from 0.78 to 0.93.
[11] Note that R&D intensity is the only regressor that is lagged. *Patents filed* and *Total patents filed* correspond to those in the file year.
[12] Because the BIC takes into account sample size when conducting model selection, I constructed a limited-sample set of patents by selecting those for which R&D ratio data were available for every lagged period. The BIC calculated from the limited sample regressions were then used to infer which of the full sample lags can provide the most information. These results are reported along with the regression output in Table 3.

prior to the filing of a patent (column 4) is associated with an increase in patent evaluation time of 0.30 months (or nine days). Similarly, for the four-year R&D intensity lag (column 5), a one percentage point increase in R&D intensity is associated with an increase in patent evaluation time of 0.37 months. It is reasonable to believe that higher R&D intensity indicates more complex patented substances or processes. Under this assumption, the results of my analysis are consistent with the work done by Harhoff and Wagner (2009). Patents that are preceded by higher levels of R&D, perhaps due to their complexity, experience longer evaluation times, after controlling for year, firm, and therapeutic class fixed effects, as well as the number of drugs a patent is used in and the number of patents filed in a given year and later granted.

Note that the results reported in Table 3 also indicate that higher R&D expenditure – to – sales revenue ratios in the file year of a patent are associated with a decrease in patent evaluation time of about 0.28 months, or just over eight days. This result is statistically significant at the 90 percent level; however, its qualitative significance is muted since most R&D expenditure that results in a patentable substance or process occurs well before the filing year itself. Furthermore, patents filed earlier in the year are less likely to benefit from research spending that occurred throughout that year. Thus, although statistical significance has been established for contemporaneous R&D expenditures, it is difficult to establish any economic relevance because complexity is unlikely to be correlated with R&D in the filing year.

While R&D intensity is a cost of pharmaceutical innovative activity at the firm level, one benefit captured in my specification is the number of drugs a single patent protects. In particular, a one unit increase in the number of drugs a patent protects decreases patent evaluation time by between 1.49 months (one-year lag) – or 1 month and 15 days – and 2.02 months (four-year lag).

Table 3: Regression Results for R&D Expenditure to Sales Revenue Ratio and Other Covariates

VARIABLES	(1)	(2)	(3)	(4)	(5)	(6)
R&D expenditure to sales	-0.28*					
	(0.14)					
R&D expenditure to sales, one year prior		-0.06				
		(0.11)				
R&D expenditure to sales, two years prior			0.14			
			(0.12)			
R&D expenditure to sales, three years prior				0.30***		
				(0.11)		
R&D expenditure to sales, four years prior					0.37***	
					(0.09)	
R&D expenditure to sales, five years prior						0.10
						(0.08)
drugs per patent	-1.49***	-1.64***	-1.65**	-1.74***	-2.02***	-1.75**
	(0.55)	(0.58)	(0.64)	(0.64)	(0.71)	(0.81)
patents per firm	-0.71*	-0.79**	-0.49	-0.69*	-0.75*	-0.94**
	(0.37)	(0.39)	(0.43)	(0.39)	(0.40)	(0.39)
total patents filed	1.10***	1.05***	1.05***	0.83***	1.01***	1.01***
	(0.15)	(0.11)	(0.20)	(0.12)	(0.14)	(0.14)
Constant	31.46**	34.47***	36.61***	29.71**	37.15***	31.28**
	(12.15)	(12.18)	(13.00)	(12.56)	(12.55)	(13.23)
Observations	954	916	777	803	729	658
R-squared	0.32	0.31	0.33	0.32	0.37	0.39
BIC	5819.86	5824.68	5819.16	5818.01	5817.43	5820.6

Robust standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

Note: Fixed effects for firm, year, and ATC group were included in the regression but are omitted from this table because their discussion is out of scope for this paper.

