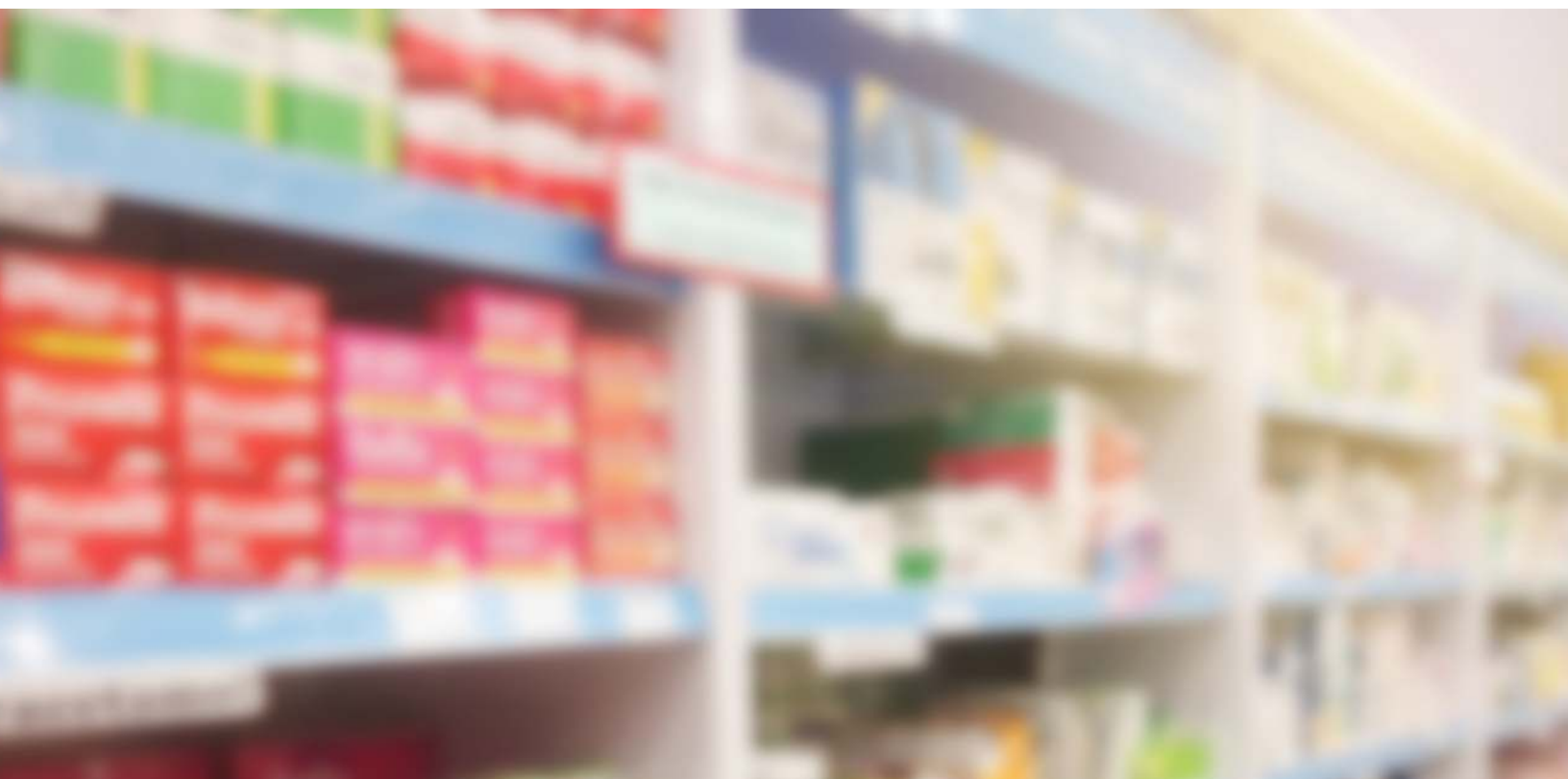


June 14, 2022



CANADIAN PATENTED DRUG PRICES: GAUGING THE CHANGE IN REFERENCE COUNTRIES



OFFICE OF THE PARLIAMENTARY BUDGET OFFICER
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The Parliamentary Budget Officer (PBO) supports Parliament by providing economic and financial analysis for the purposes of raising the quality of parliamentary debate and promoting greater budget transparency and accountability.

Regulatory changes for how the Patented Medicines Prices Review Board (PMPRB) formulates price ceilings for patented drugs have been proposed and are due to come into effect in July of 2022. This report examines the proposed change and quantifies its long-term impact. We find that a change to the median of eleven comparator countries is important, but that more flexibility to re-adjust prices would potentially contribute more to reducing expenditures by Canadians.

