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The effect of patented drug price on the share of new medicines across OECD countries

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A B S T R A C T

The Government of Canada plans to implement new controls on the prices of patented drugs sold in Canada. The literature indicates that such controls delay drug launches. The Government of Canada, in its cost benefit analysis of the proposed regulatory changes, claims that they do not. To examine this claim, we use recent OECD country level data to estimate regression models of drug launches. These estimates suggest that higher drug list prices increase the number of launches of new medicines; the estimates are larger in the short term than in the longer term. If our estimates have a causal interpretation, then, consistent with the extant literature, drug list price reductions delay availability of new medicines in the OECD countries. We explore the implications of these findings.

Introduction

Canada's Patented Medicine Prices Review Board (PMPRB), established in 1987, is a federal agency that regulates the introductory list prices of patented drugs and their rate of increase over time [1]. The regulatory regime has been criticized because the list prices for patented drugs in Canada are relatively high compared to other countries within the Organisation for Economic Co-operation and Development (OECD) [2–7]. In response, the PMPRB intends to introduce amended regulations that reduce patented drug list prices [8]. The literature indicates that a country that reduces drug list prices will wait longer for new drugs to be launched [9–13]. The PMPRB claims otherwise [14]. The literature, however, relies mostly on data prior to 2000. Since then, drug companies have increasingly used confidential rebates off list prices to conceal actual transactions prices [15]. It is therefore unclear what effect, if any, patented drug list price has on country level drug launches. To provide more evidence for policy formation, we use recent country level data to estimate regression models to assess the impact of list prices for patented drugs on drug launches across the OECD.

In this paper we first provide background on the regulation of patented drug prices in Canada. Next, we briefly review the results of the extant literature on this topic. We then present our empirical methods and results. The paper concludes with some discussion of the implications of the findings.

Patented drug price regulation in Canada

The PMPRB's current regulatory framework has resulted in list prices in Canada that are consistently among the highest in the OECD [3–7]. There are structural reasons for this: drugs that the PMPRB deems to be therapeutically novel can be priced no higher than the median of the list prices of the same drug in seven countries – the so-called PMPRB7. These seven countries are the United Kingdom, France, Italy, Sweden, Germany, Switzerland, and the United States. Historically, the latter three countries have had amongst the highest drug prices globally [3-7,16]. Thus, if the price ceiling is binding, under the current framework list prices of therapeutically novel drugs in Canada will be about the fourth highest globally.

In practice, few customers pay these list prices. Multinational drug companies price discriminate by giving drug plans confidential rebates off of public list prices [15,16]. It is therefore difficult to assess how actual, net-of-rebate prices paid in Canada compare to those paid elsewhere. Nevertheless, there is evidence that actual transactions prices in Canada are among the highest in the OECD. For example, the Government of Canada estimates that public drug plans in Canada receive discounts between 15–25 percent off list prices. Discounts of this magnitude are lower than that reported by other countries, and would make actual prices in Canada higher than the (pre-rebate) list prices paid in many OECD countries [3-7,17,18].

In response to the criticism of high drug prices, the PMPRB began a regulatory policy review which culminated in a new set of pricing rules

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that were announced in 2017 [16,19]. The coming-into-force date has been delayed several times and the proposed rules have evolved since 2017. The pricing rules are now scheduled to take effect July 2022 [8, 20]. The PMPRB intends to regulate list prices as it currently does, using international price referencing. However, it will change the set of comparator countries, replacing the two countries with the highest drug list prices in the PMPRB7 – the US and Switzerland – with six countries that tend to have lower list prices than Canada: Japan, Australia, Norway, Spain, Belgium and the Netherlands. The list price of a patented drug newly launched in Canada can be no higher than the median list price in these 11 comparator countries, or at least in the subset of these countries in which the drug has already launched [8]. In situations where no reference prices are available, the maximum list price will be set based on the domestic prices of therapeutically similar drugs [8]. The PMPRB previously proposed to regulate actual (confidential post-rebate) drug prices using estimates of the drug's therapeutic novelty, cost effectiveness and projected sales revenue. The proposal to regulate post rebate prices, which would have resulted in price reductions in the order of 20–70%, were found to be unconstitutional in Canada [21,22]. They were subsequently abandoned in April 2022 and thus the new policy amendments will only directly reduce list prices through a new set of comparator countries [20,23].

