Patented Medicine Prices Review Board

Conseil d'examen du prix des médicaments brevetés

Drug pricing and its impact on R&D investments, clinical trials and availability of medicines in Canada

PMPRB Research Webinar

July 6, 2020

Elena Lungu, Manager, Policy Development
Caroline Peterson, Policy Analyst
Naghmeh Foroutan, Policy Analyst
Patrick McConnell, Policy Analyst

Canada

Introduction

Background

- Drug prices have been historically thought to influence R&D investments levels, clinical trials location and the availability of drugs, and some stakeholders have raised concerns that the impending patented medicine price reforms would negatively impact drug access in Canada.

Objective

- This presentation provides insight on the extent to which aligning medicine prices in Canada with international norms would adversely affect R&D investments levels, the number of clinical trials and the availability of drugs in Canada.

Data Sources

- PMPRB Data, PMPRB Annual Report, PMPRB Meds Entry Watch, Health Canada Drug Product Databases, Health Canada Clinical Trial Database, GlobalData, IQVIA's MIDAS® Database, OECD, EFPIA, IMS Brogan report for Department of Foreign Affairs

Key Findings

1. The 30-year policy objective to increase R&D investments in Canada by aligning prices with premium-priced countries has not been met
2. Lower prices do not generally result in lower R&D investments, and many countries with lower prices than Canada have higher investments
3. Similarly, lower prices do not generally result in a lower number of clinical trials, and many countries with lower prices than Canada have more clinical trials underway
4. Despite low R&D investments, Canada has a sizable number of clinical trials underway, a minority of which are funded by patentees
5. There are no early signs that patented medicine price reforms are resulting in fewer clinical trials initiated in Canada
6. There are no early signs that patented medicine price reforms are resulting in fewer new medicines being launched in Canada

1 Regulatory price regime envisioned by the Patent Act

In 1987, Canada enacted a two-fold reform of its medicine patent regime (Bill C-22) that sought to balance competing industrial and social policy objectives:

- **Incentivize R&D expenditure through stronger patent protection;**
- **Mitigate the economic impact of stronger patent protection on the health system.**

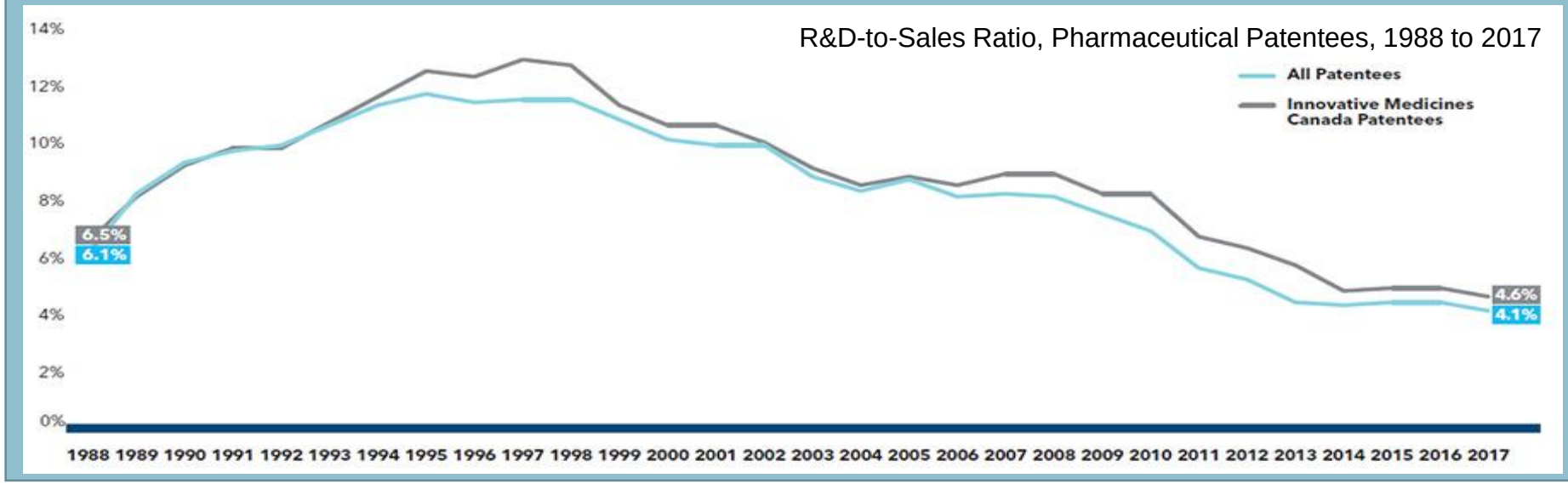
The PMPRB was conceived as C-22's "consumer protection pillar", to ensure that prices of patented medicines remain "reasonable" and "affordable".

The intent was to double R&D in Canada (to 10% of revenues) while keeping prices in line with high R&D countries (the "PMPRB7*) on the assumption we would come to emulate their level of investments.

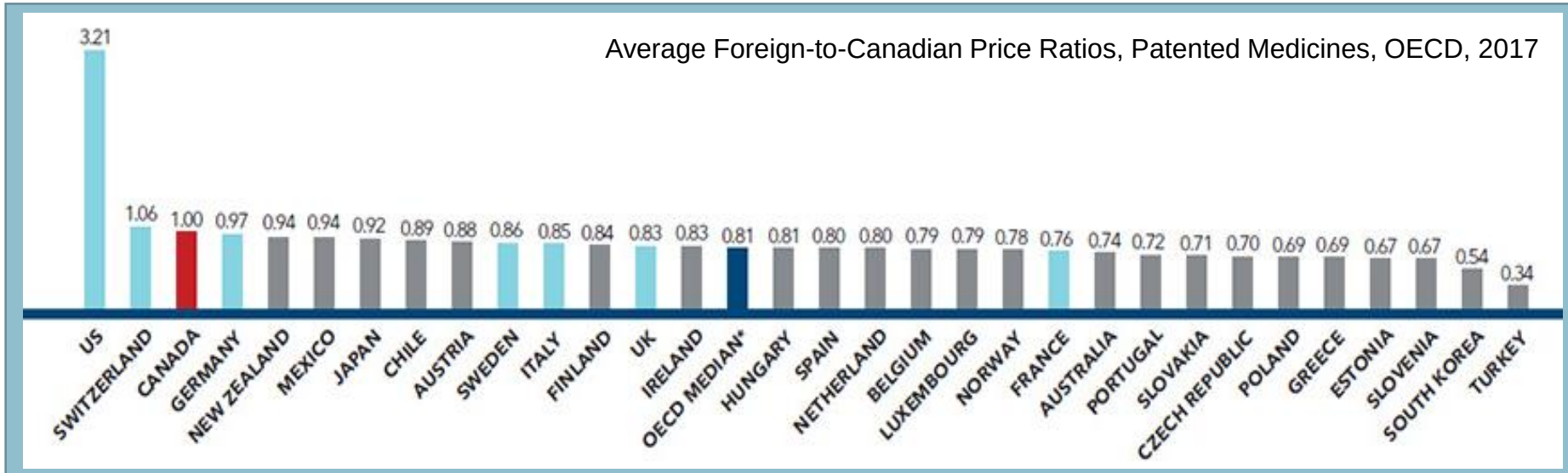
*Countries in the PMPRB7 are France, Germany, Italy, Sweden, Switzerland, the UK, and the US.

