



*Working Paper Series*  
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**Working Paper No: 150005**

[www.canadiancentrefortheconomics.ca](http://www.canadiancentrefortheconomics.ca)

**May 4, 2015**

*Canadian Centre for Health Economics*  
*Centre canadien en économie de la santé*  
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*Toronto, Ontario*

## Intellectual Property Protection and Drug Plan Coverage: Evidence From Ontario

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### Abstract

Canada has strengthened intellectual property (IP) protections for pharmaceutical drugs several times over the last three decades. These changes were intended to lengthen the period of market exclusivity for new brand drugs and thereby allow them to earn additional sales revenues that could be used to recoup R&D investments. Whether these policies achieved their objective of increasing sales revenues is unclear, however. Whether they did depends on the coverage decisions of the major drug plans. Longer periods of market exclusivity amount to a price increase for brand drugs. In response to higher prices, drug plans could have become more selective in the drugs they cover, and they could have waited longer to list these drugs on their formularies, reducing formulary exclusivity periods. To investigate, we assembled data on the coverage of brand drugs approved for use in Canada over the last 35 years by the Ontario Drug Benefit (ODB) program, the largest and most influential drug plan in Canada. We find that, except for a brief period of time, the marked strengthening of Canadian pharmaceutical IP laws over the last 25 years have not lead to an increase in the exclusivity period that brand-name drugs enjoy on the ODB formulary. In fact, exclusivity periods have been dropping more or less consistently since the mid 1970s. The causes of these changes remain to be explored.

JEL Classification: I18; I13; O34

Keywords: intellectual property, pharmaceuticals, public drug coverage, ontario

Funding: Adam Falconi and Tyler Robinson were supported by summer internship grants from the Canadian Institutes for Health Research. This study received no other financial support. The authors declare no competing interests related to this work.

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## Introduction

Canada and other industrialized countries have strengthened intellectual property (IP) protections for new pharmaceutical drugs several times over the last three decades. Although Canada made these changes to help conclude international trade agreements, the economic argument for them was to increase the incentive for drug companies to develop new drugs. In particular, stronger IP protections were intended to lengthen the period of market exclusivity for new innovative (“brand”) drugs and thereby allow them to earn additional sales revenues that could be used to recoup R&D investments. Whether these policies achieved their objective of increasing sales revenues is unclear, however. Whether they did depends on the coverage decisions of the major drug plans operating in the country. Longer periods of market exclusivity amount to a price increase for brand drugs. Economics teaches us that higher prices typically reduce the quantity that consumers wish to purchase. Thus, in the face of longer patent periods, drug plans could have reduced demand for brand drugs. This could occur in various ways: the plans could have been more selective in the drugs they cover, they could have waited longer to list these drugs on their formularies, and they could have taken steps to expedite generic entry.

In Canada, the federal government is responsible for IP policy, while most insured drug costs are paid for by provincial and territorial drug plans. Thus it is possible that the stronger pharmaceutical IP rules enacted by the federal government were muted by the countervailing responses on the part of large provincial government payers. If this is the case, policy makers may wish to re-examine the ways in which they support drug discovery and commercialization.

The impact of IP protection on drug plan generosity has received little attention in the literature. The one study we are aware of, that by Grootendorst and diMatteo (2007)<sup>1</sup>, found that drug costs did not increase markedly after Canada increased IP protections in 1987 and 1993. This study

suggests that countervailing responses on the part of drug plans, as well as the introduction of patented drug price controls by the federal government, could have played a role.

To investigate this issue more fully, we assembled data on drug plan coverage of brand drugs approved for use in Canada over the last 35 years. We focused on the formulary of the Ontario Drug Benefit (ODB) program, the provincial government plan for seniors, welfare recipients and others with high drug costs relative to income. ODB formulary coverage is particularly important to the fortunes of most branded drugs, for several reasons. First, the ODB is the single largest drug plan in Canada, accounting for 43% of the \$10.7 billion spent on prescription drugs in the province in 2010. Second, some private drug plan formularies mimic the ODB formulary. Third, Ontario physicians are more familiar with ODB formulary drugs, and may be more likely to prescribe such drugs to all of their patients, including those with private coverage.<sup>2</sup>

The federal government has made multiple changes to its pharmaceutical IP regime over the past 50 years. From 1969 to 1987 Canada allowed compulsory licensing for patented medications: Although patents were valid for 17 years after they were granted, generic companies could nonetheless sell copies of patented drugs in exchange for a royalty of 4% of the generic drug's sales revenues. Under this regime many best selling brand drugs were subject to generic competition within 5 to 7 years after market entry.