The cost savings of these new list price controls will differ by payer type, public vs private. The PMPRB estimates that the new regulations will reduce list prices by about 8–13 percent over the next decade [24]. It is unclear if these list price reductions will benefit public plans, which account for 45 percent of drug spending in Canada [17]. The reason is that public plans already pay rebated prices that are estimated to be 15–25 percent lower than list [17]. However, it is possible that a reduction in list price will further reduce actual prices.

The reduction in list price will almost certainly benefit private payers – which collectively account for 38 percent of prescription drug spending in Canada – as insurance companies that manage private plans likely negotiate smaller rebates than do public plans. Out of pocket payers – who make up the remaining 17 percent of drug spending – also typically pay list prices and will therefore also benefit [17].

These observations are consistent with the results of a cost benefit analysis (CBA) of the originally proposed reforms; this CBA was conducted by the Government of Canada in 2017. The CBA estimated the savings to payers to be approximately $2.8 billion and $3.8 billion over a 10 year period for the new rules on list prices and rebated prices, respectively [25].

Drug launch delays

One potential impact of more stringent price controls – ignored in the government's CBA – is the impact on consumers and drug payers associated with delayed or reduced launches of new drugs in Canada [9–13].

The academic literature has identified two reasons why country level drug prices may impact launch decisions by multinational pharmaceutical companies. First, drug companies typically do not have the personnel needed to obtain market authorization from all target countries at once. Thus, they will prioritize launching in countries where gross profits are expected to be greatest [10,26]. Canada's use of more stringent price controls, to the extent that they reduce actual prices, will reduce gross profits and thus lower Canada's launch priority.

Second, some countries use the PMPRB's model of international price referencing, wherein the maximum domestic drug list price depends on foreign list prices. A multinational pharmaceutical company may delay a launch in Canada to prevent a price regulator in a larger foreign market from referencing Canadian prices when the drug is launched in the foreign market.

Will the reduction in list prices of patented drugs in Canada trigger price reductions elsewhere? Currently, Canadian drug prices are used to set maximum prices in at least five other countries: Egypt, Brazil, Colombia, South Africa and Taiwan [27–30]. It seems unlikely a company would delay a launch in Canada to attain a higher list price in these relatively small markets. However, there is a risk that relatively large countries will begin to reference Canadian drug prices should Canada markedly lower its prices. For instance, both major political parties in the USA – whose pharma market is 22 times larger than Canada's – have proposed setting prices for drugs covered by its public drug plans on the basis of prices charged in Canada [3,31,32]. Thus, there is some risk that once the PMPRB regulations are enacted, drug companies will delay launches in Canada to prevent price declines in larger markets.

The PMPRB reported that, based on its analyses, patented drug prices have no material impact on drug launch decisions [14]. This finding is at odds with the literature on drug launch timing [9–13]. However, this literature may now be out of date as it relies on older data, mostly from the 1990s. The most recent data point used in the extant studies is from 2003. Since then, actual prices have diverged from list prices owing to the increased use of confidential rebates [15].

If the PMPRB claim is correct, then list price should not be an important determinant of the timing of new drug launches in a country. In this paper, we test whether this is the case using recent OECD country-level data to estimate the effect of list price on the share of new medicines available in a country.

Methods

Like the earlier studies, we model how patented drug list prices and market size affects the availability of new drugs in a country. The earlier studies estimated models of drug-specific launch lags, namely the time between first global launch of drug *j* and the drug's launch in country *i*. We model *Share New Meds*$_i$ – the percentage of new drugs launched globally over a particular time period that are launched in OECD country *i* by a certain date, where launch is defined by a commercial sale.