This negative relationship holds across all lag lengths and it is statistically significant at the 95 percent level or greater. Because pharmaceutical firms benefit greatly when years of research lead to multiple outputs, the number of drugs a patent is used in can be looked at as an indicator of value. Interpreting it in this way, these results are again consistent with Harhoff and Wagner

(2009). More valuable patents experience shorter evaluation times. Similarly, if we use the number of drugs a patent protects as an indicator of importance, these results are also consistent with Regibeau and Rockett (2010). Drugs that are more important tend to be evaluated faster than those that are relatively less important.

Interestingly, an increase in the number of patents filed by a firm in a given year is associated with a decrease in patent evaluation time. One possible reason for this result is that because firms tend to apply multiple patents to a single drug, the evaluation time may decrease as a result of prioritizing the drug. While the relationship between patents per firm and patent evaluation time is negative across all regressions, it is only marginal and statistically significant at the 90 percent level.

As expected, an increase in the total number of pharmaceutical patents filed in a given year is associated with an increase in patent evaluation time. However, I note that because this measure only includes the number of patents filed in a given year that were eventually granted, and because it fails to include those that were filed and subsequently rejected, the magnitude of the effect may be understated because unsuccessful patents bogging down the evaluation process were not included in the sample. Nonetheless, the effect of the total number of pharmaceutical patents filed on patent evaluation is consistently negative and statistically significant at the 99 percent level.

Extensions

The specification I used in this paper regresses, amongst other covariates, the R&D – to – sales revenues ratio on the patent lag using the full sample of data available from all sources. While the results discussed in the previous section are the main findings of this paper, extensions can be made to gain a deeper understanding of the data and the effect of R&D intensity on patent

evaluation times. In this section, I look at the way in which extreme values of R&D expenditure – to – sales revenues affect the estimated impact on patent evaluation time. A basic motivation for undertaking this exercise is that the range of R&D ratio estimates is high, going from a lower bound of zero to upwards of 150 percent, depending on the lag length considered. As will be discussed, the inclusion of extreme R&D intensity values tends to increase the estimated effect on patent evaluation time. An alternate motivation stems from studies that look at the increasingly collaborative work employed by pharmaceutical firms. Specifically, some firms tend to employ the services of other firms to conduct drug research, which increases their R&D intensity because R&D specialization reduces effort directed towards the marketing and selling of drugs (DiMasi, Grabowski, & Hansen, 2016).[13] For example, firms such as Pfizer, AstraZeneca, and GlaxoSmithKline have been working with relatively small biotech start-ups to research and produce new antibiotics (Gallini, 2017). Note that the PMPRB also indicates when firms have received royalties from licensed research, and when funding for R&D expenditures are provided by an associate company.

Identifying Extreme R&D Values

While the average R&D expenditure to sales revenue ratio is around 11 percent, as reported in Table 1, some firms reported R&D expenditures in excess of 100 percent of sales revenues. Because these values were reported and reviewed by the PMPRB in their annual reports, omitting them from the sample on the basis that they appear too high is unjustified.[14] Furthermore, because the only publicly available data on firm R&D spending in Canada incorporates sales revenue, it is

[13] Note that DiMasi et al (2016) refer to the employment of other firms for drug research as "licensing-in." Firms that conduct the research are the license-out firms.

[14] Annual reports from the PMPRB indicate that in some years, firms have large R&D expenditure to sales revenue ratios due to funding from other firms to undertake research. The PMPRB attributes this spending to the firm undertaking the research (license-out firm).

difficult to discern if the high ratio is because of high research and development spending or because of low sales revenues in a given year.

Figure 1 R&D Expenditure to Sales Revenue Ratio and Patent Evaluation Times, Contemporaneous and Lagged, Full Sample

