The impact of patented drug price controls on drug launches: evidence from the OECD countries

Oliver Spicer and Paul Grootendorst

Leslie Dan Faculty of Pharmacy, University of Toronto

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Agenda

- Patented drug price regulation approaches
- Patented drug price regulation in Canada
- Criticisms of Canada’s price regulation
- Proposed reforms
- Competing views on effects of proposed reforms
- Evidence from OECD countries
- Drug launch delays, CAN vs AUS

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Price regulatory approaches

- Governments in most developed countries regulate the prices of patented drugs
- Regulation occurs through variety of means, including:
  - **International price referencing**: price of new drug in country i depends on list prices of same drug in set of other countries
  - **Domestic price referencing**: price in country i depends on list prices of similar drugs in country i
  - **Economic appraisal**. Price is set so that additional cost per QALY (relative to existing therapies) is at or near max WTP per QALY.
  - **Budget impact**. Prices are reduced if unit sales exceed some threshold.

Canada's price regulatory approach

- Canada's Patented Medicine Prices Review Board (PMPRB), established in 1987, uses international and domestic price referencing to set maximum patented drug prices
- Pricing tests depend on its assessment of the therapeutic improvement of a new drug relative to existing drugs
  - This assessment made by its panel of experts
- There are 4 levels of therapeutic improvement

Canada's price regulatory approach

- *Breakthrough*: first drug to be sold in Canada that treats effectively a particular illness or addresses effectively a particular indication.
- *Substantial Improvement* over existing therapies sold in Canada
- *Moderate Improvement* over existing therapies sold in Canada
- *Slight or No Improvement* over existing therapies sold in Canada

Canada's price regulatory approach

- International price tests are based on list prices in 7 countries, the "PMPRB7"
- These countries are United States, Switzerland, Germany, UK, France, Sweden, Italy
- Domestic price tests are based on formulary prices of drugs from same therapeutic class that are sold in Canada

Price test, by level of clinical improvement

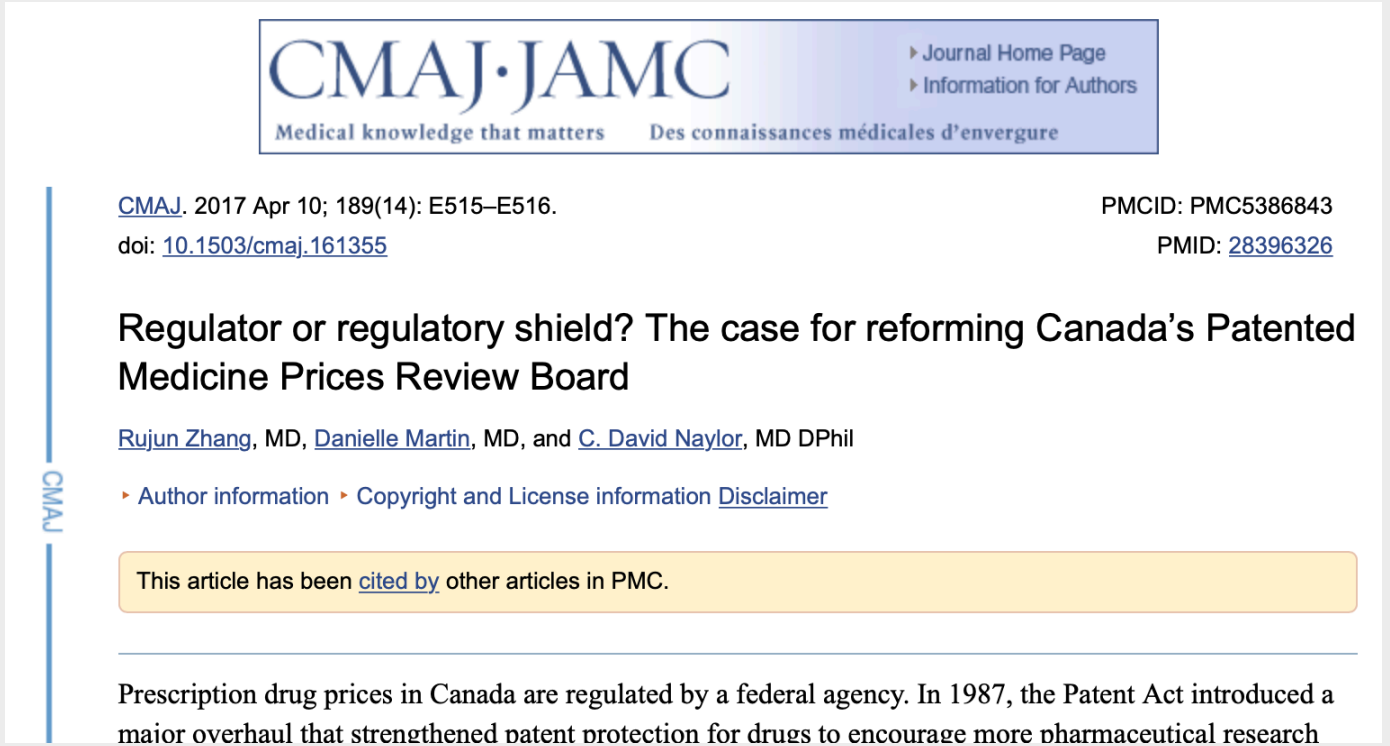
Level of Clinical Improvement	Price Ceiling	All Patented Medicines
Breakthrough	Median International Price	Prices of patented medicines can never exceed the International Maximum Price (i.e., the highest price among the PMPRB7 comparator countries
Substantial improvement	Higher of the Therapeutic Class Comparison (TCC) and the International Median	
Moderate improvement	Midpoint of the Therapeutic Class Comparison and International Median (but not lower than the TCC)	
No or little improvement	Therapeutic Class Comparison or Reasonable Relationship Test	