The outcome variable *Share New Meds*$_i$ is posited to depend on: *price*$_i$, a patented drug price index for country *i*; two measures of market size: *pop*$_i$, the population of country *i*, and *GDP*/*pop*$_i$, the (expenditure-based) per capita gross domestic product of country *i*; and, *ema*$_i$, an indicator of whether country *i* is a member of the European Medicines Agency (EMA). (EMA-approved drugs are approved for sale in all EMA member countries.) We use the statistical software package Stata to estimate the ordinary least squares (OLS) linear regression:

$$Share\ New\ Meds_i = \beta_0 + \beta_1 \log(price_i) + \beta_2 \log(pop_i) + \beta_3 \log(GDP/pop_i) + \beta_4 ema_i + \varepsilon_i \quad (1)$$

Measurement of Outcome Variable

We estimate six forms of (1), each corresponding to a different way of measuring *Share New Meds*$_i$. Our "Single Year" models all rely on data published in the "Meds Entry Watch" reports produced by Canada's National Prescription Drug Utilization Information System (NPDUIS) – a federal government research initiative [33–36]. We estimate four "single year" models: 2015, 2016, 2017, and 2018, each reflecting the time period in the denominator of *Share New Meds*$_i$. The denominator is the number of new active substances (NAS) to gain regulatory approval for use in the USA, Canada, or Europe during each year. Regulatory approval is granted by the Food and Drug Administration (FDA) in the USA, Health Canada (HC) in Canada, and the European Medicines Agency (EMA) in Europe. The numerator is the number of these NAS that accrue a sale in country *i*, during the year or 9 months after. Thus, *Share New Meds*$_i$ in the 2015 model reflects the percentage of medicines approved by the FDA, HC, or EMA during 2015 that accrued a sale in OECD country *i* over the period 2015–2016Q3. Definitions for the other single year models are provided in Table 1.

Our four single year models assess the determinants of the share of new medicinesin an OECD country in the short term. We also measure *Share New Meds*$_i$ in a way that captures the launches of new drugs over a

Table 1
Single Year Model Outcome Variable Time Interval and Regulatory Bodies.

		Single Year Models			
		Model 1	Model 2	Model 3	Model 4
Share New Meds$_i$	*numerator**	2015–2016Q3	2016–2017Q3	2017–2018Q3	2018–2019Q3
	denominator¥	2015	2016	2017	2018
Regulatory Bodies		FDA, EMA or HC	FDA, EMA or HC	FDA, EMA or HC	FDA, EMA or HC
Data Source		2016 Med Entry Watch Report	2017 Med Entry Watch Report	2018 Med Entry Watch Report	Med Entry Watch Report 5th Edition

*Numerator: Period during which drugs approved by the defined regulatory bodies accrued a sale in country *i*.
¥ Denominator: Period during which a drug was approved by any of the regulatory bodies. FDA is the United States Food and Drug Administration; EMA is the European Medicines Agency; HC is Health Canada.

7–8 year period. Our 2009–2017 model focuses on the uptake in each OECD country over the period 2009–2018Q3 of medicines approved by the FDA, HC, EMA or the Swiss regulatory authority over the period 2009–2017. Like our single year models, the data used to construct *Share New Meds*$_i$ for the 2009–2017 model were obtained from the NPDUIS [33]. Data for our 2011–2018 model were obtained from a 2019 report published by Innovative Medicines Canada (IMC) – a group representing Canada's innovative pharmaceutical industry [37]. Both the NPDUIS and IMC reports used country-level sales data collected by IQVIA, a leading pharmaceutical market research firm.