4

1 30 years later
The policy objectives sought by the Patent Act have not been met



R&D are at a 30-year low: **4.1%**

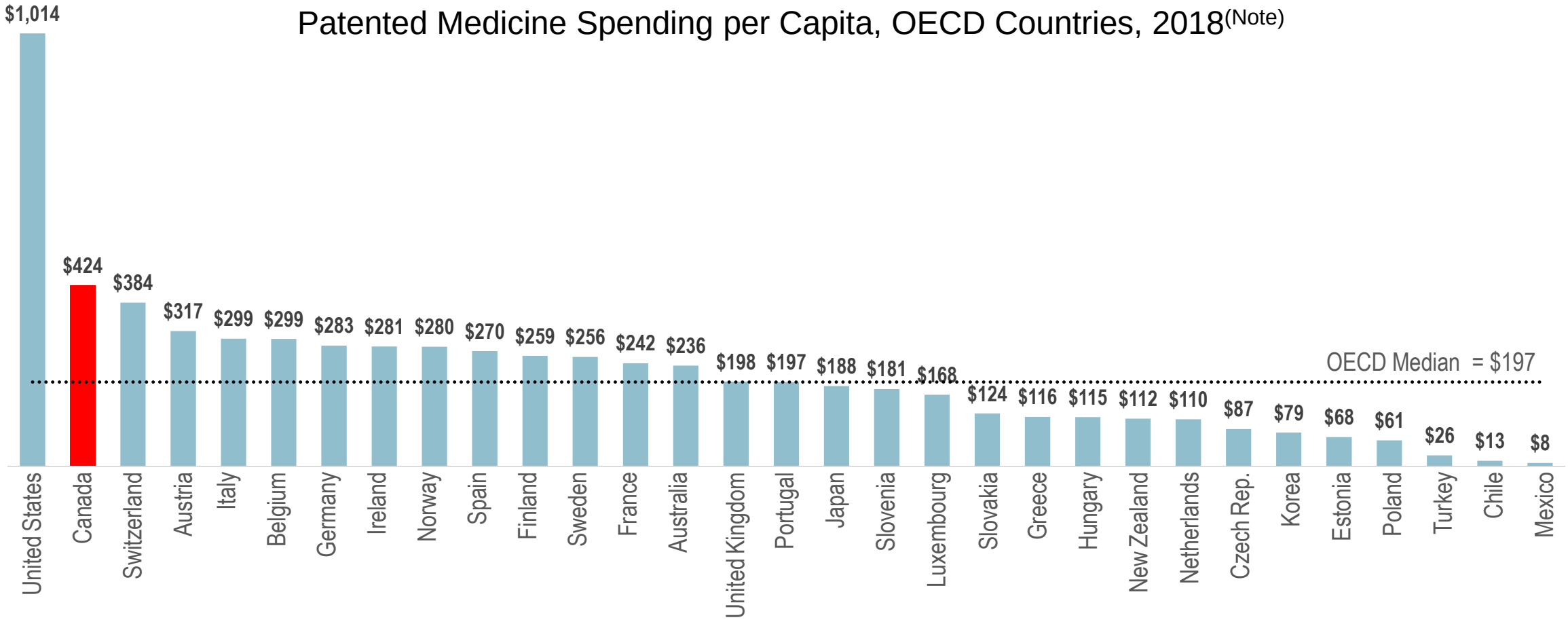


Canadian prices are **3rd** highest

Figure source:
PMPRB Annual Report, 2017

Data source:
PMPRB, MIDAS™ database, 2017, IQVIA. All rights reserved.

1 Canada has the second highest spending on patented medicines



Note: (i) Patented medicines were identified based on patents in Canada, for which sales were extracted for other countries.
(ii) Spending data for Greece, Chile, Estonia, Luxembourg and Mexico include only retail sales. and exclude hospital sales.
(iii) Includes only countries for which data are available.

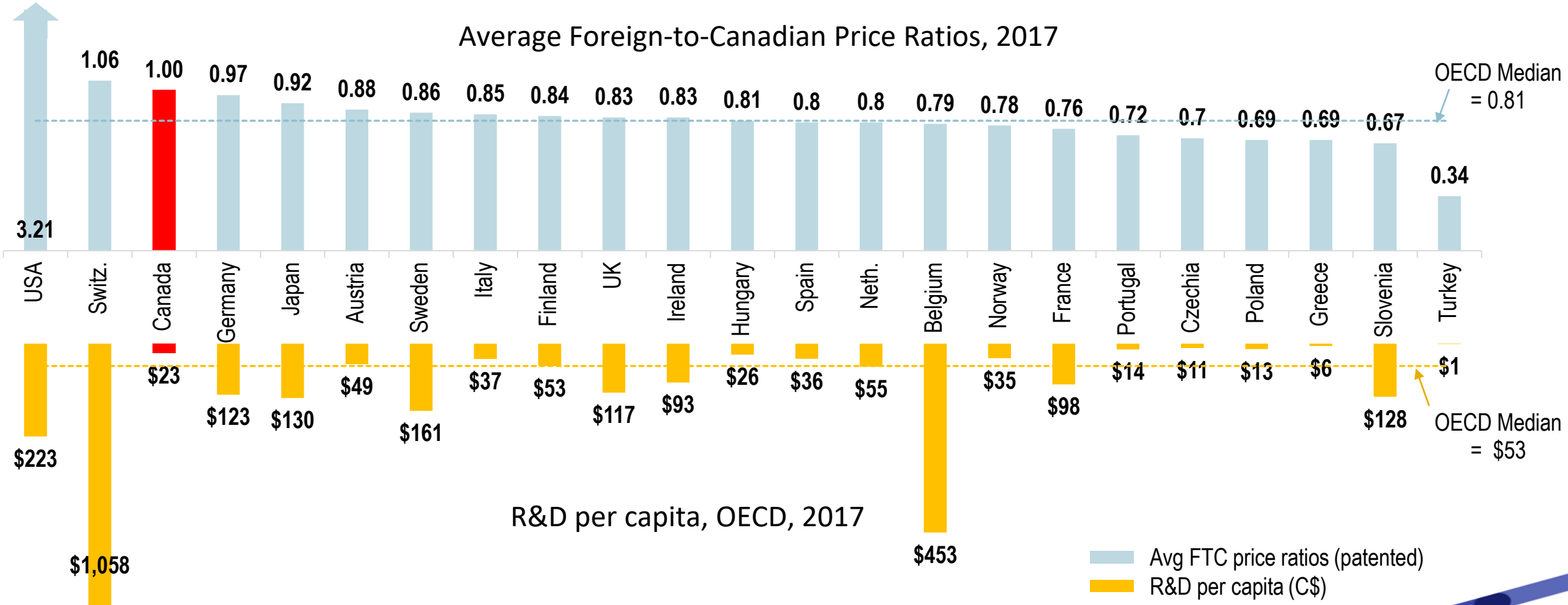
Data sources: (1) Patented medicine spending: IQVIA MIDAS® 2018; (2) Population: OECD, 2018.