Canada's IP rules were strengthened several times after 1987; the most significant of these changes were the outcomes of trade treaties that Canada negotiated with the United States (the 1987 Free Trade Agreement), the United States and Mexico (the 1993 North America Free Trade Agreement),<sup>3</sup> the 1994 Trade Related Aspects of Intellectual Property Rights (TRIPS) Agreement (a world wide agreement) and the European Union (the 2014 Comprehensive Economic and Trade Agreement, which takes effect in 2015).<sup>4</sup>

We focus on the IP changes from 1987 to 2006, which were as follows. In 1987, the Canadian government provided brand drugs with a minimum seven-year period of market exclusivity. In other words, generic drugs could not be sold until seven years after the brand drug had been approved for use. (A ten-year term applied if the generic firm imported the active pharmaceutical ingredients; the brand-name drug was provided seven years of market exclusivity if the generic firm manufactured the active ingredients domestically.) The government also changed the patent term to 20 years from the date when the patent application was filed, effective in 1989. Legislation passed in 1993, but retroactive to the end of 1991, abolished compulsory licensing. The 1993 legislation also introduced so-called “linkage” regulations; these restricted generic entry when patents deemed relevant by the brand firm were still in effect. In 2006, the federal government provided enhanced “data protection” regulations; these had the effect of providing brand firms with a minimum eight year period of market exclusivity. (The extension of data protection was not related to a trade agreement.)

We focus on the fraction of new drugs approved each year that were listed on the ODB formulary, the time between drug approval and formulary listing, and finally, the time between formulary listing and the formulary listing of the first interchangeable generic drug (i.e., “formulary exclusivity”). If ODB coverage declined in response to stronger IP in an attempt to control costs, we would expect to see a reduction in the fraction of new brand drugs that were listed, longer delays in the listing of new brand drugs, and, finally, shorter times of formulary exclusivity for listed brand drugs.

## Methods

Our focus is on oral solid dosage forms (i.e. tablets and capsules) of new molecules approved for use in Canada from January 1974 to December 2011, inclusive. Oral solid formulations account for

over 80% of prescription drug sales<sup>5</sup> and tend to be the primary targets for generic companies. We categorized new products into one of the following five dosage forms: 1) regular release tablets or capsules, 2) sustained release (including controlled delivery) tablets or capsules, 3) delayed release (including enteric coated) tablets, 4) orally disintegrating tablets, and 5) chewable tablets. For each drug (defined as unique drug molecule-dosage form combination), we assembled data on the first brand drug approval date, first ODB listing date of the brand drug, and the first ODB listing date of the generic form of the drug.

Our primary data source for drug approvals is Health Canada's Drug Product Database (DPD);<sup>6</sup> these data record regulatory activity (such as approval dates, post market drug withdrawal dates, and new therapeutic indications) of prescribed drugs for human and veterinary use. Health Canada drug approval is by way of a "Notice of Compliance" or NOC.

The DPD database for drugs approved prior to 1996 is incomplete, in two ways. First, there is no information on the NOC dates of brand drugs that were withdrawn from the market prior to 1996. For instance, the DPD contains no NOC data for Tagamet (cimetidine) tablets as this drug was withdrawn for commercial reasons prior to 1996. Second, the DPD provides just the year of approval for some drugs; for others NOC years are incorrect. We thus double-checked the NOC dates provided in the DPD using information from other sources. First, we compared NOC dates in the DPD with those given in Health Canada's NOC database.<sup>7</sup> The NOC database accurately records NOC dates for drugs receiving NOCs from 1991 and onwards. We also added drugs identified in the NOC database that were not found in the DPD. Pre-1991 NOCs were compared to information contained in the "top 200 prescription products tables" of the periodical *Pharmacy Practice*. Each year, starting in 1992, *Pharmacy Practice* provides a list of the most commonly prescribed drug products, along with the year and month of the first sale of these drugs. The data were generated

by IMS Health Canada. These data were supplemented by a list of all prescription drug sales in 2006; these data were given to us by IMS-Brogan.