Measurement of covariates

In all models, *Share New Meds*$_i$ was posited to depend on an index of patented drug prices, market size, and market entry costs. The patented drug price index, *price*$_i$, used in the single year models and the 2009–2017 model were obtained from the 2014–2018 PMPRB Annual Reports [3–7]. The price index reported by the PMPRB for country *i* is a weighted average of the ratio of country *i* price to the Canadian price for each patented drug sold in both countries during a particular year. The PMPRB obtained the price data from IQVIA's MIDAS database [3–7]. The MIDAS data are derived from the purchase invoices of a sample of pharmacies in each country. Invoiced prices reflect wholesaler markups; IQVIA removes estimates of these markups in order to determine the prices paid to drug manufacturers. Foreign prices are converted into Canadian dollars using 36-month average exchange rates. The prices do not reflect off-invoice rebates paid by drug manufacturers to drug payers. For the 2011–2018 model, pricing data was obtained from IMC, which reports the country level weighted average price of global drugs per standard unit during 2017 [37]. For this reason, other covariates included in the 2011–2018 model were also measured in 2017.

The two measures of market size, expenditure-based GDP per capita and population size – GDP/pop_i and pop_i – were measured using the Penn World Tables database [38]. Market entry costs for country *i* were measured using ema_i, an indicator equal to one if country *i* is a member of the EMA. EMA-approved drugs are approved for sale in all EMA member countries. Thus, the cost of obtaining EMA regulatory approval is amortized over unit sales in the entire EMA region [39]. However, companies still face the cost of obtaining reimbursement in each of the countries.

A limitation of the 7–8 year models is that the covariates reflect conditions in just one year. Degrees of freedom and data constraints preclude the inclusion in these models of covariates that reflect prices in each year of the accrual period. For instance, the PMPRB only began reporting price index data for all OECD countries in 2014 (prior to this, they only reported the PMPRB7 price indexes). Given these constraints, for the 2009–2017 model, we use the average of the 2014–2017 data for all covariates. As a robustness check, we estimated a model using the same outcome variable but measuring the covariates at each individual year between 2014 to 2017. These results are reported in the Appendix (Table S1).

Table 2

Table 2
Model 5 and 6 Outcome Variable Time Interval and Regulatory Bodies.

		7–8 year models	
		Model 5	Model 6
Share New Meds$_i$	*numerator**	2009–2018Q3	2011-Aug 2018
	denominator¥	2009–2017	2011-Aug 2018
Regulatory Bodies		FDA, EMA, HC or Swiss	FDA, EMA or JPMDA
Data Source		2018 Med Entry Watch Report	2019 IMC Report

*Numerator: Period during which drugs approved by the defined regulatory bodies accrued a sale in country *i*.
¥Denominator: Period during which a drug was approved by any of the regulatory bodies. Swiss refers to Swissmedic, the medicines regulatory authority for Switzerland. JPMDA refers to the Japanese Pharmaceuticals and Medical Devices Agency

We also estimate variants of the models that account for the influence of potential outliers in our data set. Specifically, the USA and New Zealand have extreme values of drug launches and drug prices; the USA has particularly large values of both variables (Fig. 1). In contrast, New Zealand is often cited as having particularly low numbers of drug launches, though its prices as reported by the PMPRB are quite similar to Canada [3-7,13,37]. To assess the degree to which these two countries – or any other – were driving the results, we estimated our models after sequentially excluding a country-specific observation. As a further sensitivity test to assess the effects of outliers, we perform conditional quantile regression at the 25th, 50th, and 75th percentile for each model. One would expect to see a significant difference between the OLS and quantile regression estimates if outliers are strongly influencing our OLS estimates.