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Executive Summary

Evolving markets for pharmaceuticals in Canada and around the world have made it challenging for the Patent Medicines Prices Review Board (PMPRB) to achieve what its mandate defines as non-excessive prices for patented medicines. This includes reference to the average of the medians of prices in seven other countries. Two trends in particular underlie that difficulty,

- (1) Higher prices in the US and an high proportion of drugs for which it is the only external reference; and
- (2) Increasingly less informative *ex factory* price information.

These are distinct from the general rise in the price of pharmaceuticals, which has multiple and complicated sources and is outside the scope of the PMPRB's mandate.

To respond to those trends, in 2019 Health Canada proposed changes to the PMPRB's regulatory framework. They were challenged in court, and following unfavourable rulings, most of the proposed changes were withdrawn. Only the change in reference countries – whose median is often used to set Canadian prices – was retained.

The composition of reference countries will therefore move from the current seven (PMPRB7), to a broader group of eleven countries (PMPRB11). The United States and Switzerland will be removed from the list and six others added. Whether by coincidence or design, Canada's GDP per capita (in purchasing power parity) is near the median of that new group.

In this report, we assess the potential long-term impact that changing comparator countries for median targeting could have on expenditures by Canadian consumers. Given the complicated and time-dimensioned nature of implementing the proposed change, we abstract from the difficult-to-measure short-term impacts and focus on the potential proportionate impacts.

While we acknowledge that the new rules are not yet final. Nonetheless, we estimate that, *ceteris paribus*, Canadian expenditures would have been lower by approximately nineteen per cent in 2018 had pricing at the median of PMPRB11 been in place at that time. For a representative year like 2018, for which reliable data for Canada and other countries exist, this would have represented a \$2.8 billion reduction. Data from 2021 confirm the general magnitude of that result, though the Covid pandemic makes data from that year less reliable.

Canada's gap to PMPRB11 median, 2018

Patented drugs	PMPRB11
ATC4* classes where Canada's price exceeds median	83%
Value of pricing <u>over</u> or under median**	\$2.8 billion
Percentage of total sales in 2018	19%

Sources: OBPO using PMPRB data¹

Note: * ATC4 defines the 4th level of detail in the Anatomical Therapeutic Chemical classification system (see http://whocc.no/atc/structure_and_principles).
 ** Combining cases where Canada's prices are more than 5% above or below the comparator country median.

We note, however, that if mechanisms such as grandfathering of existing drugs are used, there could be a substantial delay in realising the full change. For example, if the transition allows their current prices to continue for the duration of their patent(s), it would be more than a decade before grandfathering ended.

We calculate a similar gap of twelve per cent between Canadian prices and the PMPRB7 median. That is, expenditures in 2018 would have been twelve per cent lower if PMPRB7 prices had prevailed in Canada. This means that of the nineteen per cent gap relative to PMPRB11 countries, some two thirds are not related to the change in comparator countries but instead are due to lower prices in PMPRB7 countries (confirmed in Figure 36, PMPRB, 2019).

Since *ex factory* prices are used by PMPRB to determine maximum prices, and *ex factory* prices are used in the PMPRB7 medians, the discrepancy between Canadian prices and PMPRB median prices is unexpected. An important reason for it is that once prices are set in Canada, they rarely fall. Indeed, manufacturers are allowed to raise them each year at the rate of inflation. This contrasts to other countries where prices can be renegotiated and tend to fall if the drug is particularly successful.

We conclude that the proposed change may, over the long-term, lower expenditures on patented drugs by seven per cent, reaching nineteen per cent if reassessment of prices occurs more frequently.

Our analysis is based on prices in the IQVIA's MIDAS dataset.¹ Thus, the comparison is consistent in what is being measured across countries: *ex factory* prices for retail and hospital use.

Proposals to change the regulatory framework have in the past engendered resistance, both from the industry itself, and from patient advocacy groups. The latter have been concerned that lower prices will slow the introduction of new drugs into Canada. This report does not delve into those issues, but it is

recognized that both lower prices for new innovative drugs may reduce timely access to those drugs for Canadians, and that Canada must inevitably balance the interest of consumers who ultimately pay for pharmaceuticals with obligations to help fund R&D and incentivise the development of future products.