We also determined NOC dates from various issues of the Compendium of Pharmaceutical Specialties (CPS). This publication of the Canadian Pharmaceutical Association, published since 1960 and annually since 1971, provides product monographs and other information on the approved uses and dosing for prescribed drugs available in Canada. A drug's NOC date can in some cases be ascertained by the date printed on the first product monograph available for the drug. If no product monograph is available, NOC dates can be bounded within a 12 month interval by identifying the issue of the CPS in which the drug first appeared. A drug that first appears in, say, the April 1987 CPS was likely launched between the publication of the previous issue of the CPS and March 1987. We used the midpoint of these dates as the NOC date. Drugs that appeared in the 1973 CPS could not have been launched after 1974 and were thus excluded. A number of drugs whose NOC dates could not be ascertained using the IMS or CPS data had NOCs listed as December 31 of the relevant year; this date appeared to be incorrect. To minimize expected measurement error, we changed the NOC to July 1 of the relevant year.

As noted, we flagged the earliest NOC date for each molecule-dosage form combination. We therefore retained the earliest NOC date of co-marketed drugs, such as lisinopril. We also excluded "repurposed" drugs. For example, finasteride was initially approved to treat benign prostatic hypertrophy in 1992 (under the brandname Proscar), and then approved to treat hair loss in 1998 (Propecia). We thus included Proscar but excluded Propecia. We also excluded birth control pills.

Next, we identified the ODB formulary listing date, if any, of approved brand drugs. List dates of drugs approved after 1996 were obtained from the ODB's on-line formulary<sup>8</sup>. We obtained the listing dates of other approved drugs from the printed ODB formularies starting with the first edition

in 1974 to the Dec. 19, 2006 update of the 35th edition. Since the printed formularies do not give the actual date that the drug was first reimbursed, we used the formulary's publication date. We then searched the formularies for the date that an interchangeable generic competitor first appeared. The ODB removed some brand drugs from the formulary prior to the listing of interchangeable generics. As an example, the sustained release forms of the beta blockers metoprolol and propranolol were delisted in October 1993. We identified the delisting dates, if any, of the brand drugs that appeared on the formulary. Formulary exclusivity was then defined as the time between formulary listing and the earlier of generic entry and brand delisting. ODB formulary listing dates were independently obtained by three pharmacists: AF and TR (acting as a team) and EI. Discrepancies were resolved by MS.

We excluded molecules that were withdrawn from the market for safety reasons prior to generic entry. Examples here include cisapride and valdecoxib. We identified the list of withdrawn molecules from two articles published by Lexchin.<sup>4,9</sup> The withdrawal dates listed in these papers were corroborated using data from the DPD and NOC databases.

The two duration outcomes we focus on, i.e., the time between drug approval and formulary listing ("time to listing"), and the duration of formulary exclusivity, were censored for some drugs. We retained observations on drugs with censored formulary exclusivity values, and computed durations observed at the time we last checked the ODB formulary, October 25 2014. We computed summary statistics of the listing outcomes by year of brand drug NOC. We reported the duration outcomes as medians to account for any outliers that may distort means. We visually inspected graphs of the fraction of approved drugs that were listed, the median time to listing and median period of formulary exclusivity to detect any abrupt changes in the ODB formulary listing outcomes for drugs receiving a NOC in 1987-89 and 1991-93, the dates when, and just after, the most



important changes were made to the IP policies. To reduce the number of censored observations, we focused on drugs with NOCs issued over the period 1974 to 2005 when computing the median number of years of formulary exclusivity. We focused on drugs with NOCs issued 1974 to 2011 when computing the median time to listing. All computations were performed using Stata version 13.<sup>10</sup>

## Results

We identified 575 new oral solid drugs that were launched between 1974-2011. Of these drugs, 402 were found in both the DPD and NOC database, 157 were found in the DPD database only and 16 were found in the NOC database only. We could not ascertain the NOC date for 2 drugs; these were dropped, leaving 573 for analysis. Figure 1 displays the number of new drug approvals by year.

From 1974-1990, the number of new drug approvals fluctuated between 5-15 per year. Approvals increased markedly after 1991, peaking at 26 in 1994. Approvals declined thereafter, although there was a large increase in 2011. The fraction of new drugs listed on the ODB formulary, displayed in Figure 2, has declined over the years, although there has been marked variation around the trend line. In the mid 1970s, ODB covered almost all drugs; about 40% of drugs approved in 2011 were covered.

From 1974 to 2005, the median time between NOC and ODB listing for listed drugs was generally between 1-2 years. There were exceptions however: for 11 years, median time to listing was under 1 year while the median time to listing for drugs approved in 1991 was almost 5 years (Figure 3). Since 2005, the median time to formulary listing increased slightly.