Estimation of standard errors of the OLS parameter estimator

It is possible that the error terms in our models are heteroskedastic, in which case the default "iid" standard error estimators are invalid. One approach is to use the so-called "robust" standard error estimator; in large samples this estimator is consistent in the face of heteroskedasticity of unknown form [40]. However, inference based on robust standard errors can be misleading in samples of the size used in this paper. Roodman et al. (2019) report that the wild bootstrap is a more reliable approach to inference in smaller samples. We therefore used this procedure, as implemented using Roodman's "boottest" Stata program, to generate p-values associated with the restriction that β_1, the parameter associated with $\log(price_i)$ in our regression models, is equal to zero [41]. Specifically, we generated 999 wild bootstrap samples using the Rademacher distribution, with the restriction imposed. The bootstrapped p-value is the percentage of bootstrapped t-ratios, $t^b_{\beta_1}$, $b = 1, \ldots, 999$ that are more extreme (in either direction) than the t-ratio

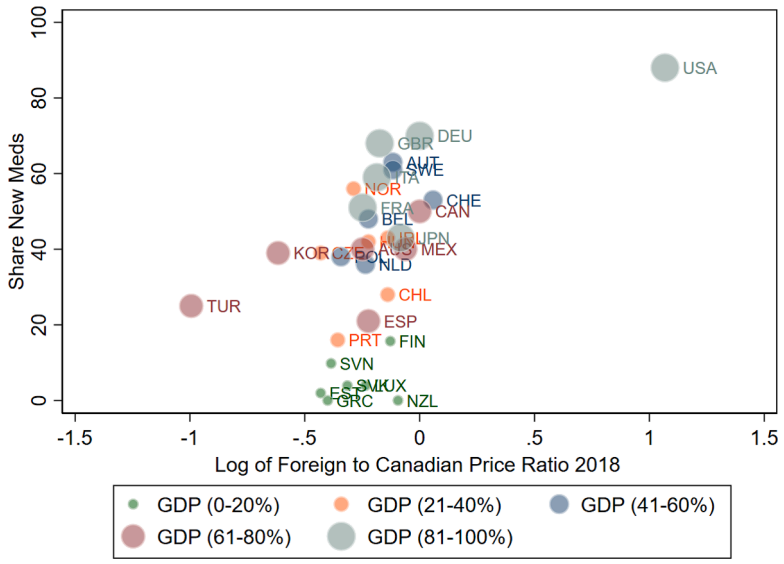

Fig. 1. Share of New Medicines and log foreign to Canadian price, by country, in 2018. Marker size is proportional to total GDP. Quintile of GDP in parentheses. Model 4 *Share New Meds* definition used.

calculated using the original data, t_{β_1}:

$$\frac{1}{999}\sum_{b=1}^{999}\left(\left|t^b_{\beta_1}\right| > \left|t_{\beta_1}\right|\right) \tag{2}$$

Here, $\|\ (|t^b_{\beta_1}| > |t_{\beta_1}|)$ equals 1 if the expression in the parentheses is true and equals 0 otherwise. The t-ratios in this expression are calculated using the heteroskedasticity-robust variance estimator of Eicker and White [40,42]. We also used this procedure to test the restrictions that the other parameters were equal to zero and report the resulting p-values with our parameter estimates below.

Impact of missing data on actual transactions prices on our regression model

As noted earlier, both list and actual prices presumably affect *Share New Meds*$_i$, albeit through different channels. One limitation of our regression model is that it does not control for actual transactions prices. How will this affect the OLS estimator of the effect of list price on *Share New Meds*$_i$?

To begin, express the index of actual patented drug prices in country *i*, act_i, to be a fraction α_i of the list price index $list_i$:

$$act_i = \alpha_i list_i \tag{3}$$

This fraction α_i reflects a weighted average across payers and different types of drugs. Suppose further that the Data Generating Process (DGP) is:

$$Share\ New\ Meds_i = \beta_0 + \beta_1 \log(list_i) + \beta_2 \log(act_i) + \nu_i \tag{4}$$

where ν_i is the error term for country *i*. Substituting, we have:

$$Share\ New\ Meds_i = \beta_0 + \beta_1 \log(list_i) + \beta_2 \log(\alpha_i list_i) + \nu_i \tag{5}$$

Rearranging:

$$Share\ New\ Meds_i = \beta_0 + (\beta_1 + \beta_2)\log(list_i) + \beta_2 \log(\alpha_i) + \nu_i \tag{6}$$

The estimable form of this model is:

$$Share\ New\ Meds_i = \beta_0 + \gamma_1 \log(list_i) + \varepsilon_i \tag{7}$$

where γ_1, the parameter on $\log(list_i)$, reflects the sum of the impacts of the logarithm of list and actual prices on *Share New Meds*$_i$. The error term ε_i is the original error ν_i plus $\beta_2 \log(\alpha_i)$.