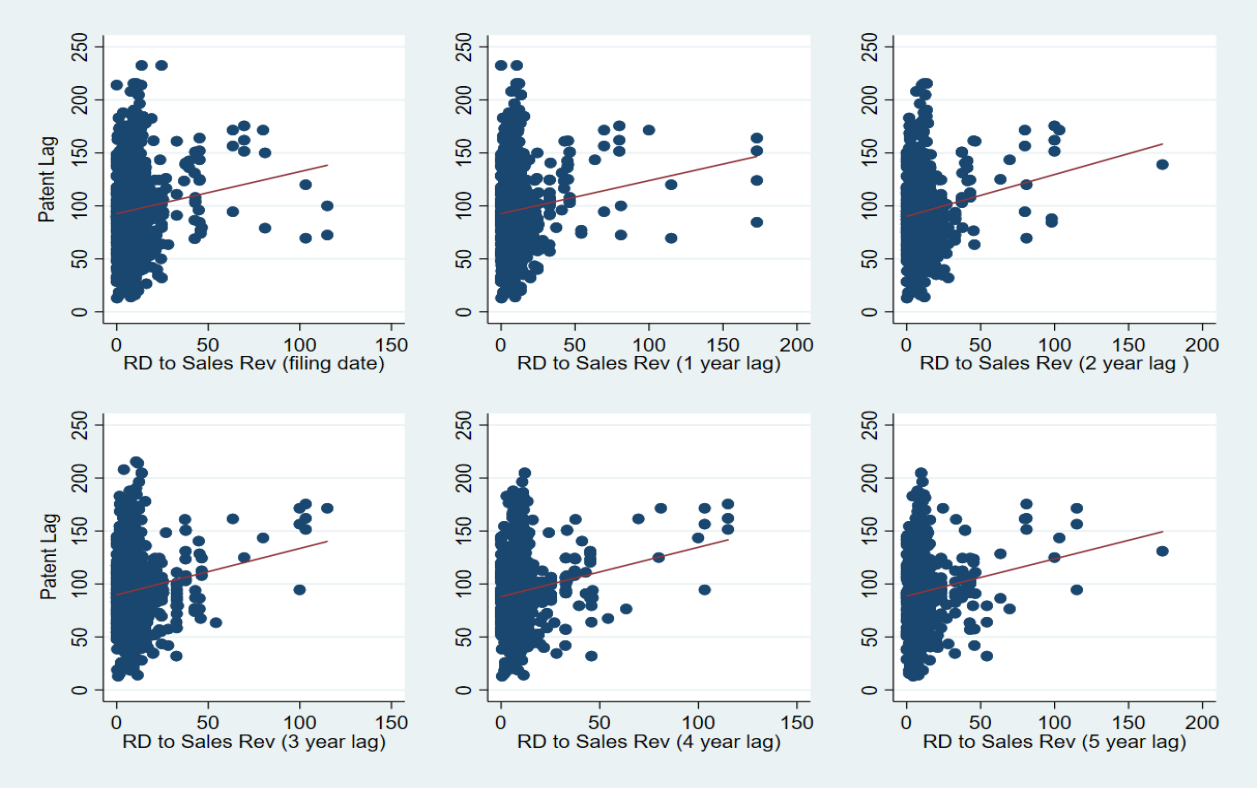


Figure 1, which presents the R&D intensity and patent lag for the full sample of data, indicates that extreme values of R&D intensity exist across all lag lengths. In order to identify extreme values, I identify quantiles for each R&D – to – sales revenue ratio to determine the ratios that were unusually high relative to the rest of the sample. The summary statistics reported in Table 1 indicate that for all lag lengths, R&D ratios in the top ten percent of data reflect extreme values because the maximum values differ from the 90th percentile to a large extent.[15] Removing

[15] To ensure that the upper ten percent of data are indeed extreme values, I considered the kurtosis measures reported in Table 1 (full sample). For all lag lengths of R&D, the kurtosis measures in Table 3 were large, indicating a heavy right tale and possible outliers (DeCarlo, 1997, pp. 298). Omitting the highest 10% of observations, Table 4 reveals kurtosis measures closer to normal distribution.

the highest 10 percent of observations reveals a distribution of R&D ratios closer to normal – see summary statistics reported in Table 4.