International Comparisons

(7 comparator countries)

Criticisms of Canada's price regulatory approach

- Various commentators have noted that list prices of patented drugs in Canada are relatively high



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Regulator or regulatory shield? The case for reforming Canada's Patented Medicine Prices Review Board

Rujun Zhang, MD, Danielle Martin, MD, and C. David Naylor, MD DPhil

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Prescription drug prices in Canada are regulated by a federal agency. In 1987, the Patent Act introduced a major overhaul that strengthened patent protection for drugs to encourage more pharmaceutical research

Criticisms of Canada's price regulatory approach

- The reason is that United States, Switzerland, Germany -- three of the PMPRB7 -- have among highest prices internationally. Thus breakthrough and substantial improvement drugs – priced at the PMPRB7 median – will have high list prices.
- Drugs used in the domestic price tests include those that were previously deemed to be breakthrough or substantial improvement, so these list prices will also be relatively high

But who pays list prices?

- Drug manufacturers will often provide confidential rebates off of public list prices
- Actual, net of rebate prices are therefore lower than list prices
- However probably the case that actual, net of rebates prices in Canada are relatively high
- Public plans said to get rebates in order of 25%
- Private plans likely get smaller rebates since they can't credibly threaten to exclude new drug from private plan formularies
- Thus, overall, rebates likely <20%

PMPRB changes

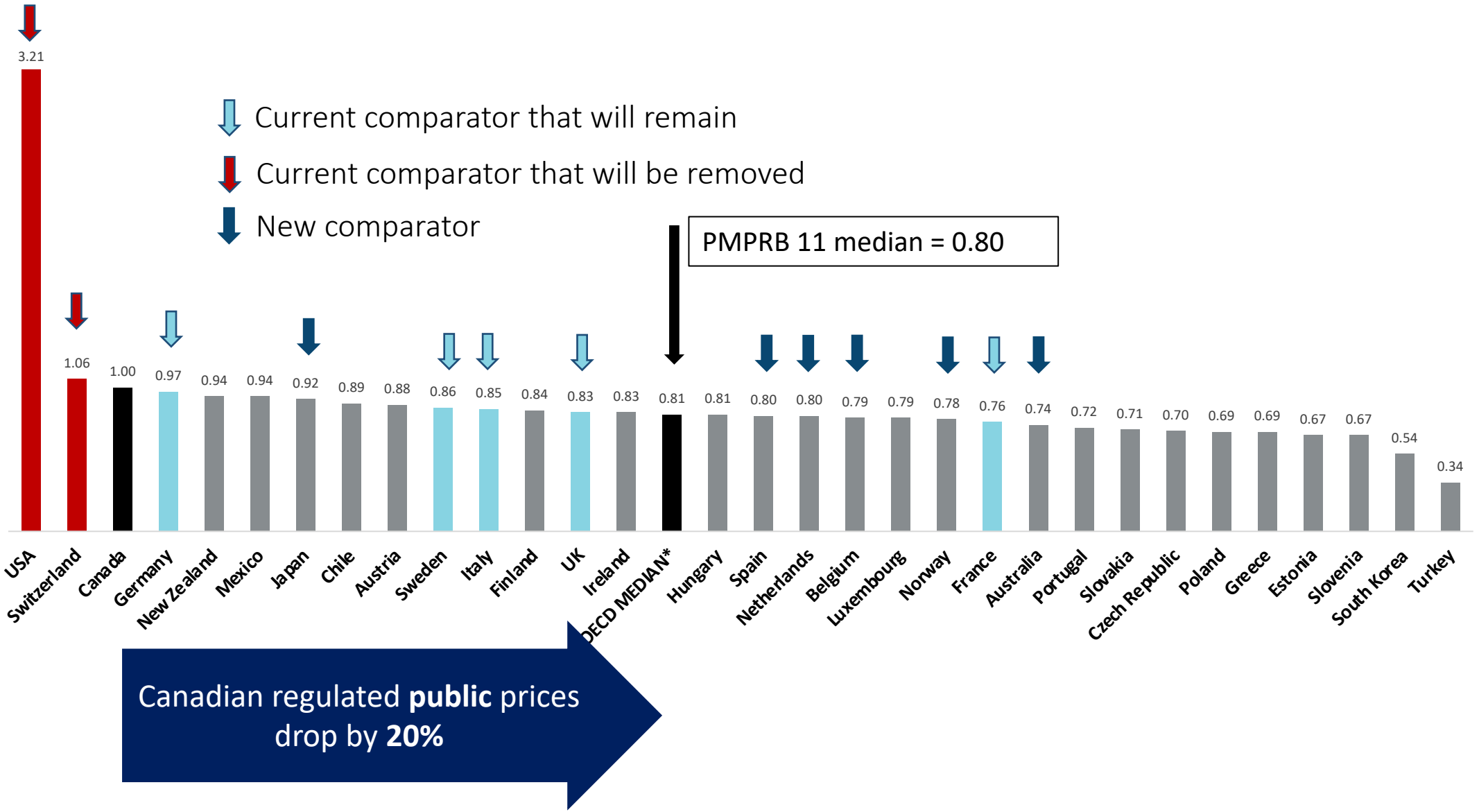
- The PMPRB intends to overhaul the rules in July 2020.
- Price ceiling will now be determined through