Unbiasedness requires that the expected value of ε_i not vary with $list_i$. But it seems plausible that α_i (a component of ε_i) does indeed vary with $list_i$. One may expect that the proportional rebate in a country, $1 - \alpha_i$, is larger, the greater is the list price, if only because there is more negotiating room. In this case, α_i and thus actual prices tend to be smaller, the higher are list prices. This will attenuate the estimator of γ_1. On the other hand, if rebate percentages tend to be higher the *lower* is $list_i$ then the model will over-estimate the impact of prices on *Share New Meds*$_i$.

Results

Fig. 1 shows the *Share New Meds*$_i$of each country included in the 2018 Model. This graph reveals a cluster of EMA member countries with higher *Share New Meds*$_i$ but lower patented drug prices than in Canada. *Share New Meds*$_i$ and prices in Switzerland – which is not a member of the EMA – are similar to those in Canada. South Korea and Turkey have relatively low prices and also relatively low *Share New Meds*$_i$. Conversely, the USA have the highest drug prices and the highest share of new medicines. Countries in the lowest quintile of overall GDP appear to have low *Share New Meds*$_i$..

We next turn to the estimates of the linear regression models to quantify the roles of drug price, market size and EMA membership on the share of new medicines available globally entering a country.

Single Year Models

Our single-year models suggest that list price has an economically meaningful and statistically significant impact on the percentage of new medicines available in a country (Table 3). In the short term, a ten-percentage increase in price is associated with a 2.2 to 3.7 increase in *Share New Meds*$_i$. Larger markets – those with larger values of GDP per capita and population – are also associated with a larger shares of new medicines in an OECD country. Finally, EMA membership is associated with 9-to-15-point increase in the percentage of NAS that are sold in the country. The four models have adjusted R^2 values between 0.65–0.70.

7–8 Year Models

The final two models capture the influence of list price, market size and EMA membership on *Share New Meds*$_i$.over a period of 7–8 years (Table 4). In these models, price has a smaller, although statistically significant, impact on an OECD country's share of new medicines. Per

Table 3
Parameter estimates of single year models.

Variable	2015 Ψ β (p-value)	2016 Ψ β (p-value)	2017 Ψ β (p-value)	2018 Ψ β (p-value)
log(price$_i$)	37.071*	21.805***	26.940***	28.306*
	(0.0170)	(0.0000)	(0.0000)	(0.0140)
log(population$_i$)	6.694	5.871*	6.343*	6.857*
	(0.0701)	(0.0240)	(0.0450)	(0.0310)
log(GDP$_i$/capita$_i$)	20.191*	12.155	19.631*	15.513
	(0.0991)	(0.0621)	(0.0300)	(0.0551)
ema$_i$	15.246**	15.311**	9.243	9.171
	(0.0220)	(0.0080)	(0.1061)	(0.1351)
Constant	-207.118*	-129.998*	-206.145**	-169.534*
	(0.1261)	(0.0701)	(0.0400)	(0.0490)
N	29†	31	31	31
R^2 adjusted	0.668	0.652	0.662	0.702

wild bootstrap p-value legend: * p<0.05, ** p<0.01, *** p<0.001
†Launch Data for Greece and Turkey not available
ψThe outcome variable reflects the percentage of drugs which obtain global regulatory approval in the specified year that are sold in an OECD country during the specified year or 9 months after.

Table 4
Parameter estimates of 7–8 year models.