Figure 4 plots the median number of years of exclusivity of brand drugs listed on the ODB

formulary, by year of NOC, 1974-2005, inclusive. While there was substantial variation between years, two trends appear. First, there was a gradual downward decline in exclusivity from the mid-1970s to about 1990. To get a sense of the decline, brand drugs approved in the late 1970s received about 15 years of exclusivity on the ODB formulary; drugs approved in 1990 received 6.2 years exclusivity. Second, after 1990, there was a dramatic increase in median exclusivity, peaking at 15.5 years for drugs approved in 1994. This increase was short lived, however; median exclusivity periods began to decline after 1994. Drugs approved in 2004 received 8.7 years of exclusivity, and drugs approved in 2005 received 3.9 years of exclusivity.

## Discussion

We did not detect any systematic effect of Canada's stronger pharmaceutical IP laws on the coverage decisions of the ODB, the largest and most influential Canadian drug plan. The fraction of approved oral solid brand drugs reimbursed by the ODB has declined steadily over the last several decades, but these declines appear to be independent of the IP policy changes. Also, we did not see any pronounced changes in the period of time between drug approval and ODB listing for the drugs that were listed. We did observe a slight increase after 2005 but this is plausibly related to the introduction of the Common Drug Review.<sup>11</sup>

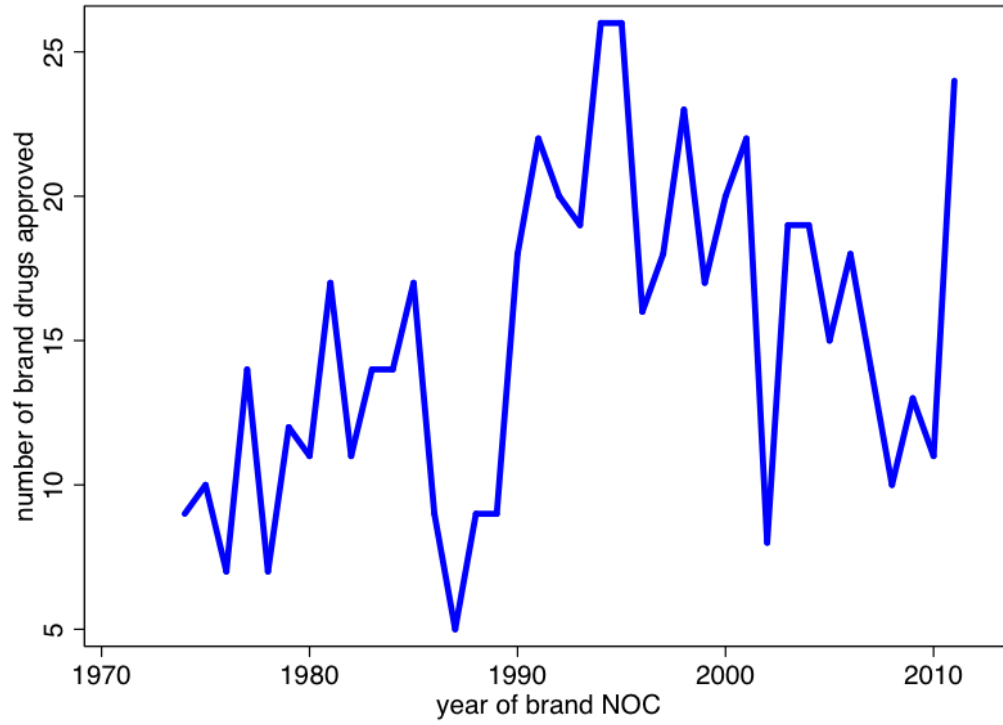
The median period of formulary exclusivity for brand drugs reimbursed by ODB has also declined steadily over the last several decades. The IP changes introduced in 1993, which abolished compulsory licensing and introduced a US-style linkage system, increased periods of formulary exclusivity for all drugs approved after 1993 to levels that are higher than what they would otherwise would have been. However the rate of decline observed before 1993 was also observed after 1993.

The causes of the secular decline in the median period of ODB formulary exclusivity is an

interesting question in its own right. There are several possibilities. First, generic drug companies may have become more proficient at navigating the IP regulations and gaining market entry. Second, it is possible that an increasing share of the new brand drugs are being granted exclusivity on the basis of weaker patents; this would be the case, for instance, for a sustained release formulation of a drug that was previously available in regular release form. Finally, it could be the case that governments are delisting drugs prior to the end of the normal patent term.