Table 4. Summary Statistics Omitting Top 10% of Observations

R&D/sales	Summary Statistics				Quantiles					
	N	Mean	S.D.	Kurtosis	Min	0.25	Mdn	0.75	0.9	Max
File year	860	8	4.3	2.308	0	4.9	8.4	11.3	13.4	17
One-year prior	827	8.05	4.36	2.459	0	5.2	8.4	11.3	13.4	19
Two- years prior	700	8.37	4.76	2.855	0	5.1	8.9	11.5	13.6	21
Three – years prior	723	8.19	4.36	3.009	0	5.8	8.6	10.7	13.4	20.9
Four – years prior	655	8.37	4.39	2.949	0	6.1	8.7	11.4	13.5	21
Five – years prior	602	9.27	4.95	3.693	0	6.8	9.1	11.7	15.6	23.24
Patent evaluation duration	971	97	36.81	3.44	13	72	95	117.5	143.5	232.5

Results from Omitting Extreme Values

Table 5 presents the regression results from the truncated sample of observations that exclude extreme values. Like the full sample regression, the contemporaneous effect of R&D intensity and the one-year lagged R&D intensity are associated with a decrease in patent evaluation time. Although these results are statistically significant at the 90 percent level when excluding high values of R&D intensity, economic intuition suggests that earlier years of spending matter more to the development of a patented substance or process. When looking at earlier R&D, which is more likely to have meaningfully contributed to the research process of the patent, we see that omitting the extreme R&D values leads to a decrease in patent evaluation time for the second and third lags – a result that contrasts the full sample estimates, and although the relationship has changed, the results are no longer statistically significant. Omitting the extreme R&D ratios does not qualitatively impact the results from the full sample regression – at the fifth lag, I still find that increases in R&D are associated with increases in patent evaluation times. The earliest lag length

in this model – four and five years prior to the filing of a patent – still yield positive coefficients for the associated effect of R&D intensity on patent evaluation time. Overall, the results of the truncated sample regression, and Figure 2, indicate that identifying a relationship between patent complexity and evaluation duration can be challenging. Firms with large R&D expenditures may be producing more innovative drugs, as opposed to improvements on existing drugs. Thus, their associated patents likely protect the most complex compounds, leading to a stronger impact of R&D intensity on patent evaluation length.

Table 5: Regression Results for R&D Expenditure to Sales Revenue Ratio and Other Covariates, Omitting top 10% of R&D Ratio Observations