1. Reference to a new set of comparison countries, with high price countries (US, Swiss) removed and lower price countries (such as Australia, Belgium) added
2. Application of maximum cost-per-QALY rules
3. Further price cuts for high cost drugs

Modified list of comparator countries

- All medicines, including those currently marketed in Canada, will be subject to the new basket (the PMPRB11) as of July 1, 2020
- The new basket would bring Canada's public list prices to around the OECD median (about 20% reduction)

Average Foreign-to-Canadian Price Ratios, Patented Medicines, OECD, 2017



Calculated at medicine level for medicines with prices available in at least three foreign markers
Source: From Figure 21 of the PMPRB Annual Report 2017; MIDAS™ database, 2017, IQVIA. 40-70%

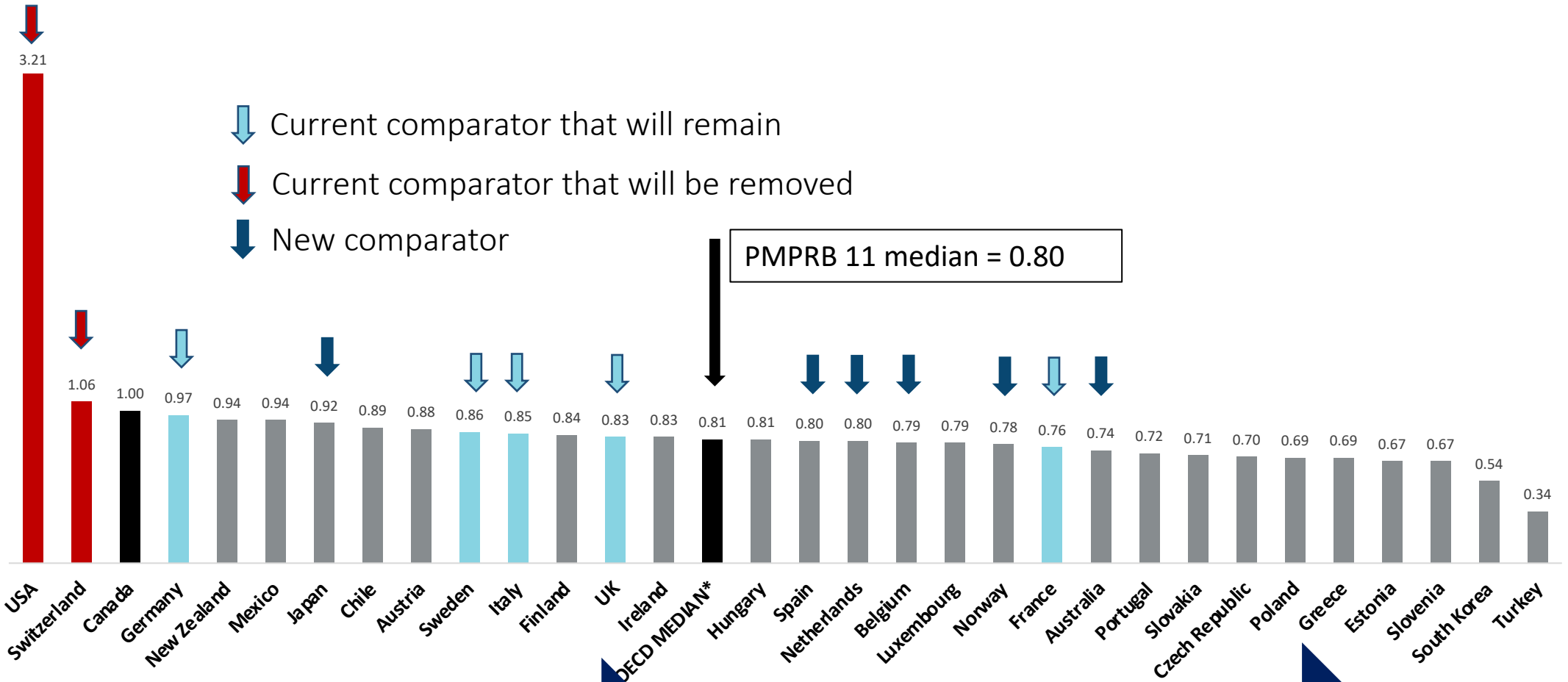
New factors: max cost-per-QALY

- New “high-cost” meds (annual tx cost higher than 50% of GDP/capita) will be subject to max additional cost-per-QALY constraint
- According to the RIAS
  - $35k threshold for drugs that treat highly prevalent diseases (e.g. high cholesterol)
  - $50k threshold for drugs that treat standard diseases (including cancer)
  - $150k threshold for drugs that treat rare diseases
- These price ceilings will be kept confidential

New factors: max price = f(expenditures)

- Market size in Canada: adjustments may apply to all medicines to reduce maximum rebated price by 10% for every $10M in sales over $20M up to max impact of 50%