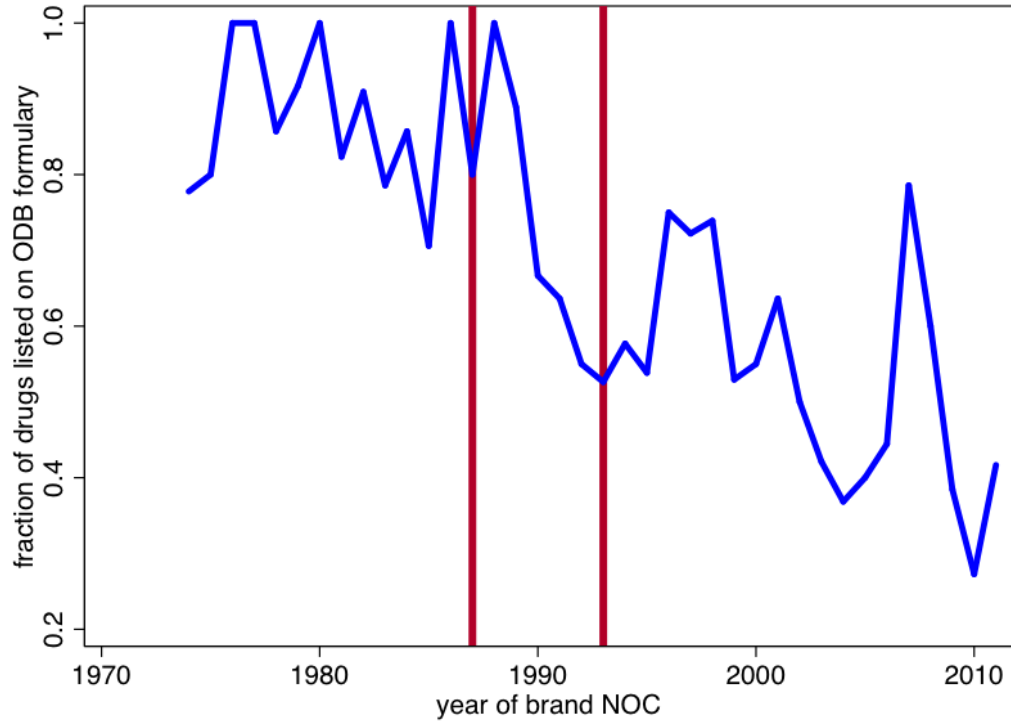
In conclusion, we have shown that except for a brief period of time, the marked strengthening of Canadian pharmaceutical IP laws over the past 25 years have not lead to an increase in the exclusivity period that brand-name drugs enjoy on the ODB formulary. In fact, exclusivity periods have been dropping more or less consistently beginning with drugs receiving a NOC in the mid 1970s with the exception of the period 1992 to 1994. The causes of these changes remain to be explored.

Figure 1: Number of brand drugs approved by Health Canada, by year, 1974-2011. Oral solids only.



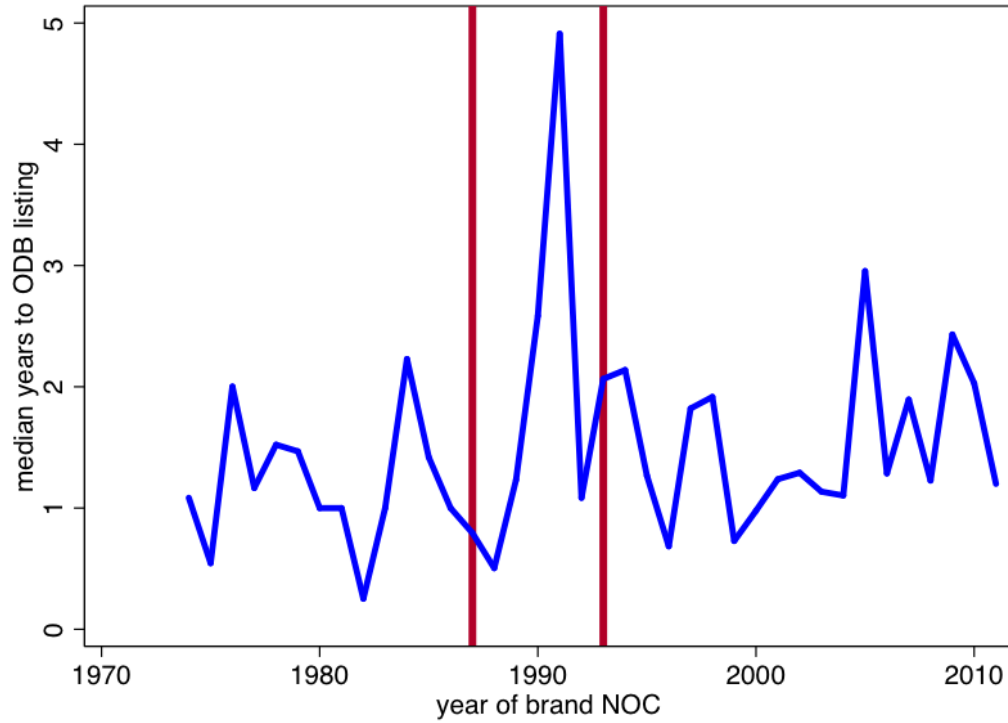
Note: drug defined as a unique combination of molecule and dosage form. Health Canada approval is by way of a Notice of Compliance (NOC).