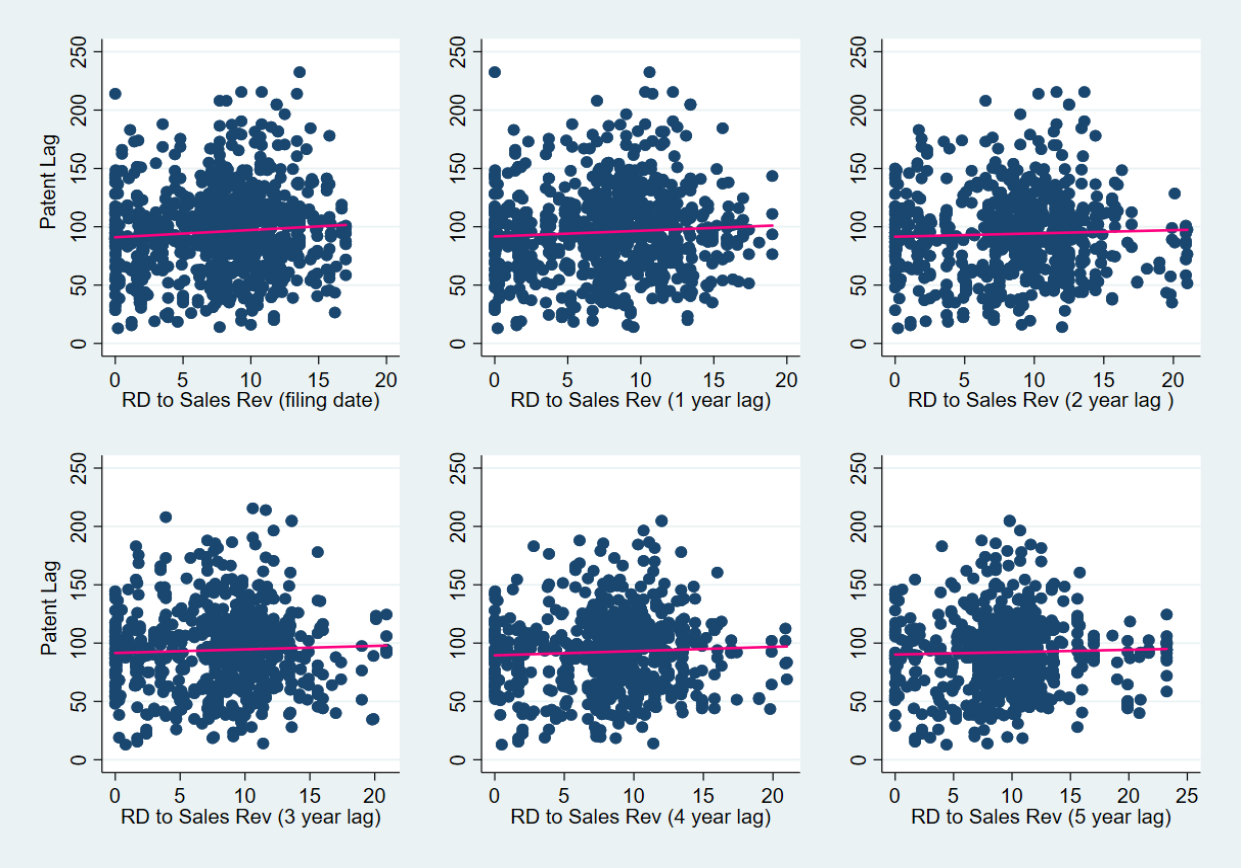
VARIABLES		(2)	(3)	(4)	(5)	(6)
R&D expenditure to sales	-1.25**					
	(0.57)					
R&D expenditure to sales, one year prior		-1.25*				
		(0.67)				
R&D expenditure to sales, two years prior			-0.19			
			(0.56)			
R&D expenditure to sales, three years prior				-0.19		
				(0.61)		
R&D expenditure to sales, four years prior					0.62	
					(0.49)	
R&D expenditure to sales, five years prior						0.80*
						(0.47)
drugs per patent	-1.69***	-1.90***	-1.81**	-1.85***	-2.13***	-1.85**
	(0.61)	(0.66)	(0.74)	(0.65)	(0.74)	(0.83)
patents per firm	1.18***	1.12***	1.13***	0.88***	0.98***	0.98***
	(0.16)	(0.12)	(0.23)	(0.12)	(0.15)	(0.16)
total patents filed	-0.52	-0.65	-0.53	-0.76*	-0.77*	-1.01**
	(0.41)	(0.43)	(0.47)	(0.42)	(0.46)	(0.44)
Constant	31.14**	30.68**	29.29**	23.04*	37.87***	28.99**
	(12.64)	(12.81)	(13.77)	(13.32)	(13.23)	(14.23)
Observations	860	827	700	723	655	602
R-squared	0.31	0.30	0.32	0.30	0.35	0.36

Robust standard errors in parentheses

*** p<0.01, ** p<0.05, * p<0.1

It is important to note that the other variables of interest are also impacted by the exclusion of observations with extreme R&D ratios. The number of patents filed by a firm in a given year has a positive effect on patent evaluation time that is statistically significant at the 99 percent level, whereas the effect derived from the full sample regression was negative, and statistically significant when including only certain lagged periods in the model. This result indicates that firms with extreme R&D intensity decrease the impact of the number of patents per firm relative to the full sample regression.

Figure 2. R&D Expenditure to Sales Revenue Ratio and Patent Evaluation Times, Contemporaneous and Lagged, Top 10% Excluded



Meanwhile, the total number of pharmaceutical patents filed and subsequently granted is associated with a decrease in patent evaluation time when looking at the truncated sample of observations. Although this result is no longer statistically significant, save for the three-to-five-year lagged periods, it is still counter-intuitive. Nonetheless, the result implies that including the high R&D intensity observations in the sample increase the estimated effect of total number of pharmaceutical patents on patent evaluation time.