- These price cuts will be kept confidential

Average Foreign-to-Canadian Price Ratios, Patented Medicines, OECD, 2017



Canadian regulated **public** prices drop by **20%**

Further reductions of net (confidential) prices bring total regulated reductions to as much as 50% off international median price

Calculated at medicine level for medicines with prices available in at least three foreign markers
Source: From Figure 21 of the PMPRB Annual Report 2017; MIDAS™ database, 2017, IQVIA. 40-70%

Impact of the reforms

- Obviously will benefit drug payors – estimated savings unclear but likely around $2 billion/year
- One potential cost is the reduction in drug R&D globally but this will not be large impact due to Canada's small size
- Another cost is the likely delay in the launch of new drugs into Canada

Different perspectives on launch delays

- **Existing literature**: lower prices delay access to new drugs, for two reasons

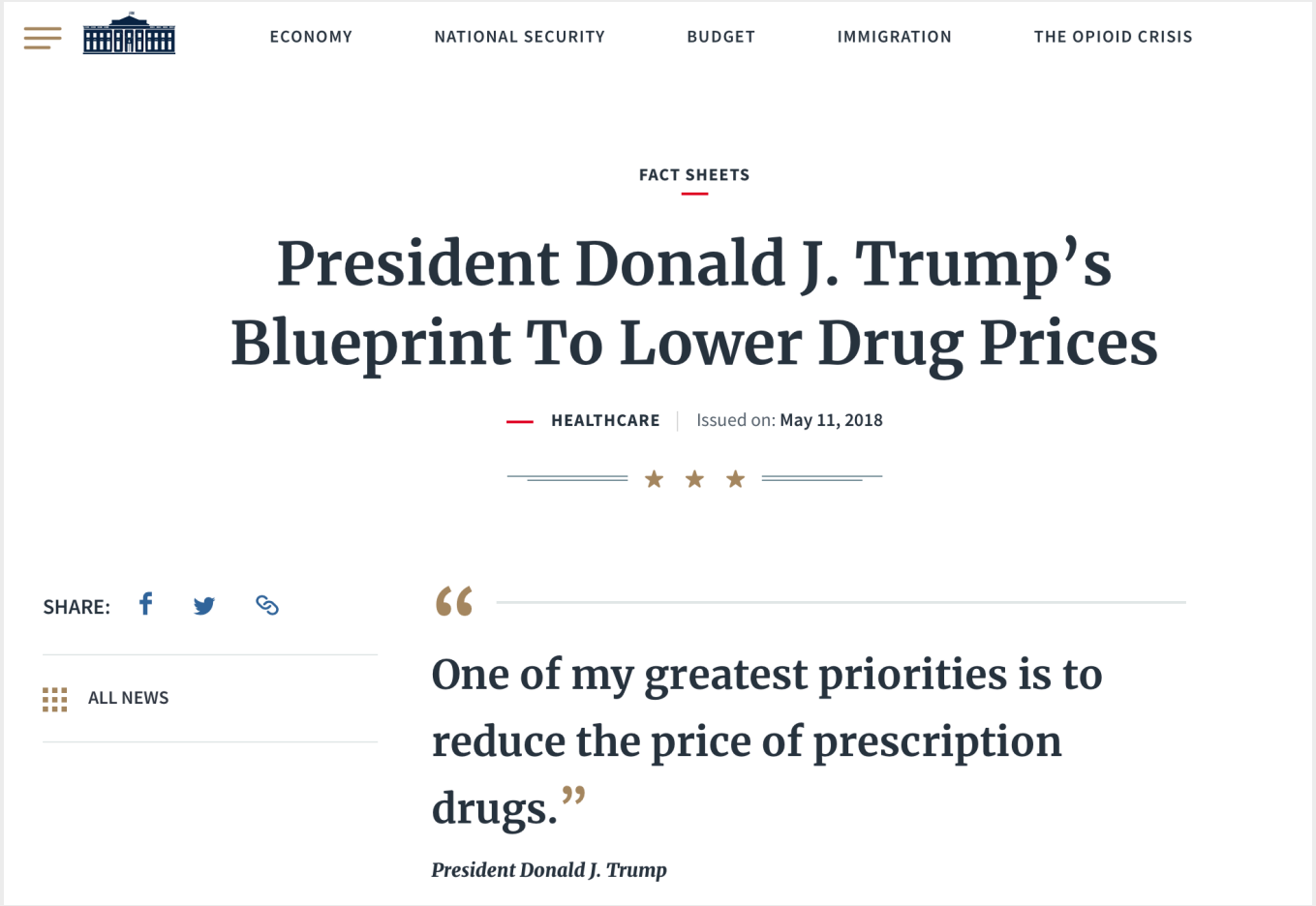
1. **Launch prioritization:**
   - drug companies typically do not have the personnel needed to obtain market authorization from all target countries at once. Thus, they will prioritize launches in countries where gross profits are highest.
   - Canada's use of more stringent price controls will reduce gross profits and thus lower Canada's launch priority.