1. Introduction

Canada's market for medicines transitioned in 1987 from what had been a system of compulsory licensing to one that granted market exclusivity to a patent holder (Lexchin, 1993). With the expectation that patents would support R&D in Canada, the subsequent regulatory framework was focused on the potential harm to Canadian consumers that might come from unrestrained prices (Shulman and Richard, 1988). The Patented Medicine Prices Review Board's (PMPRB) mandate under the Patent Act was explicitly to avoid *excessive prices* for patented drugs. That mandate has withstood constitutional legal challenges.²

From a broad economics perspective, there are arguments for and against the notion of that harm, so there is no clear analytical view. Nonetheless, Parliament signaled its intent and PMPRB was mandated from the start to use external reference pricing (ERP).^{3,4} This set a price ceiling in Canada in relation to a medicine's price in other countries: the median of a group of seven countries, including the United States.

Given its regulatory framework to implement that mandate, two trends over the past fifteen or so years have made attaining PMPRB's price-ceiling objective challenging: (1) the United States has become an acute outlier in drug prices globally, and (2) prices globally are less informative than they used to be, notably given increased use of undisclosed rebates, etc.

To respond to those trends, in 2019 Health Canada proposed revising its regulations, which are due to come into effect in July of 2022.⁵

Modifications were made after judicial review, but the change in comparator countries is proceeding, even if the final rules implementing that change are not ready. They will be expanded from the current seven to eleven (Figure 1-1). Two countries will be removed that have historically had high prices for pharmaceuticals, while six other countries will be added that have GDP per capita comparable to Canada's; indeed, Canada's GDP per capita falls in the median of the new group.

Figure 1-1 Changes to comparator countries

PMPRB7	France	Germany	Italy	United Kingdom	Sweden	Switzerland					United States
PMPRB11	France	Germany	Italy	United Kingdom	Sweden	Australia	Belgium	Japan	Netherlands	Norway	Spain

Source: PMPRB

The removal of the United States is particularly significant given the integrated nature of the Canadian and American drug markets, and the outlier status of prices in the United States. Depending on how the change is implemented, its impact may be substantial.

In this report we attempt to quantify the potential impact of the change in comparator countries on the assumption that median PMPRB11 prices will be the new targets. Specifically, we estimate what the proportionate change in Canadian expenditures would have been in 2018 if prices had been at the median of PMPRB11 countries. That proportion is generally supported by results for 2021 – though the Covid pandemic makes those data less reliable. A focus on proportionate change is more likely to be reflective of structural differences between PMPRB7 and PMPRB11.

We find a proportionate expenditure reduction of 19 per cent, which is what we claim is a useful first order approximation of the long-term impact of the change in comparator countries.⁶

2. Canada’s patented drug prices landscape

We begin our analysis with an outline of how non-excessive prices for patented drugs have been determined. This gives context to the proposed regulatory change as well as provides background to the changes that have been withdrawn following judicial review.

2.1. How are PMPRB prices currently determined?

Excessiveness of drug prices is currently linked to how innovative a drug is, as well as how its price compares to that in other countries (Table 2-1). When a breakthrough drug is first introduced, the non-excessive price is the median

in the seven comparator countries. For non-breakthrough drugs, the maximum price takes into account that of existing drugs in the same therapeutic class.

Table 2-1 Previous PMPRB pricing of patented drugs

Designation*	Price calculation	Note
Breakthrough	Median international price among PMPRB7 nations	Where price comparison is possible
Substantial Improvement	MAXIMUM [MEDIAN (PMPRB7), TCC]	Where the TCC price is determined from Canadian sources for comparable therapeutic classes (AQPP, ODB, IMS Health, McKesson Canada, PPS Pharma, RAMQ).
Moderate Improvement	MAXIMUM [AVERAGE (TCC, MEDIAN (PMPRB7)), TCC]	The price is centered on TCC, but accounts for PMPRB7 if that price is higher.
Slight or No Improvement	Either MAXIMUM (TCC) or MINIMUM [broader TCC, MEDIAN (PMPRB7)]	A broader TCC may also be used if necessary.
Existing drug	Price _{t-1} *(1+ MINIMUM [LOGARITHM (CPI _t /CPI _{t-1}), 1.5* LOGARITHM (CPI _{t-1} /CPI _{t-2})])	Allowable annual change. If CPI inflation is more than 10%, alternative rules become effective.

All subject to a hard cap of highest price among PMPRB7

Note * Refers to therapeutic change

TCC - price from a Therapeutic Class Comparison. Price is based on either cost per treatment, or cost per day. CPI - consumer price index, AQPP - Association québécoise des pharmaciens propriétaires, ODB - Ontario Drug Benefit Program, IMS Health (www.iqvia.com), McKesson Canada (www.mckesson.ca), PPS Pharma (www.gopps.ca), RAMQ - Régie de l'assurance maladie du Québec.