When excluding extreme values of R&D expenditure – to – sales revenue ratios from the dataset used in this analysis, the results for most variables of interest change, either in terms of direction, statistical significance, or both. While my main qualitative conclusions are based on the full-sample regressions, the use of the truncated sample indicates that the overall findings are sensitive to the sample of patents observed. This is likely because firms with very high R&D ratios patent more complex compounds but file fewer patents each year relative to low R&D ratio firms. As a result, their patents disproportionately slow the entire patent evaluation process.

Limitations

This paper has estimated the effect of R&D expenditure on pharmaceutical patent evaluation times in Canada. While the results in this paper offer insights inferring causality, a few limitations must be acknowledged.

Because the data in this paper rely on patents voluntarily submitted to the Patent Register, a possible selection bias exists in this analysis. In other words, because submitting patents to the Patent Register is not obligatory, it may be the case that patents that were submitted are more likely to be used in certain types of drugs – for example, drugs that are more marketable or of higher value. Furthermore, because the sample of patents used in this paper consist of patents

that have been granted and correspond to drugs that have been approved for sale in Canada, no information can be gleaned on the effects of R&D intensity on patent evaluation time for patents that turn out to be unsuccessful – ones that have been filed but not granted. This implies that the results of this paper are better suited to offer insights for patents that are considered of high value with a high probability of being approved.

Another limitation of this study stems from the use of data on R&D expenditure – to – sales revenue ratios, rather than firm level R&D expenditure alone. While this data is the best alternative in the absence of easily accessible time series R&D expenditure data for Canada, it does have implications for the findings in this paper. As previously mentioned, because it is difficult to determine if a high R&D expenditure to sales revenue ratio is due to low sales revenues or large R&D expenditures, establishing a causal relationship between R&D expenditures alone and patent evaluation times is not possible. Additionally, because firms are only required to submit revenue and R&D expenditures in years in which they sell patented medications, R&D expenditure to sales revenue ratios from firms not engaged in the marketing of their drugs, but still engaged research endeavours, are not included in this analysis, further complicating the identification of a causal relationship between R&D intensity and evaluation time.

An important patent characteristic not accounted for in this paper is the novelty and usefulness of the patented pharmaceutical. Novelty and usefulness affect patent evaluation times by way of either value or importance, or both. Specifically, this paper does not differentiate between patents that protect improvements to existing drugs (referred to as abbreviated new drug submissions (ANDS) in Canada) and patents that are protecting new innovations that have not yet been used in pharmaceuticals – i.e. breakthrough products or new drug submissions. While

this distinction likely affects patent evaluation duration, data is not readily available in a usable format.[16] As a result, the effect of drug novelty, which can act as another indicator of value in the patenting process, is omitted from this paper. Due to the increasing attention being paid to patents that only slightly improve an existing drug, but are filed later in the drug's lifespan to increase it patent protection, including this element in future studies may prove to be an interesting area of further research.

Conclusion

Pharmaceutical patenting activity has been the subject of numerous studies due to its impact on various facets of the economy. The history of pharmaceutical research and patenting in Canada has seen numerous policy changes aimed at changing the duration of patents and implementing restoration to recover time lost in the filing and approval process.[17] While most studies within the Canadian context tend to highlight these policy changes and their effect on innovative activity and public health practices, far fewer aim to highlight the determinants and importance of patent evaluation time. However, this area is increasingly relevant given that patent examination times have been shown in the empirical literature to signal information about the complexity, value, and importance of a patent.