Different perspectives on launch delays

2. To mitigate the impacts of price referencing:

- Suppose that
  - A country with a large market (A) sets its price equal to the list price in a smaller market (B)
  - The list price in B is regulated to be low
- Then drug company will rationally not list in B to prevent price erosion in more profitable A
- Price referencing is common in EU. Few countries formally reference Canadian prices but the US is considering this

Overtures in the US to reference CAD drug prices



Different perspectives on launch delays

- **Federal government** view:
- Its (unpublished) analysis of the recent data indicates that reductions in drug list prices have no material affect on launch delays.

THESE AMENDMENTS WILL **NOT**:

- reduce or delay access to new innovative medicines—in fact, several countries with lower prices have faster access to new medicines than Canada;

Different perspectives on launch delays

- **Which perspective is correct, literature or Federal government?**
- It could be the case that the results of the literature, which relies mainly on data prior to 2000, no longer fully applies.
  - Possible that harmonization of list prices, and increased use of secret rebates, neutralizes price referencing.

Our analysis

- Using recent data for the OECD countries, estimate impact of list price on drug launch delay, holding constant market size
- Use LRM:

$$druglaunch\%[i] = \beta_0 + \beta_1 \log(priceratio[i]) + \beta_2 \log(population[i]) + \beta_3 \log(GDP[i]) + \beta_4 ema[i] + \varepsilon[i],\ i = 1, 2, \ldots, 31$$