The international price comparison that PMPRB undertakes is constrained by limits on federal powers. It can only consider *ex factory* prices for comparison to prices in other countries. Even that metric indicates that Canada's prices are among the highest (Figure 26, PMPRB 2020). A misleading metric that appears in the PMPRB Annual Reports compares transacted prices in Canada with list prices elsewhere (Figure 27, PMPRB 2020). Since list prices are generally higher than transacted prices, it misleadingly implies that Canada's prices are lower.

The use of prices in other countries to determine a price threshold is referred to as external reference pricing (ERP; Box 2-1).

Box 2-1 External Reference Pricing and R&D

The Canadian system of external reference pricing (ERP) – based on seven other countries – has been in effect for more than three decades. Alternatives such as “internal” reference pricing or no reference pricing at all, are in use to varying degrees in other countries as well as ERP.

Relying on ERP has two drawbacks. The first is that if all countries rely on ERP, then the system has no anchor – or at best a weak anchor. The second is that under ERP excessiveness in pricing is not tied to Canadian consumers – it relies on what consumers in other countries have negotiated. In effect, through ERP Canada strives to ensure that its consumers are not disadvantaged relative to international peers who may have national drug plans.

That strategy has some potentially important shortcomings. Confidential rebates (Morgan, *et al*, 2013), which are explicitly intended to avoid making the transacted price public, would lead to bias in the ERP. Though the evidence is not solid, estimates put confidential rebates at 15 per cent of the list price (Health Canada, 2019; page 86).

Another potential bias from ERP concerns pharmaceutical R&D. While ERP strives to level prices across countries for consumers, it does not address regional imbalances in R&D expenditures. Indeed, maintaining a robust pharmaceutical R&D industry was Canada’s explicit objective in eliminating compulsory licensing. Patent exclusivity seems to have not been sufficient since after Canada removed compulsory licensing, R&D rose a little, then gradually declined relative to sales.

The high value-added created by pharmaceutical R&D was deemed important enough that PMPRB was tasked with reporting on the sector’s R&D expenditures on a regular basis.

Though median price should be unaffected by extremes within the ERP group, the United States has nonetheless consistently had a significant impact on Canadian prices. This is a consequence both of the United States often being the only available comparator country (see various issues of the PMPRB Annual Report in their international comparison), as well as it being a distant outlier in prices. When it is the only comparator, the price there becomes the Canadian price even though overall drug prices in the United States are higher (Box 2-2 below).

The magnitude of that effect is such that overall Canadian expenditures on patented drugs are about 10 per cent higher than they otherwise would be (see Figure 28 in PMPRB, 2021).

Even in the case where the drug is available in all countries, its price can diverge significantly from the comparator countries. PMPRB's annual reports inevitably show a divergence for many drugs between Canada's then-current prices, and the equivalent PMPRB median. This is in part because exchange rates may change, and TCC can be less constraining, but also because allowing Canadian prices to increase with inflation can lead to a significant gap when they are falling in other countries (e.g., Lucentis and Avastin; PMPRB, 2018, Figure 4.1).

Nonetheless, there are a number of cases where prices go up more in other countries, so Canada's inflation-indexed prices lead to a benefit for consumers of those products. To illustrate, in 2018 some 18 per cent (by value) of ATC4-aggregated patented drugs had median prices that were lower in Canada than elsewhere.⁷

2.2. What motivated the regulatory change?

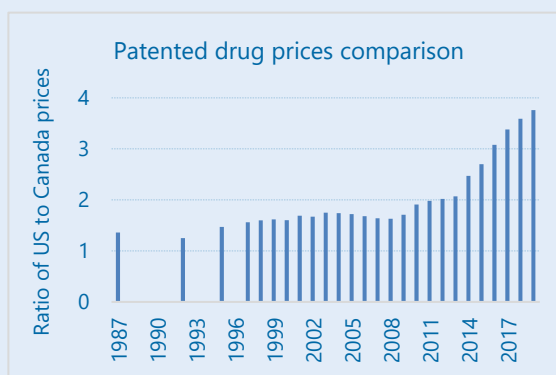
Trends have developed over the past few decades that have had profound effects on drug prices in Canada:

- 1) Newer drugs are increasingly available for treating rare diseases and are more expensive to develop,
- 2) Drug prices in the US have increased substantially relative to Canada's; and,
- 3) Non-disclosed rebates are increasingly common in all countries.

The first and second trends are inter-related (Box 2-2) and have created an environment of increasing prices for new medicines. This has given impetus to acting on the second and third trends. The third trend has a more diffuse source – perhaps motivated by the widespread use of ERP – indeed, Canada itself has become a reference country for some developing countries (e.g., Brazil, South Africa, and Egypt).