This paper has looked at the role of R&D intensity on pharmaceutical patent evaluation times in Canada, using hand collected data from Health Canada's Patent Register and a variety of other sources that provide patent-specific information. Incorporating therapeutic class fixed

[16] Health Canada produces a Notice of Compliance (NOC) database that is available for download and does contain information on drug submission types. However, NOC dates are not matched to DINs in the database.
[17] Bill C-22, which eliminated compulsory licensing and Bill C- 30 (following CETA), which allows drugs companies to request certificate of supplementary protection (CSP) that extend drug exclusivity on the market, for examples.

effects, year fixed effects, and firm fixed effects, the analysis in this paper finds that an increase in R&D intensity in the years leading up to the filing of a patent is associated with an increase in patent evaluation time. In particular, the three and four years of R&D intensity prior to the file date of a patent have the most significant impacts on evaluation time. In addition, the results show that as the number of drugs a patent protects increases, its evaluation time decreases. Interpreting R&D intensity as an indicator of complexity, and drugs per patent as an indicator of value or importance, these results are in line with previous research that indicates greater complexity increases evaluation time while greater value and importance decreases evaluation time. While limitations exist in the approach used in this analysis, the results reveal an interesting relationship between research and development, and patent evaluation time that is of importance to pharmaceutical firms because it carries strategic implications for competitors that can see evaluation times but not necessarily the value and complexity of the patented compound or process. The results discussed also provide a good starting point for further investigation into pharmaceutical patenting and the role patents play within the greater context of healthcare practice in Canada.

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Appendix

Table 6 shows the results of the regression when dummying the highest ten percent of R&D to sales revenue ratios. From these results, we can see that the largest 10 percent of R&D intensity observations increase the associated effect of R&D intensity on patent evaluation duration. The intercept for these observations is also lower, corresponding to Figure 1 in which we see a strong positive relationship between patent evaluation duration and R&D intensity.

After dummying the high R&D observations, the three- and four-year lags still show that an increase in R&D intensity is associated with an increase in patent evaluation duration. These results are also statistically significant at the 95 and 99 percent level, respectively. The contemporaneous effect of R&D intensity on patent duration is still negative; however, when dummying the highest 10 percent of observations, it becomes statistically significant at the 95 percent level.

While an increase in the number of drugs a patent protects is still associated with a statistically significant decrease in patent evaluation duration, an increase in the total number of patents filed (that were also eventually granted) corresponds to a decrease in patent evaluation time. These results are counterintuitive but are consistent with the results when omitting the top ten percent of observations from the sample observed.

Overall, the results of Table 6 indicate that extreme values of R&D intensity increase the associated impact of R&D intensity and the number of patents filed on examination duration.

Table 6: Regression Results for R&D Expenditure to Sales Revenue Ratio and Other Covariates, Dummying Top 10% of R&D Ratio Observations

VARIABLES	(1)	(2)	(3)	(4)	(5)	(6)
R&D expenditure to sales	-0.34**					
	(0.17)					
R&D expenditure to sales, one year prior		-0.02				
		(0.12)				
R&D expenditure to sales, two years prior			0.22			
			(0.14)			
R&D expenditure to sales, three years prior				0.36**		
				(0.14)		
R&D expenditure to sales, four years prior					0.44***	
					(0.13)	
R&D expenditure to sales, five years prior						0.17
						(0.10)
Extreme value, one year	3.62					
	(5.53)					
Extreme value, two year		-5.09				
		(6.31)				
Extreme value, three year			-8.42			
			(7.31)			
Extreme value, four year				-4.62		
				(9.43)		
Extreme value, five year					-6.27	
					(8.29)	
						-6.84
						(6.32)
drugs per patent	-1.47***	-1.65***	-1.63**	-1.74***	-2.02***	-1.77**
	(0.56)	(0.58)	(0.65)	(0.64)	(0.71)	(0.81)
patents per firm	1.10***	1.06***	1.06***	0.83***	1.01***	1.01***
	(0.15)	(0.11)	(0.20)	(0.12)	(0.14)	(0.14)
total patents filed	-0.68*	-0.82**	-0.53	-0.68*	-0.73*	-1.00**
	(0.38)	(0.39)	(0.44)	(0.39)	(0.41)	(0.40)
Constant	31.79***	33.99***	35.75***	29.51**	36.92***	29.91**
	(12.13)	(12.14)	(13.03)	(12.55)	(12.69)	(13.21)
Observations	954	916	777	803	729	658
R-squared	0.32	0.31	0.33	0.32	0.37	0.39

Robust standard errors in parentheses
*** p<0.01, ** p<0.05, * p<0.1