Figure 2: Fraction of brand drugs listed on the ODB formulary, by year of brand NOC, 1974-20011. Oral solids only.



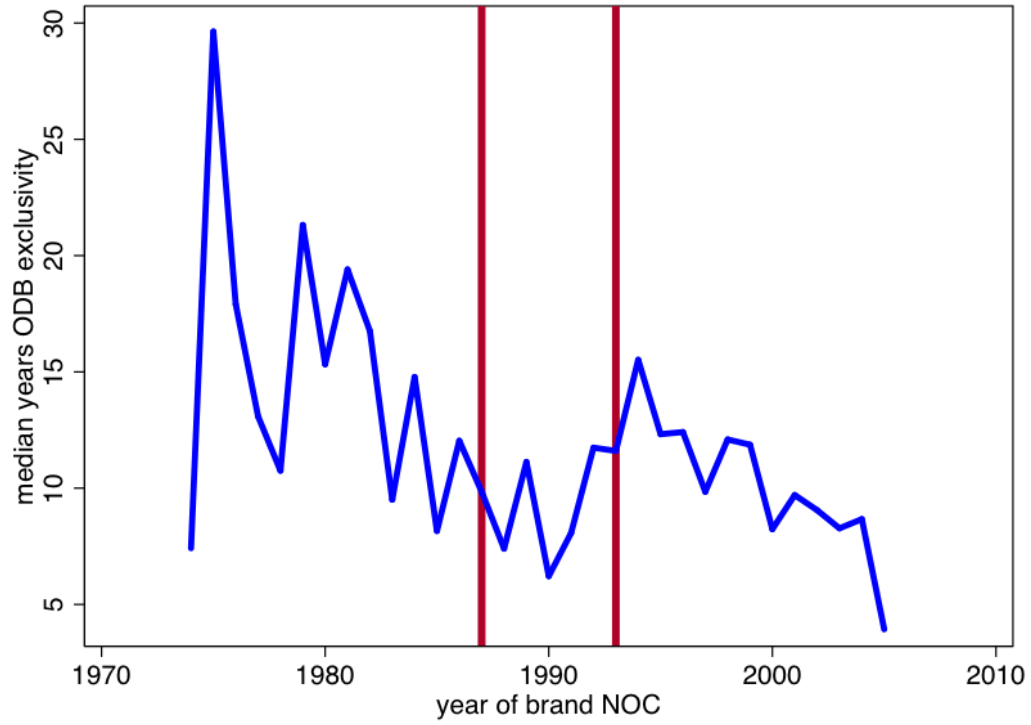
Note: drug defined as a unique combination of molecule and dosage form. Health Canada approval is by way of a Notice of Compliance (NOC). The two red vertical lines indicate the introduction of two policies that strengthened pharmaceutical intellectual property protections.

Figure 3: Median number of years to ODB listing, for brand drugs that were listed, by year of brand NOC, 1974-2011. Oral solids only.



Note: drug defined as a unique combination of molecule and dosage form. Health Canada approval is by way of a Notice of Compliance (NOC). The two red vertical lines indicate the introduction of two policies that strengthened pharmaceutical intellectual property protections.

Figure 4: Median number of years of exclusivity on the ODB formulary, for the brand drugs that were listed, by year of brand NOC, 1974-2005. Oral solids only.



Note: drug defined as a unique combination of molecule and dosage form. Health Canada approval is by way of a Notice of Compliance (NOC). The two red vertical lines indicate the introduction of two policies that strengthened pharmaceutical intellectual property protections.

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