Box 2-2 - Drug prices in the US

Drug prices in the United States have historically been higher than in Canada but until recently the gap changed only moderately. For example, in 1987 US prices were on average 36% higher than in Canada and in 2008 they were 63% higher. But after 2007, US prices began to climb much more rapidly (Box Figure).



Source: PMPRB Annual Reports

The reasons underlying that recent divergence have not been studied in detail, but some broad factors offer insight into what may be underlying it. These include the US Hatch-Waxman Act of 1984 that made it easier for generics to enter the market and thus forced innovators to recover R&D costs almost entirely within the patent exclusion period. The share of new drugs facing generic competition within the first year after patent-expiration went from 9% in 1995, to 81% in 2012 (Grabowski, et al., 2014).

The creation of Medicare Part D (effective 2006) further led to pressure on prices. It expanded drug coverage to potentially all Medicare recipients while precluding price negotiation. It also required Medicare to cover all drugs in certain disease categories (Olsen and Sheiner, 2017).

The Orphan Drug Act of 1984 also added to long-term price pressure by giving an additional seven years of market exclusivity to drugs that treat rare diseases. By 2015 some 47% of new drugs were treating rare diseases (Yin, 2008).

All of these measures were intended to expand access to effective therapeutics while continuing to encourage innovation within the pharmaceutical sector. Indeed, the US is currently the world leader in biopharmaceuticals (Wu and Ezell, 2016) and in business pharmaceutical R&D spending (Box Table).

Business R&D expenditure, pharma (2016)

Region	\$ billions
United States	64.6
Europe	20.1
Japan	13.2
Other OECD	3.1
China	14.1

Source: OECD, 2019

Even though Canada's prices have not grown as quickly as those in the United States, treatment costs have nonetheless increased significantly. The weighted-average treatment cost of the 20 top-selling drugs went from \$2,240 in 2006 to \$19,266 in 2019 – a more than eightfold increase (PMPRB, 2021) – though the drugs of 2006 were generally treating different conditions than those of 2019.

As drugs have become more expensive, misalignment of Canada's prices (whatever the cause) leads to significantly higher expenditures relative to what they would have been with comparable PMPRB7 median prices.

The third trend listed above is particularly problematic for Canada's implementation of ERP. The use of confidential rebates in comparator countries can cause upward bias when using ERP to set non-excessive prices.

The opaqueness of prices has been documented extensively (see Morgan, et al, 2013; Health Canada, 2019; and the references therein). Moreover, Health Canada (2019b) illustrated a flattening of prices across comparator countries – consistent with the proposition that prices have become less informative in the face of confidential rebates.

2.3. Proposed change

In 2019 Health Canada proposed changes to the regulations that had operationalised PMPRB. Most of them were subsequently withdrawn.⁸

The proposed change to the comparator countries was retained and is potentially consequential, but issues remain to be addressed.

In particular, the significance of removing the United States from the comparators will depend on how the comparison will be done afterwards. Currently, it is at the level of the drug identification number (DIN). This means that a match must occur in both the dosage and delivery form. Even in two markets as integrated as those of the United States and Canada only 78 per cent of drugs have such a match (Table 9, PMPRB, 2020). Illustrative of ways to overcome that obstacle is an increased flexibility to match prices in cases where the chemical compounds are the same and the drug is otherwise identical.

Another issue that remains relevant is linked to the reasons for Canada's timely access to some drugs. If current Canadian prices for those drugs was the main reason for that access, then it would likely be curtailed (e.g., Spicer and Grootendorst, 2020; Palmer, 2019). This means that Canada would only have access to some new drugs as they became more widely available internationally. This potential delay in new drug availability also engendered opposition to the proposed changes from patient advocacy groups.⁹

3. Potential impact of changing comparator countries

Given the challenge of projecting something as inherently unpredictable as the development of new drugs, this analysis proceeds by gauging how important the regulatory changes might be for the long term. We do that by highlighting how much it would have affected expenditures in 2018 if regulations to target PMPRB11 median prices had already been fully in place. The general magnitude of the result is confirmed using 2021 data – though the Covid pandemic makes data from that year less reliable.

The utility of that analysis is that, in principle, that estimated proportionate change should apply to most long-term projections – it is a structural impact. The main objective of the exercise is not to attempt to provide an accurate measurement, but rather to gauge the importance of the change.

Using data provided by PMPRB, we compared the value of Canadian expenditures on patented medicines under both prevailing prices in 2018, and the median prices of PMPRB7 or PMPRB11 (Table 3-1).^{1,10}

That data limited our analysis to ATC4 categories, but the sample is sufficiently large to avoid significant bias.