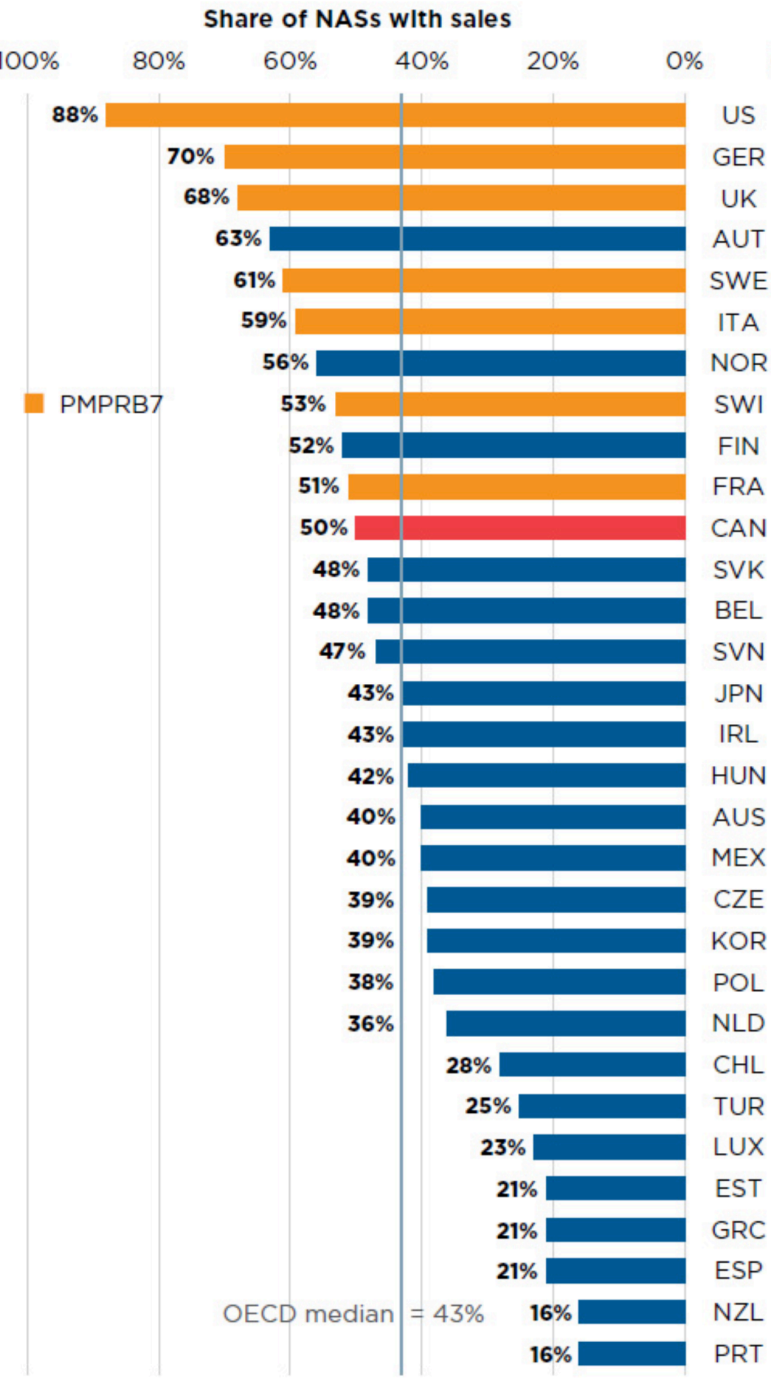
variables

- LRM

$$druglaunch\%[i] = \beta_0 + \beta_1 \log(priceratio[i]) + \beta_2 \log(population[i]) + \beta_3 \log(GDP[i]) + \beta_4 ema[i] + \varepsilon[i],\ i = 1, 2, \ldots, 31$$

- percentage share of the 252 new active substances (NASs) that were launched between 2009 and 2015 in Canada and the PMPRB7, sold in country i by the 4th quarter of 2016
- Source: NPDUIS Meds Entry Watch 2016

Share of new active substances (NASs) launched in Canada and the PMPRB7 from 2009 to 2015 with available sales, by country, Q4-2016



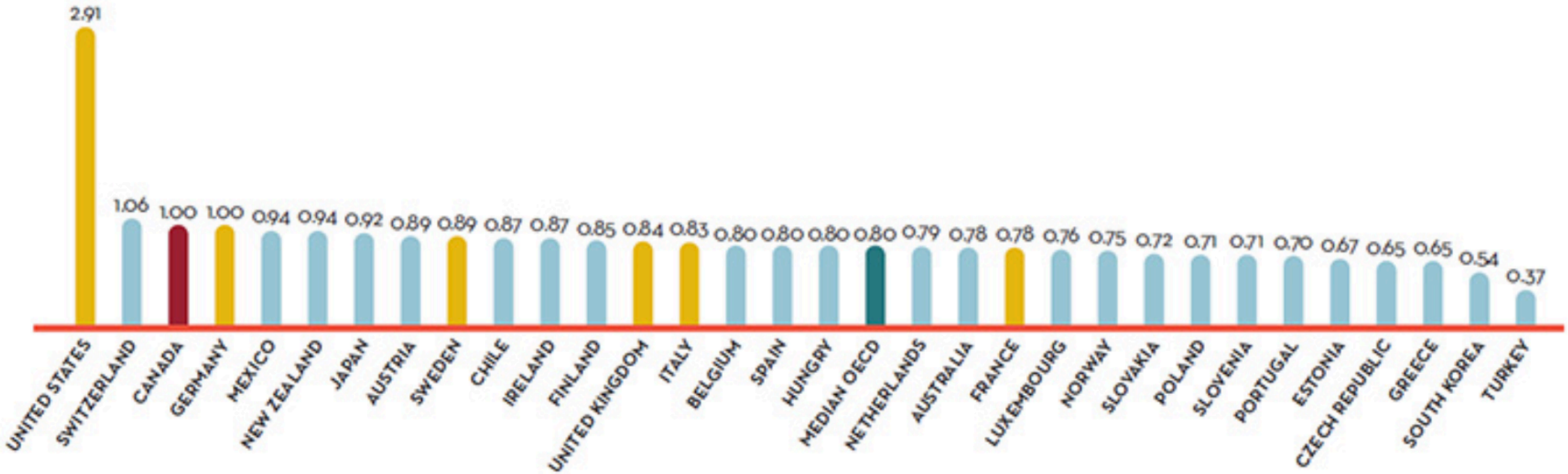
variables

- LRM

$$druglaunch\%[i] = \beta_0 + \beta_1 \log(priceratio[i]) + \beta_2 \log(population[i]) + \beta_3 \log(GDP[i]) + \beta_4 ema[i] + \varepsilon[i],\ i = 1, 2, \ldots, 31$$