Key Findings

1. The 30-year policy objective to increase R&D investments in Canada by aligning prices with premium-priced countries has not been met
2. Lower prices do not generally result in lower R&D investments, and many countries with lower prices than Canada have higher investments
3. Similarly, lower prices do not generally result in a lower number of clinical trials, and many countries with lower prices than Canada have more clinical trials underway
4. Despite low R&D investments, Canada has a sizable number of clinical trials underway, a minority of which are funded by patentees
5. There are no early signs that patented medicine price reforms are resulting in fewer clinical trials initiated in Canada
6. There are no early signs that patented medicine price reforms are resulting in fewer new medicines being launched in Canada

2 Higher prices do not generally result in greater R&D investments

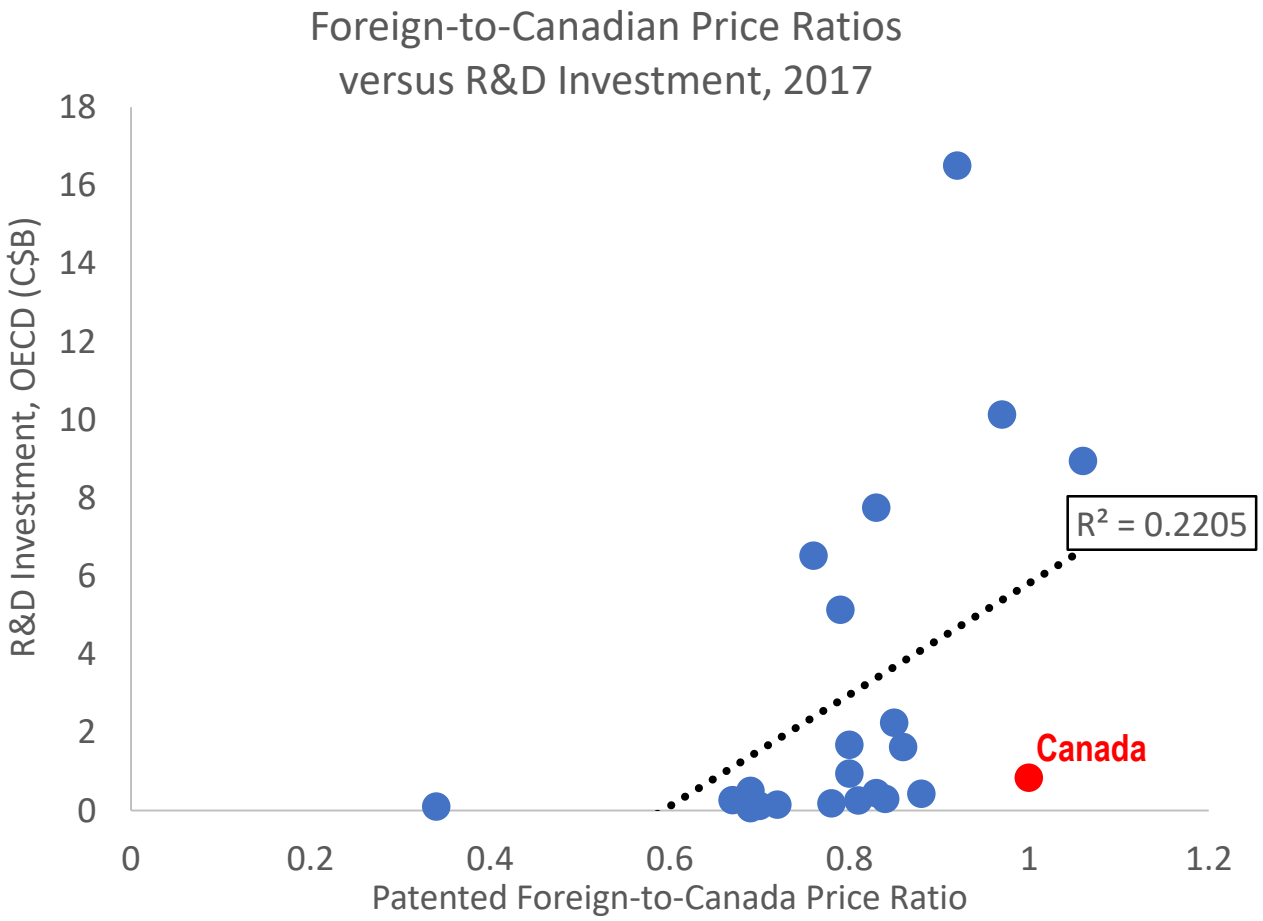
Many countries with lower patented drug prices than Canada have higher per capita R&D investments

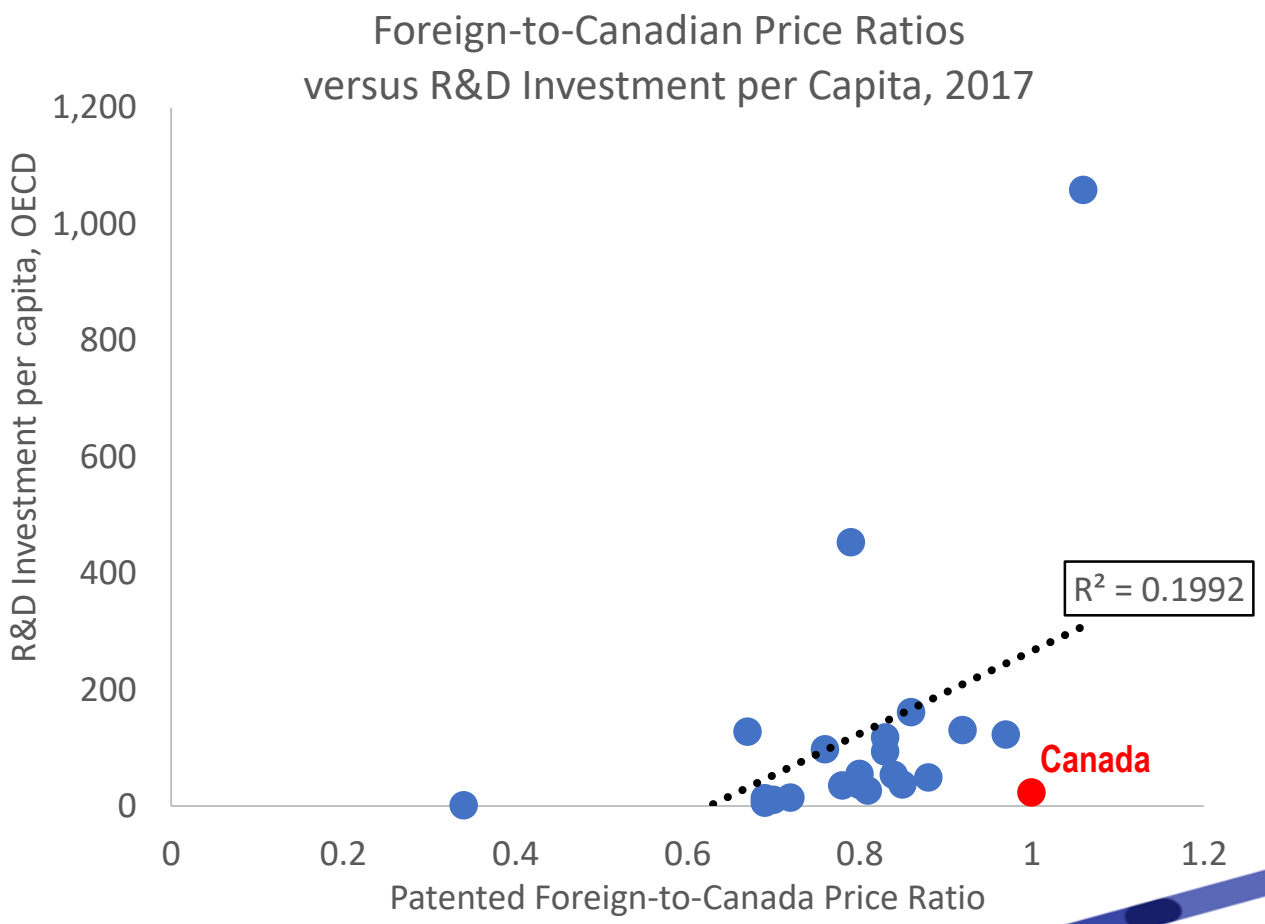


Data sources: PMPRB (FTC, R&D); OECD (Population).
Note: Total R&D investments, e.g. by patentees, other companies, universities, hospitals, other.