Table 3-1 Canada's gap to international median, 2018*

Patented drugs	PMPRB7	PMPRB11
ATC4 classes where Canada's price exceeds median	71%	83%
Value of cases where price is <u>over</u> median	\$2.0 billion	\$3.0 billion
<i>Percentage of total sales over median in 2018</i>	14%	21%
Value of cases where price is <u>under</u> median	\$361 million	\$212 million
Combined percentage of total sales in 2018**	12%	19%

Source: OPBO using PMPRB data¹

Note: *The analysis is done using ATC4 category aggregates.

**Combining cases where Canada's prices are more than 5% above or below the comparator country median.

The table confirms that there is a potentially large expenditure reduction that could occur by moving to PMPRB11 median prices: 19 per cent. Whether that

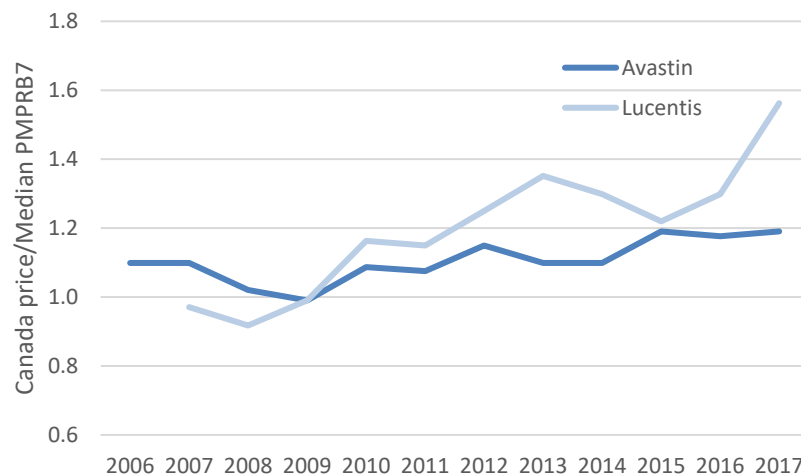
reduction actually occurs when the regulatory change is implemented will depend on the specific rules that are adopted. One that is particularly important concerns grandfathering of existing drugs. If, for example, those drugs were allowed to continue to be priced at their current levels, the reduced expenditures could take more than a decade to be fully realised.

The distinction between PMPRB7 and PMPRB11 also reveals some important characteristics of current pharmaceutical prices. Much of the 19 per cent reduction (almost two thirds) can be attained by achieving PMPRB7 median prices. This means that actual Canadian prices and PMPRB7 median prices are drifting apart over time. At present, when a drug is approved for use in Canada its initial (reviewed) price is only allowed to vary in line with inflation. In other countries, prices can be revised as the market evolves.

Reassessment of prices after initial introduction was a potentially significant part of the now-withdrawn proposed guidelines. They included a broader set of conditions that could trigger reassessment. Our finding (using *ex factory* prices, IQVIA MIDAS database for 2018), that Canadian expenditures for patented drugs were about 12 per cent higher in 2018 than they would have been if PMPRB7 median prices had prevailed means that more latitude to reassess prices could lead to significant reductions in expenditures.

To illustrate, consider the time profile of the relative price (the median of PMPRB7 to Canada's) of two drugs: Lucentis and Avastin (Figure 3-1).

Figure 3-1 Profile of median PMPRB7 prices for Lucentis and Avastin



Source: Calculated from PMPRB (2018), Figure 4.2.

Note: The ratio of Canadian price to median PMPRB7 is shown. Values above 1.0 mean Canada's price is higher. The annual changes are caused by short-term factors such as exchange rate changes that can also lead to a change in the median country. But these factors do not underpin the longer upward trend.

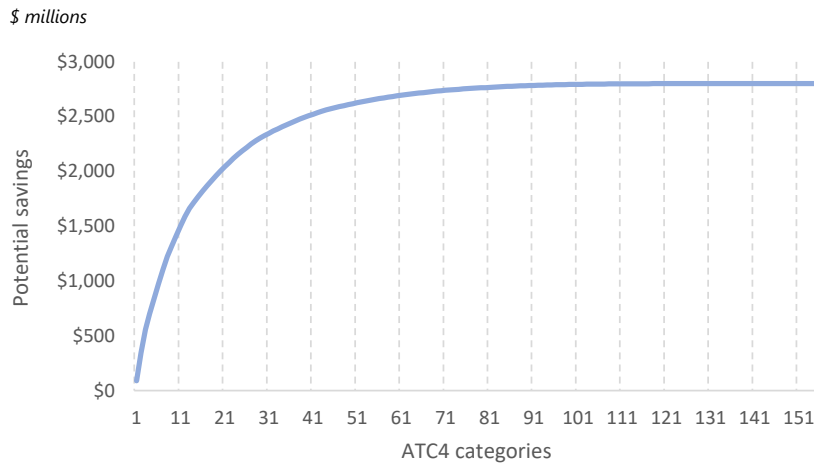
In both cases, the median price in PMPRB7 is falling over time, while Canada’s price is not. This is primarily due to the one-sided rule that allows prices to increase with inflation but does not require downward revisions when they occur elsewhere.