- weighted average of the ratios of country i to Canada patented drug list prices in 2016
- Source: PMPRB Annual Report 2016

Figure 13. Average Foreign-to-Canadian Price Ratios, Patented Drugs, OECD, 2016



Source: MIDAS™ database, 2005-2016, IMS AG. All rights reserved.

variables

- LRM

$$druglaunch\%[i] = \beta_0 + \beta_1 \log(priceratio[i]) + \beta_2 \log(population[i]) + \beta_3 \log(GDP[i]) + \beta_4 ema[i] + \varepsilon[i],\ i = 1, 2, \ldots, 31$$

- Population of country i in 2016
- Source: Penn World Tables

variables

- LRM

$$druglaunch\%[i] = \beta_0 + \beta_1 \log(priceratio[i]) + \beta_2 \log(population[i]) + \beta_3 \log(GDP[i]) + \beta_4 ema[i] + \varepsilon[i],\ i = 1, 2, \ldots, 31$$

- Expenditure-side real GDP at chained PPPs (in US$) for country i in 2016
- Source: Penn World Tables

variables

- LRM

$$druglaunch\%[i] = \beta_0 + \beta_1 \log(priceratio[i]) + \beta_2 \log(population[i]) + \beta_3 \log(GDP[i]) + \beta_4 ema[i] + \varepsilon[i],\ i = 1, 2, \ldots, 31$$

- $ema[i] = 1$ if new drugs in country i approved by European Medicines Agency, $= 0$ otherwise
- reflects relatively low market entry costs in EMA member countries

Results

Source	SS	df	MS		
Model	5091.5045	4	1272.87612	Prob > F	0.0001
Residual	3775.85034	26	145.225013	R-squared	0.5742
				Adj R-squared	0.5087
Total	8867.35484	30	295.578495	Root MSE	12.051

ps20092015	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
lprice_ratio2016	23.46235	8.433667	2.78	0.010	6.126703	40.79801
lpop2016	5.727002	1.851001	3.09	0.005	1.922214	9.531789
lrpcgdp2016	14.81325	7.159365	2.07	0.049	.0969607	29.52953
ema	11.2376	5.167377	2.17	0.039	.6159038	21.85929
_cons	-132.0972	78.42253	-1.68	0.104	-293.297	29.1026

effect of 20% reduction in *priceratio*

- Evaluate LRM at *priceratio* $= 1$ and *priceratio* $= 0.8$ and find difference in *druglaunch%*
- This difference is $\beta_1 \log(\textit{priceratio} = 1) - \beta_1 \log(\textit{priceratio} = 0.8)$

  $= \beta_1 \{\log(1) - \log(0.8)\}$

  $= \beta_1 \log(1/0.8)$

  $= 23.46 \times 0.223$

  $= 5.23$

  about 5% absolute reduction in % of drugs launched in Canada within 8 years of first global launch

Results: effect of 50% reduction in *priceratio*

- Evaluate LRM at *priceratio* $= 1$ and *priceratio* $= 0.8$ and find difference in *druglaunch%*
- This difference is $\beta_1 \log(\textit{priceratio} = 1) - \beta_1 \log(\textit{priceratio} = 0.5)$

  $= \beta_1 \log(1/0.5)$

  $= 23.46 \times 0.693$

  $= 16.26$

  about 16% absolute reduction in % of drugs launched in Canada within 8 years of first global launch

Sensitivity analysis

- What if we use covariates for 2015?

Results

Source	SS	df	MS	Number of obs	=	31
				F(4, 26)	=	8.84
Model	5109.65066	4	1277.41266	Prob > F	=	0.0001
Residual	3757.70418	26	144.527084	R-squared	=	0.5762
				Adj R-squared	=	0.5110
Total	8867.35484	30	295.578495	Root MSE	=	12.022

ps20092015	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
lprice_ratio2015	24.67839	8.644524	2.85	0.008	6.909313	42.44746
lpop2015	5.606353	1.854354	3.02	0.006	1.794673	9.418033
lrpcgdp2015	15.61654	6.994357	2.23	0.034	1.239434	29.99365
ema	11.2337	5.149137	2.18	0.038	.6494948	21.8179
_cons	-139.19	76.58392	-1.82	0.081	-296.6105	18.23047

Sensitivity analysis

- What if we use covariates for 2014?