Variable	**2009–2017 Ψ β (p-value)**	**2011–2018 β (p-value)**
log(price$_i$)	**15.636***	**21.692***
	(0.0310)	**(0.0100)**
log(population$_i$)	**7.048***	**5.715***
	(0.0210)	**(0.0360)**
log(GDP$_i$/capita$_i$)	**15.579**	**4.206**
	(0.0851)	**(0.7788)**
ema$_i$	**13.855***	**10.126**
	(0.0110)	**(0.0631)**
Constant	**-148.612**	**-1.569**
	(0.2282)	**(0.9940)**
N	**31**	**31**
R^2 adjusted	**0.668**	**0.704**

wild bootstrap p-value legend: * p<0.05, ** p<0.01, *** p<0.001
ψThe outcome variable reflects the percentage of drugs which obtain global regulatory approval in the specified years that are sold in an OCED country during the specified year or 9 months after.

capita GDP does not have a statistically significant effect in either of the longer-term models.

Sensitivity Analysis

In a sensitivity analysis, we re-estimated each model after sequentially excluding one country observation to identify influential observations. We found that the exclusion of the USA had the largest impact on model estimates of log($price_i$), reducing the model R-squared values, parameter estimates, and increasing p-values of the estimates. We report model estimates and the estimated impact of price reductions when excluding the USA in the Appendix. Without the USA, the estimated effect of price is smaller, and only 3 of the 6 models show it to be a statistically significant covariate at conventional levels. However, in 5 of 6 models the p-value is no higher than 0.074. Overall, we find that the USA is indeed a particularly important observation.

We also report conditional quantile regression estimates at the 25th, 50th, and 75th quantile in the Appendix. Quantile regression is less sensitive to outlier error term values. Comparison of the conditional quantile results to the linear regression results therefore can assess the impact of outliers in our OLS estimates. In our comparisons, reported in the Appendix, we found no instances where the OLS estimates fall out of the 95% confidence interval of the quantile regression.

Estimated impact of price reductions

We next used the parameter estimates to estimate the impact on expected *Share New Meds*$_i$ of a 5%, 15%, 25%, 35%, and 45% decrease in patented drug prices (Table 5). Recall that our model estimates the effect of a percentage reduction in *both* list and actual prices. The price reductions reported in the table are meant to be illustrative; the price reduction for a given drug will depend on the specifics of how the new pricing controls are applied.

The single year models show that a 25% price decrease will result in an estimated 6–10% decrease in *Share New Meds*$_i$ for a given country included in the model. The 7–8 year models show a 4.5–6% decrease in *Share New Meds*$_i$ with the same price decrease. Our models therefore suggest that the effect of price cuts on new medicines entering a country is greater in the short-term than in the long-term, a result indicative of launch delays.

Discussion

The Government of Canada plans to implement new controls on both the list and actual transaction prices of patented drugs in July 2022 [8]. The literature indicates that reductions in drug list prices delay drug launches [9–13]. The Government's analysis indicates that the proposed price controls will not delay drug launches [14,43]. It is possible, however, that the results of the extant literature no longer apply. The literature uses data that is now almost 20 years out of date, drawn mostly from the 1990's.

We produced new evidence on the issue to assess the possible effects of the PMPRB's new regulatory regime. Using recent OECD country level data, we estimated 6 regression models of the percentage share of new medicines approved globally that are launched in a country by a given date. The models show that list price is an important covariate, and the impact of list price on the share of new medicines within this group of countries is greater in the short term than the long term.

If our estimates can be given a causal interpretation, then we predict that a 25% decrease in list prices in an OECD country will lead to a 6–10% and 4.5–6% decrease in drugs launched over 1- and 7–8-year periods, respectively. Though our methods and data sources differed, these findings are consistent with previous studies on this topic. Our estimates also suggest that larger market sizes and EMA membership increase the share of new medicines entering an OECD country.