A conclusion that we draw from Table 3-1 is that the change in comparator countries is potentially secondary to the price reassessment (Section 2.3 above).

The last row of Table 3-1 also shows that greater flexibility of prices can have some adverse consequences. Drugs whose prices have increased by more than inflation in other countries have been restrained in Canada. Moving to the median prices of PMPRB11 countries would *increase* the cost of those medicines.

It is also notable that much of the gain outlined in moving to median PMPRB11 prices could be achieved through just a few categories of drugs (Figure 3-2 and PMPRB, 2020). Of the 155 ATC4 categories included in this analysis, some 20 account for \$2 billion (more than two thirds) of expenditures above what would occur with PMPRB11 prices.

Figure 3-2 Expenditure difference using PMPRB11 prices



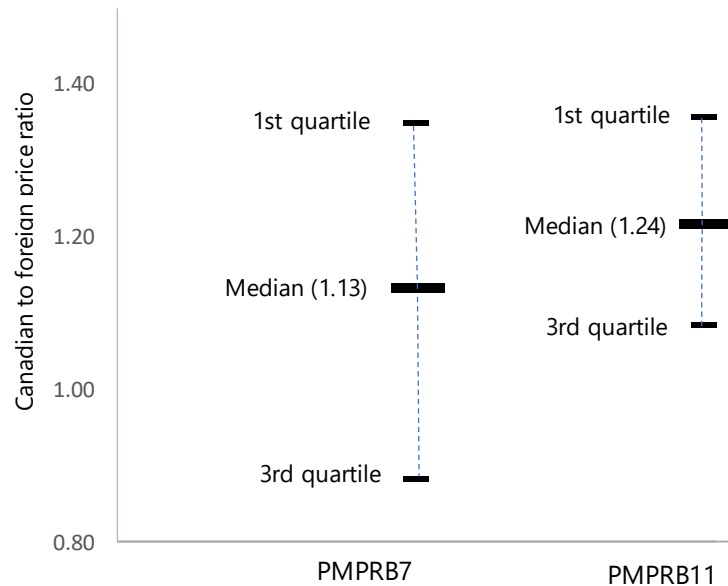
Source: OPBO using PMPRB data¹.

Note: The total expenditure difference is \$2.8 billion. In all, 155 ATC4 categories were included. They were sorted into decreasing expenditure difference between actual expenditures in 2018, and those same drugs valued at PMPRB11 median prices (from 2018).

The upshot of Figure 3-2 is that just a few drugs falling out of line with international peers can lead to large consequences for expenditures in Canada. Introducing a mechanism to reassess non-excessive prices and focusing the subsequent administrative effort on prominent cases could yield substantial reductions in expenditures.¹¹

The move toward PMPRB11 could also help to reduce the amplitude of any price misalignment caused by time-lapses in reassessment. The range of prices in comparator countries is significantly lower amongst PMPRB11 than it is for PMPRB7 as is evident in the gap between the lowest and highest quartiles (Figure 3-3). This potentially means that misalignment when targeting PMPRB11 median prices is likely to be less costly than when PMPRB7 is being targeted.

Figure 3-3 PMPRB7 vs PMPRB11: Medians and dispersion of prices of a broad basket of drugs



Source: OPBO using PMPRB data¹.

Note: In each case we report results based on a sales-weighted average; i.e., the median is reporting the sales weighted average of medians of ATC4 groupings. A value greater than one means that Canada's price is higher than the international price. For PMPRB7, the 3rd quartile below 1 means that prices there would cause even higher expenditures for Canadians.

Moreover, to explore the envelope of higher prices in PMPRB7 versus PMPRB11, we looked at what expenditures would have been under both comparator groups when Canada's drugs were priced at the highest international price (HIP) in 2018. That is, we compared expenditures at PMPRB7 HIP prices versus PMPRB11 HIP prices. We found that expenditures would have been some 57 percentage points lower under PMPRB11 HIP prices. This implies that the environment for ERP is more constrained under PMPRB11 than under PMPRB7.

Finally, notice that the estimated reduced expenditure (19 per cent) is a substantial portion of the saving that an earlier OPBO analysis had calculated

could be gained through a national Pharmacare program (more discussion in the next section).