2 Higher prices do not generally result in greater R&D investments

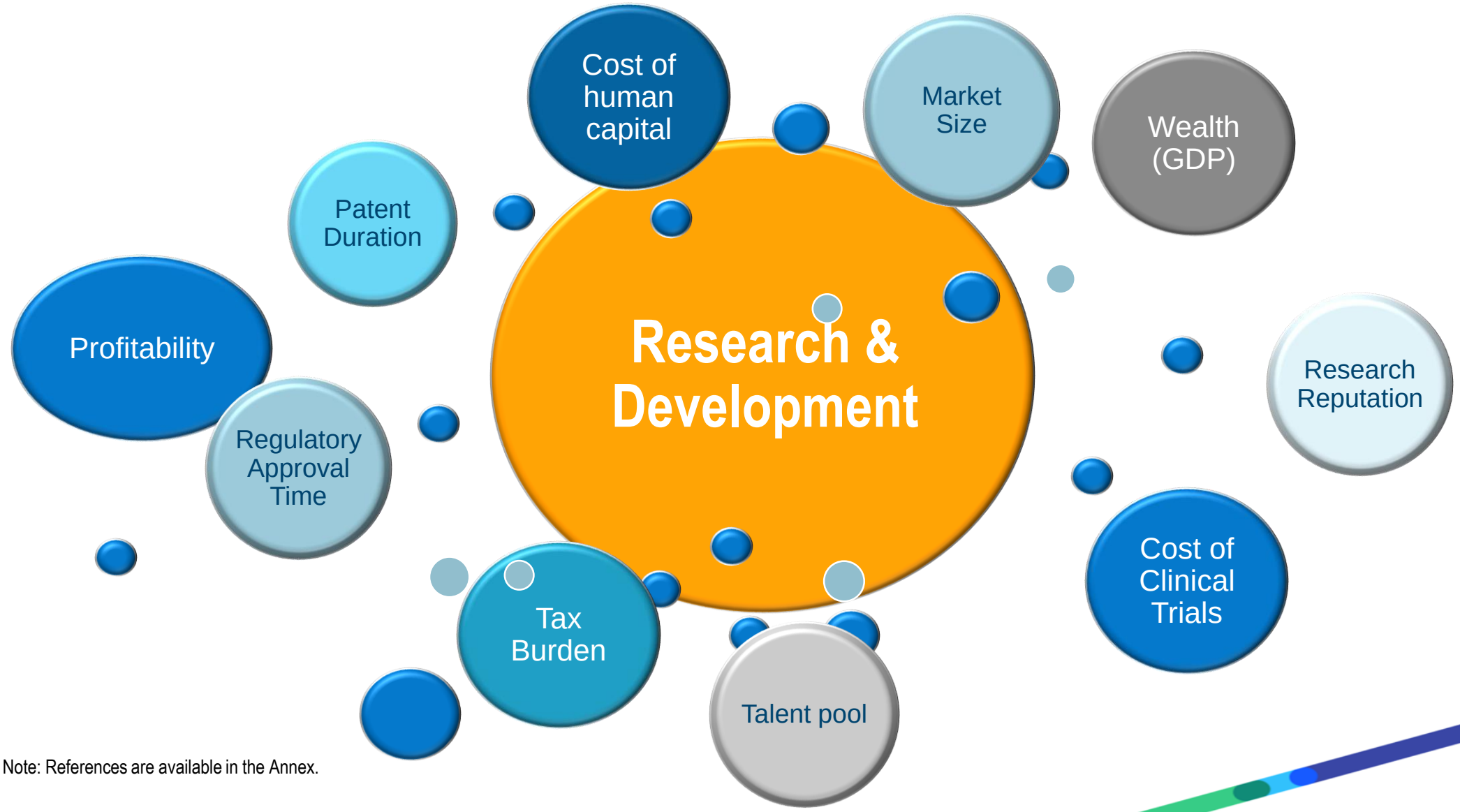
The variability in R&D investments levels across the OECD countries is only minimally explained by price levels (very low R squared)





Data sources: PMPRB Annual Report, 2017 (FTC, R&D); OECD (population).
Notes: R^2 is the percentage of the response variable variation that is explained by a linear model.
The United States is not included as with its FTC price ratio of 3.21 it is a significant outlier (see Annex).

2 What is driving R&D?



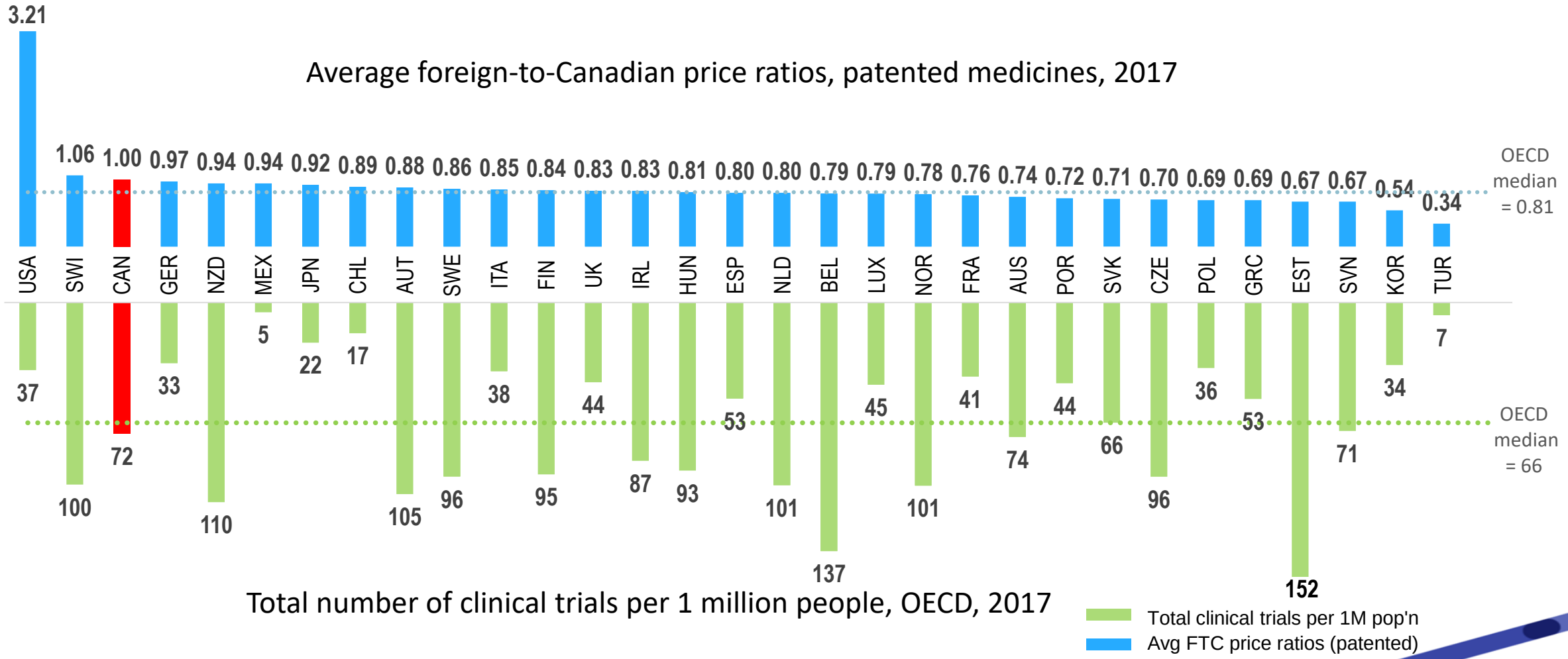
Note: References are available in the Annex.