To what extent do these empirical results inform the impacts of the proposed PMPRB regulatory reforms? This depends on whether our results directionally indicate the causal impact of price reductions on launch delays. It is possible that our results are spurious, and simply reflect correlations between unmodelled determinants of drug launches and list prices. We would be surprised if this were the case. One unmodelled determinant of drug launches are actual drug prices; these are list prices less any confidential rebates. If rebate percentages are higher with higher list prices (a situation we find plausible), then our estimator is attenuated. If this is the case, other unobserved factors

Table 5
Estimated percentage point decrease in expected launch percentage from a 5%, 15%, 25%, 35% and 45% decrease in list prices.

Price Decrease	2015 %	2016 %	2017 %	2018 %	2009–2017 %	2011–2018 %
5%	1.902*	1.118***	1.382***	1.452*	0.802*	1.113*
15%	6.025*	3.544***	4.378***	4.600*	2.541*	3.525*
25%	10.666*	6.273***	7.750***	8.143*	4.498*	6.240*
35%	15.97*	9.393***	11.606***	12.19*	6.736*	9.344*
45%	22.163*	13.036***	16.106***	16.922*	9.348*	12.968*
N	29†	31	31	31	31	31

wild bootstrap p-value legend: * p<0.05, ** p<0.01, *** p<0.001
†Launch Data for Greece and Turkey not available

would need to overwhelm this downwards bias to produce the estimates we obtain. Of course, we cannot rule out the possibility that our results are spurious.

Proceeding on the assumption that our estimates do have a causal interpretation, how do they affect the CBA of the new price regulations? A lot depends on the therapeutic novelty of the drugs whose launch in Canada is delayed. Delays in access to therapeutically important new medicines will harm patients. Perhaps recognizing this, the Government of Canada exempted COVID-19 treatments from the new pricing rules [8]. However, most drugs currently entering the Canadian market are those offering only small improvements over existing therapies, colloquially known as "me-too" drugs. From the period of 2010–2018, the PMPRB reports that 5% of 811 NAS evaluated by its Human Drug Advisory Panel were categorized as either a breakthrough drug (2.3%) or a drug offering a substantial improvement over other medicines in Canada (2.7%) [3]. The remaining drugs were either a moderate improvement (12.1%) or a "me-too" drug (82.9%) [3]. The welfare effects of delayed "me too" drug entry into Canada are likely smaller than that of delayed entry of breakthrough drugs. Moreover, as a referee pointed out, during the delay period additional information on the therapeutic properties of new drugs can be generated from jurisdictions where the drug is already approved.

The price reductions will also vary across payer types, i.e., the public drug plans (which insure mainly seniors, the indigent and those with high drug costs relative to income), private plans (which insure mainly those with employment related benefits) and the uninsured. The proposed new price ceilings will likely have their greatest effect on prices paid in the private plans since the public plans likely currently secure larger rebates. We might therefore expect to see the largest delays in those drugs used primarily by beneficiaries of private plans, who tend to under 65 years of age.

It is unclear if the incorporation of drug delay costs would change the net benefit to Canada of implementing the more stringent price controls. Regardless of the net benefit to Canada, however, Canada's new price controls will weaken the international system of financing pharmaceutical R&D if it causes other countries to reduce their prices. International agreements that ensure that each high-income country carries its fair share of the global pharmaceutical R&D burden would appear to be better than the current system of price referencing and confidential discounts [44].

Declaration of Conflicting Interests

Paul Grootendorst has provided expert testimony and or reports in legal proceedings on behalf of both innovator and generic drug companies. Oliver Spicer is a PhD candidate at the University of Toronto and paid employee of Astellas Pharma Canada, Inc. (Astellas). This article is intended for informational purposes only and does not replace independent professional judgment. Positions taken and opinions expressed are those of the author individually and, unless expressly stated to the contrary, do not necessarily reflect the opinion or position of the author's employer, Astellas, or any of its subsidiaries and/or related entities. Other than the author's direct contribution, Astellas had no role in the study design, interpretation of results, or decision to publish.

Author Contributions

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.healthpol.2022.05.003.

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