4. General discussion

The expenditure reduction implied by the analysis here represents a counterfactual that has some *ceteris paribus* constraints. For example, responses by pharmaceutical companies as well as consumers to the regulatory change were not accounted for in the analysis. For pharmaceutical companies, there is analysis that constraining prices will lead to slower introductions of new medicines in Canada (Spicer and Grootendorst, 2020).

For consumers, reduced prices can lead to increased use of medicines (e.g., when affordability leads to a higher rate of completion of prescribed regimens).

These results are also informative from the perspective of a national Pharmacare. The savings from such a program were estimated to be on the scale of 25 per cent at a national level on all prescription pharmaceuticals (OPBO, 2017). Those estimates were calculated without fully accounting for recent changes in public plans,¹² making the results somewhat comparable.

The analysis in this report also requires further context. Pharmaceutical companies expend large sums to develop new products, often without success. Even once a candidate drug has reached Phase 1 trials, its probability of final approval is roughly 10 per cent (Takebe, et al, 2018).¹³ Alzheimer's disease is illustrative of that effort. It has been the subject of decades of intense pharmaceutical research and many failed drug trials. These efforts have been forthcoming because the potential rewards (rents) for a successful drug are very large – particularly in the US market. At present, more of that R&D occurs in the US than in the rest of the world. A strategy by Canada of free-riding on R&D expenditures in the US and elsewhere is not tenable.¹⁴

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Notes

1. PMPRB provided aggregated data based in part on data obtained under license from MIDAS database proprietary to IQVIA Solutions Canada Inc. and/or its affiliates ("IQVIA"). The statements, findings, conclusions, views and opinions expressed in this report are exclusively those of the OPBO, and are not attributed to the PMPRB or IQVIA.
2. E.g. Canada (Attorney General) v. Sandoz Canada Inc., 2015 FCA 249
3. As well as a few other factors such as comparison to other drugs in the same therapeutic class.
4. See Shulman and Richard (1988) for an outline of the debate that occurred around Bill C-22 *An Act to Amend the Patent Act*.
5. They were originally due to come into effect in July of 2020, but have been postponed four times and substantially modified.
6. Complicating PMPRB's efforts to revise its regulations is Canada's increased status as a reference market for other national price-setting regimes. Any reductions of prices in Canada will have an outsized impact on drug manufacturers. Moreover, a 2018 Special Report by the Office of the United States Trade Representative singled out the upcoming regulatory changes as part of the reason it put Canada on a priority watchlist, signalling that the US strongly opposed the proposed regulations.
7. ATC4 defines the 4th level of detail in the Anatomical Therapeutic Chemical classification system (see http://whocc.no/atc/structure_and_principles).
8. Judicial review of those proposed changes substantially reduced their scope. The principal judgement stemmed from the constitutional limits of federal powers over healthcare. The federal government could only use its power over patents to regulate abuse of patents, not to set prices generally (Merck Canada inc. c. Procureur général du Canada, 2022 QCCA 240 (CanLII), <<https://canlii.ca/t/jmjbm>>, consulté le 2022-04-19). Those proposals also included a requirement for confidential rebates to be reported to PMPRB, however, that was struck down by a federal court given that it would involve disclosure of contracts with third parties.
9. www.raredisorders.ca/open-letter-to-prime-minister-justin-trudeau-regarding-pmprb-regulations/
10. The data from PMPRB was compared to the OECD median, which was confirmed by PMPRB to be identical to the PMPRB11 value of 0.83 in 2018. See slide 22 www.canada.ca/content/dam/pmprb-cepmb/documents/legislation/guidelines/PMPRB%20final%20Guidelines%20-%20Public%20Webinar%20Deck%20November-20-2020-EN.pdf

11. Indicative of how a few widely-used and/or expensive drugs can dominate the market, the top 10 drugs in 2018 had sales of \$3.8 billion which represented 23 per cent of patented drug sales (PMPRB, 2019).
12. The pan-Canadian Pharmaceutical Alliance (pCPA) negotiates drug prices on behalf of provinces on the basis of analysis from the Canadian Agency for Drugs and Technologies in Health (CADTH) and the Institut national d'excellence en santé et en services sociaux (INESSS)
13. Since the major components of a drug's costs are in the later phases of trials and approval, this is not a statement concerning average drug costs.
14. Nonetheless, a link between higher prices for pharmaceuticals in Canada and more R&D in Canada is not clear. For example, R&D expenditures were proportionately higher under compulsory licensing than they were subsequent to its removal. Presumably compulsory pricing created relatively low drug prices in Canada. Unless PMPRB has been able to lower prices by more than what compulsory licensing was achieving, it is not self-evident that higher prices would lead to more R&D expenditures in Canada.