Key Findings

1. The 30-year policy objective to increase R&D investments in Canada by aligning prices with premium-priced countries has not been met
2. Lower prices do not generally result in lower R&D investments, and many countries with lower prices than Canada have higher investments
3. Similarly, lower prices do not generally result in a lower number of clinical trials, and many countries with lower prices than Canada have more clinical trials underway
4. Despite low R&D investments, Canada has a sizable number of clinical trials underway, a minority of which are funded by patentees
5. There are no early signs that patented medicine price reforms are resulting in fewer clinical trials initiated in Canada
6. There are no early signs that patented medicine price reforms are resulting in fewer new medicines being launched in Canada

3 Higher prices do not generally result in more clinical trials

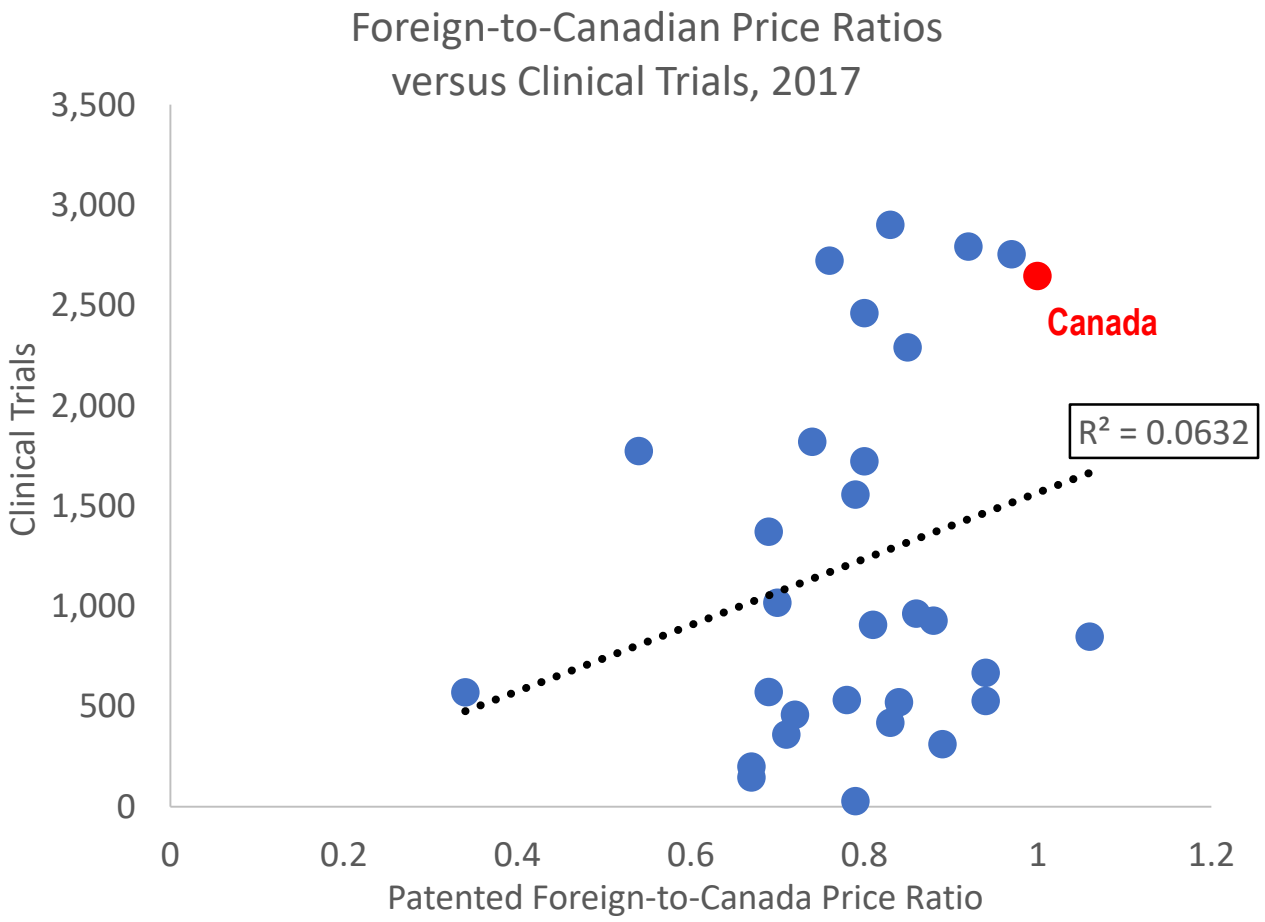
Many countries with lower patented drug prices than Canada have a higher number of clinical trials per 1 million people