Results

Source	SS	df	MS		
Model	4941.27511	4	1235.31878	Prob > F	0.0002
Residual	3926.07973	26	151.003067	R-squared	0.5572
Total	8867.35484	30	295.578495	Root MSE	12.288

Number of obs	=	31
F(4, 26)	=	8.18
Prob > F	=	0.0002
R-squared	=	0.5572
Adj R-squared	=	0.4891
Root MSE	=	12.288

ps20092015	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
lprice_ratio2014	20.69251	8.695166	2.38	0.025	2.819337	38.56568
lpop2014	6.157595	1.866559	3.30	0.003	2.320828	9.994363
lrpcgdp2014	17.2731	7.382601	2.34	0.027	2.097947	32.44826
ema	12.6622	5.335833	2.37	0.025	1.694238	23.63016
_cons	-158.1272	80.61661	-1.96	0.061	-323.837	7.582608

Sensitivity analysis

- What if we drop USA and New Zealand?

Results

Source	SS	df	MS	Number of obs	=	29
				F(4, 24)	=	4.58
Model	2648.07262	4	662.018154	Prob > F	=	0.0069
Residual	3468.686	24	144.528583	R-squared	=	0.4329
				Adj R-squared	=	0.3384
Total	6116.75862	28	218.455665	Root MSE	=	12.022

ps20092015	Coef.	Std. Err.	t	P>|t|	[95% Conf.	Interval]
lprice_ratio2016	26.93313	11.99272	2.25	0.034	2.181367	51.6849
lpop2016	4.759261	1.991199	2.39	0.025	.6496284	8.868894
lrpcgdp2016	13.45029	7.20911	1.87	0.074	-1.428586	28.32916
ema	8.221987	5.565855	1.48	0.153	-3.265373	19.70935
_cons	-111.451	79.64488	-1.40	0.175	-275.83	52.92792

So what?

- One common reaction to prospect of launch delays: who cares? Aren't most drugs "me-toos", offering little in way of added benefit?
- Three responses:
- Me too drugs can be helpful clinically due to individual differences in drug effectiveness
- Even if there are more me-toos than breakthrough drugs, both will be delayed
- Entry of me-toos helpful for drug plans since me-toos need to compete on price

What is the impact of policies on launches of important drugs

- What will the actual delay time be for important new drugs?
- Australia seems to resemble Canada's pharmaceutical market once the new PMPRB regs are enforced in july 2020
- Lets examine drug regulatory approval dates of PMPRB-designated important drugs (breakthroughs and substantial improvement) in Australia and Canada

Australia vs Canada, 2017

country	real per capita GDP	pop (m)	priceratio	real pc HC spending	fraction pop 65+
Canada	44,493	36.6	1	4,418	0.17
Australia	48,142	24.5	0.74	4,056	0.16

Reg approval of important new drugs 2008-18, AUS vs CAN

Generic Name	Brand Name	days difference	interpret
Sofosbuvir	Sovaldi	-1102	AUS delayed on 12/21 drugs
Boceprevir	Victrelis	-400	-321.75
Ocriplasmin	Jetrea	-393	
Collagenase clostridium histolyticum	Xiaflex	-368	
Midostaurin	Rydapt	-300	
Ivacaftor*	Kalydeco	-285	
Vemurafenib	Zelboraf	-233	
Methylnaltrexone	Relistor	-230	
Sapropterin	Kuvan	-181	
Pomalidomide	Pomalyst	-162	
Asfotase Alfa	Strensiq	-153	
Pertuzumab	Perjeta	-54	
Lenalidomide	Revlimid	28	CAN delayed on 6/21 drugs
Multicomponent meningococcal B vacine	Bexsero	114	700.1666667
Obinutuzumab	Gazyva	194	
Ibrutinib*	Imbruvica	211	
Sacubitril, Valsartan	Entresto	1282	
Galsulfase	Naglazyme	2372	
Canakinumab	Ilaris	NA	3/21 drugs not launched in AUS
Boceprevir, peginterferon alfa-2b, ribavirin	Victrelis Triple	NA	
Pariseotide	Signifor	NA	

Conclusions

- Some evidence that new PMPRB rules will delay entry of new drugs into Canada
- Effects will depend on the implementation of two new factors and how they reduce actual prices
- If Australia is a good analog to Canada then some therapeutically novel drugs will be delayed into Canada, perhaps by a year
- On other hand we might still get some important new drugs without delay
- Delays will be much longer if US elects to reference Canadian drug prices

Figure I.1 Share of NASs launched by OECD country, Q4-2015