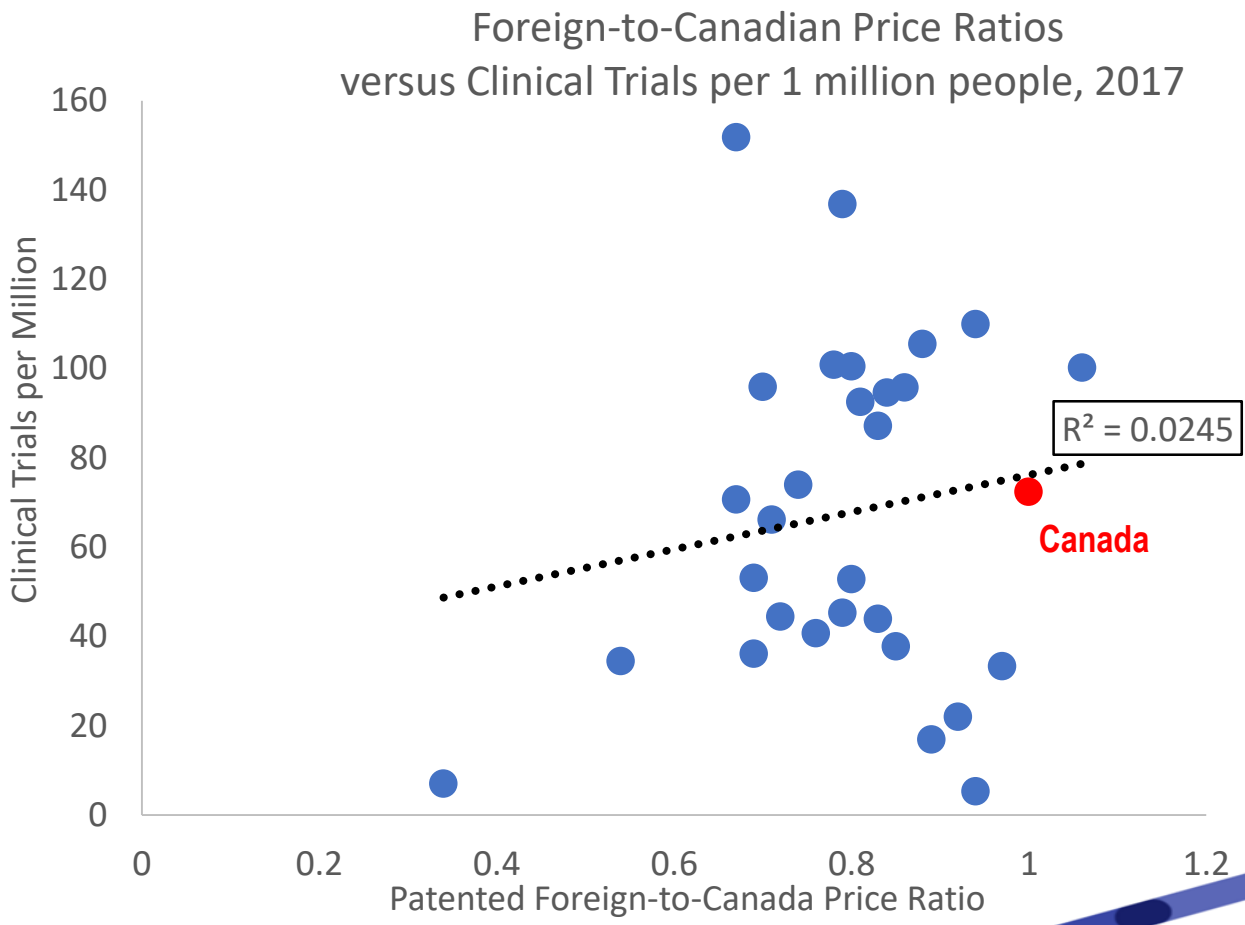


Data sources: PMPRB Annual Report, 2017; GlobalData®; OECD (population).

3 Higher prices do not generally result in more clinical trials

The variability in the number of clinical trials across the OECD countries is not explained by price levels (R squared close to zero)



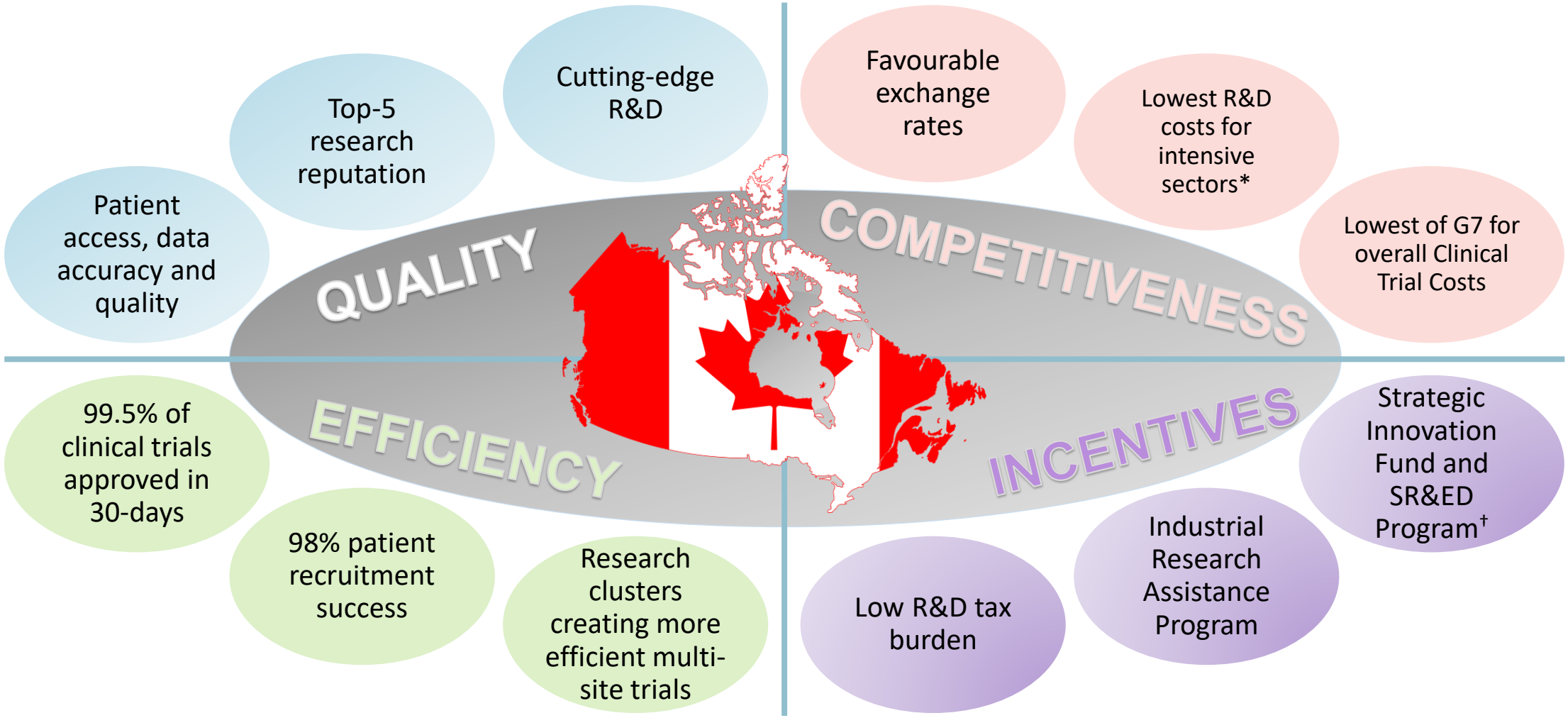


Data sources: PMPRB Annual Report, 2017; GlobalData®; OECD (population).
Notes: R^2 is the percentage of the response variable variation that is explained by a linear model.The United States is not included as with its FTC price ratio of 3.21 it is a significant outlier (see annex).

Key Findings

1. The 30-year policy objective to increase R&D investments in Canada by aligning prices with premium-priced countries has not been met
2. Lower prices do not generally result in lower R&D investments, and many countries with lower prices than Canada have higher investments
3. Similarly, lower prices do not generally result in a lower number of clinical trials, and many countries with lower prices than Canada have more clinical trials underway
4. Despite low R&D investments, Canada has a sizable number of clinical trials underway, a minority of which are funded by patentees
5. There are no early signs that patented medicine price reforms are resulting in fewer clinical trials initiated in Canada
6. There are no early signs that patented medicine price reforms are resulting in fewer new medicines being launched in Canada

4 Clinical Trials: the Canadian advantage

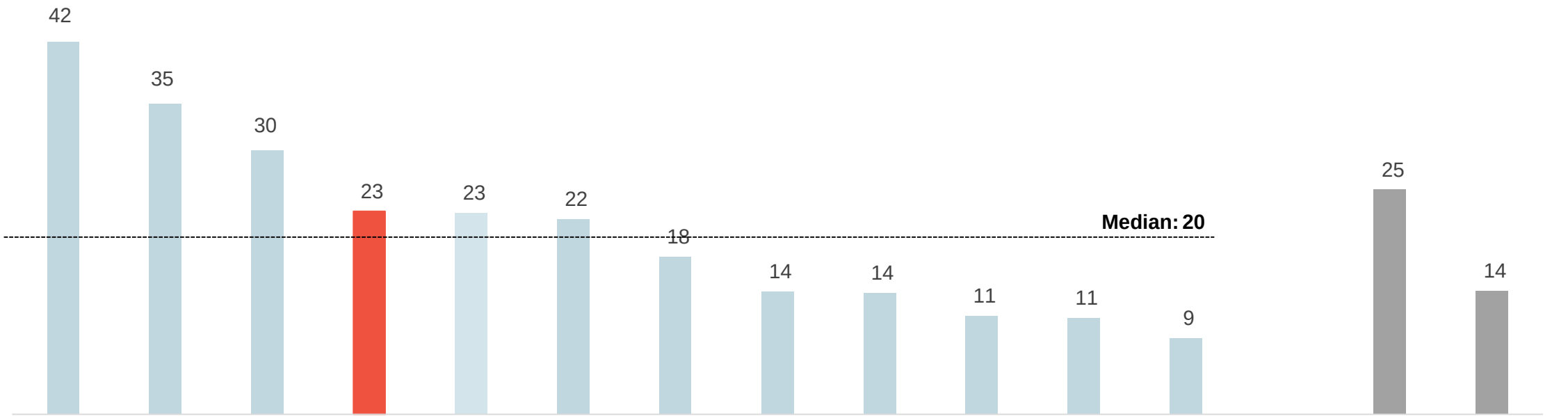


Sources: *Investment case on the value of conducting clinical trials in Canada* IMS Brogan for Department of Foreign Affairs, Trade and Development & Canadian Clinical Trials Coordinating Centre, Oct 2014. *Clinical Trials: The Canadian Advantage* Canadian Clinical Trials Coordinating Centre, June 2018
Notes: *Lowest R&D costs for intensive sectors among 10 developed countries & BRIC, †Scientific Research and Experimental Development Tax Incentive Program

4 Canada has one of the highest number of new clinical trials

Both in terms of the total number of new clinical trials as well as the clinical trials per 1 million people Canada ranks highly among the PMPRB11 counties

Number of new clinical trials per 1 million people, 2019



Total number of new clinical trials	Belgium	Australia	Netherlands	Canada	Sweden	Norway	Spain	UK	France	Germany	Italy	Japan	Switzerland	US
	475	868	509	834	231	116	824	912	909	914	653	1078	212	4521

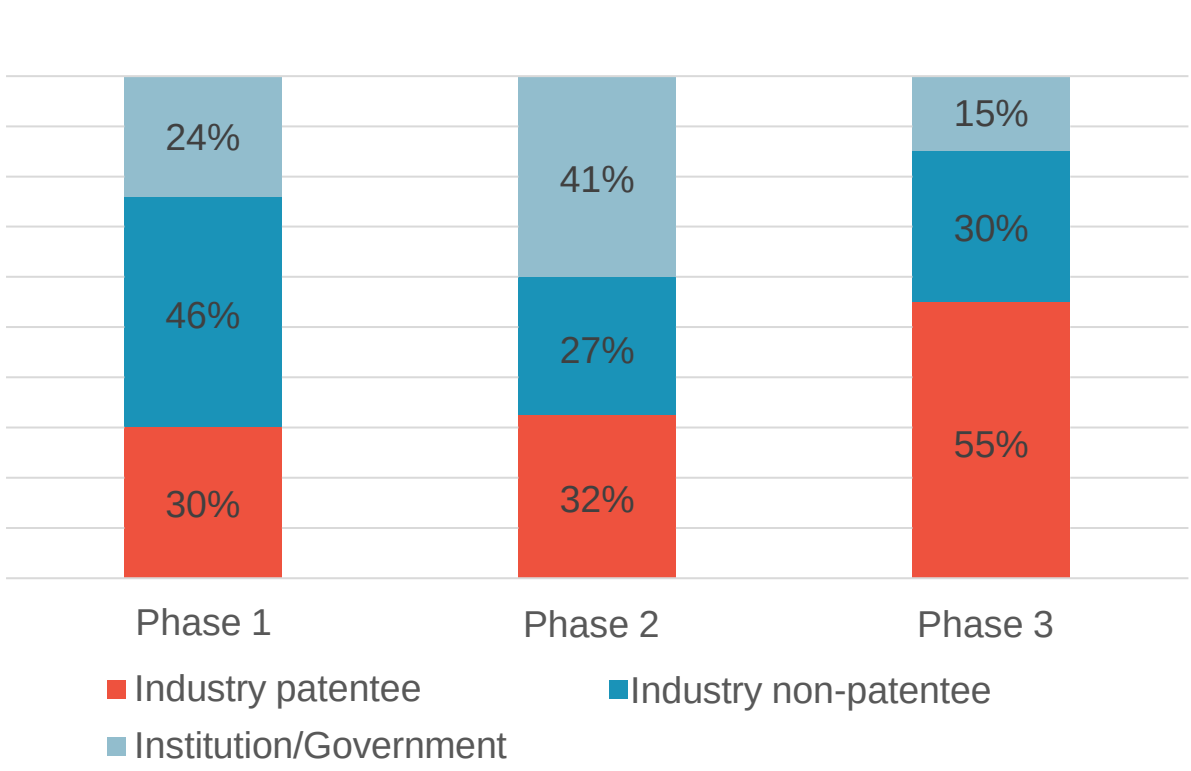
PMPRB 11

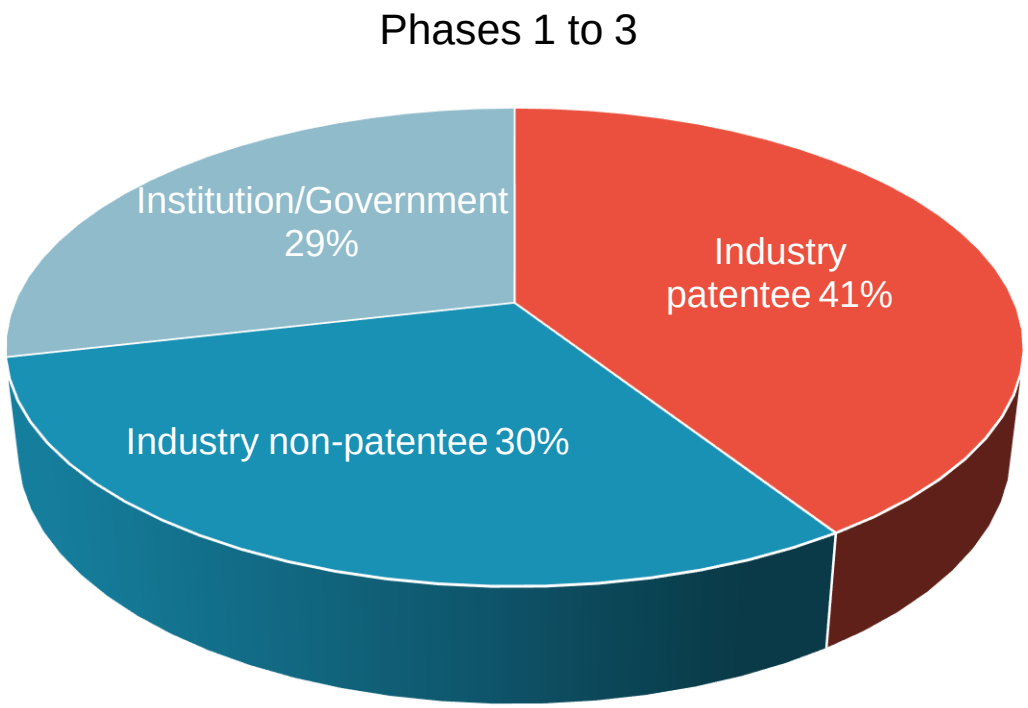
Data source: GlobalData ®,Access date: 2020/06/11

4 A minority of new clinical trials in Canada are funded by patentees

A smaller share of new clinical trials are being sponsored by the patentees in the early phases than in the later phase

Share of new clinical trials by source of funding, Canada, 2019





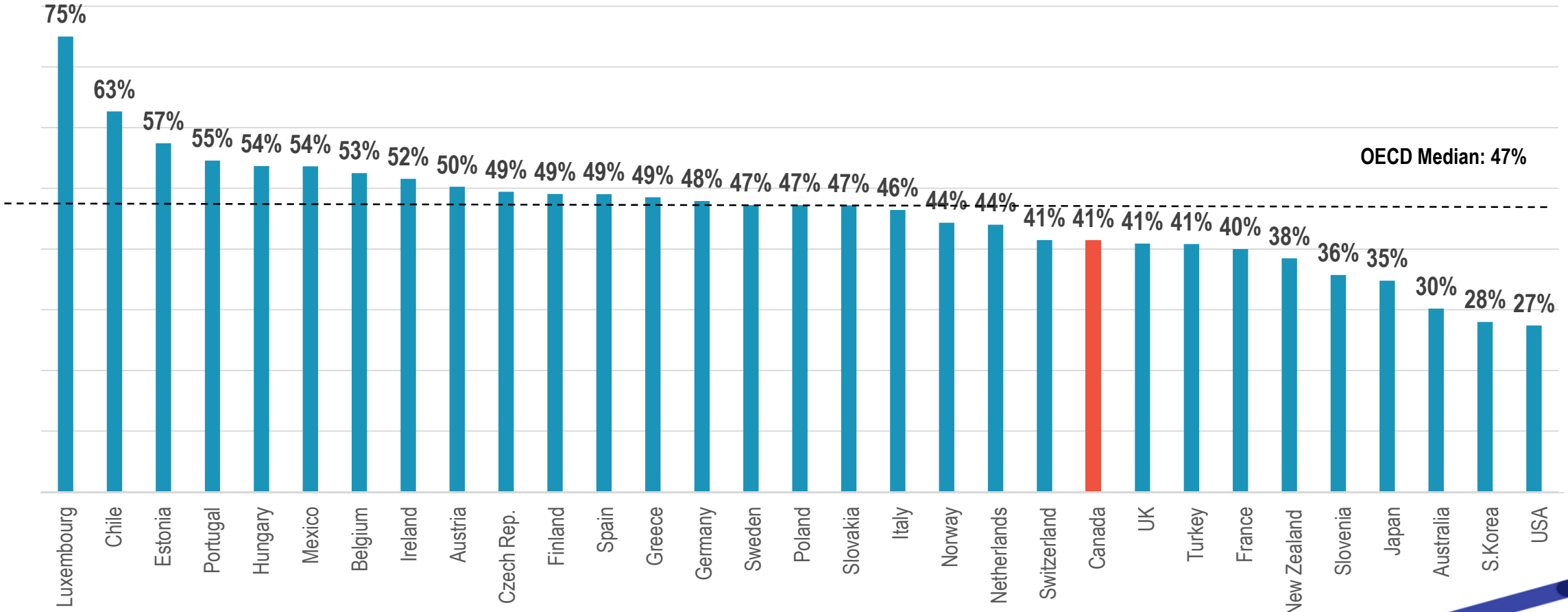
Data source: PMPRB Annual Report 2017, GlobalData®

Note: Institutions include universities, research centers, individual investigators, disease associations, etc.

4 A minority of new clinical trials are funded by patentees in Canada

41% of all the new clinical trials in Canada are sponsored by patentees, below the OECD median of 47%

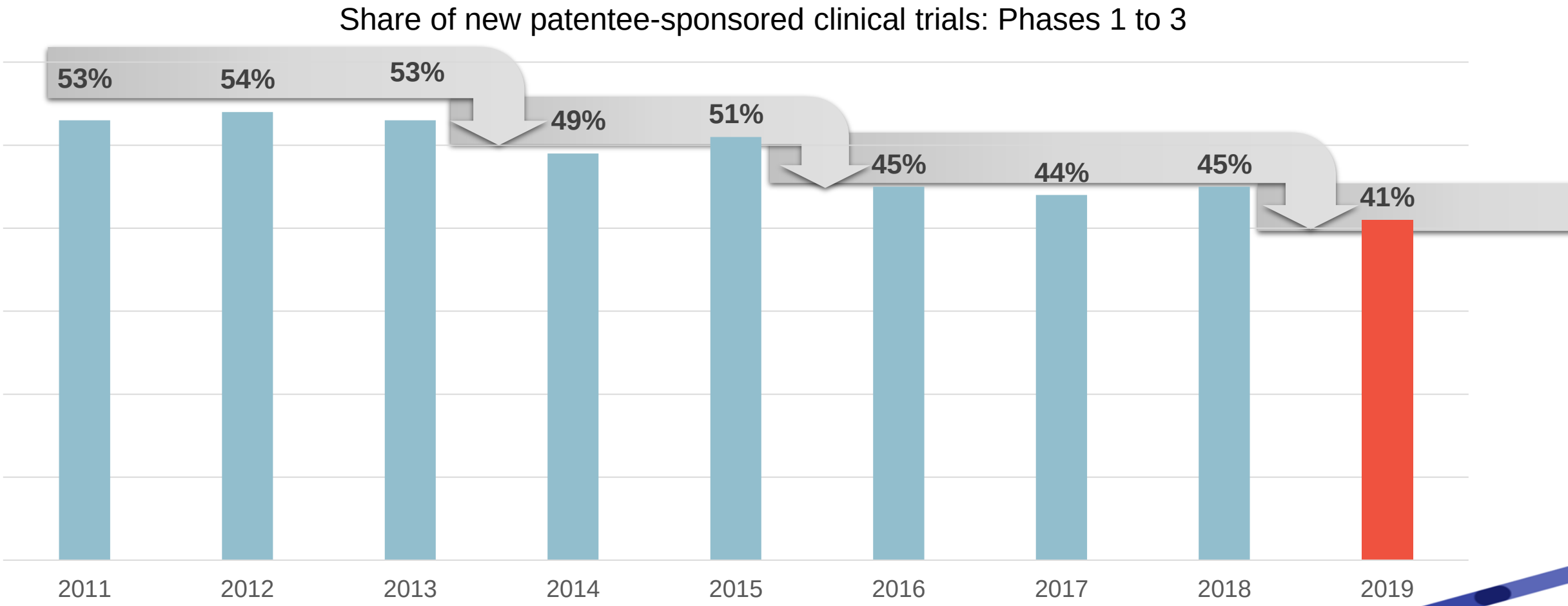
Share of new patentee-sponsored clinical trials: Phases 1 to 3, OECD, 2019



Data source: PMPRB Annual Report 2017, GlobalData®

3 Share of patentees funded clinical trials in decline in Canada

While over half of all new clinical trials commenced in Canada were sponsored by patentees earlier in the decade, by 2019 the share dropped to 41%



Data source: PMPRB Annual Report 2017, GlobalData®

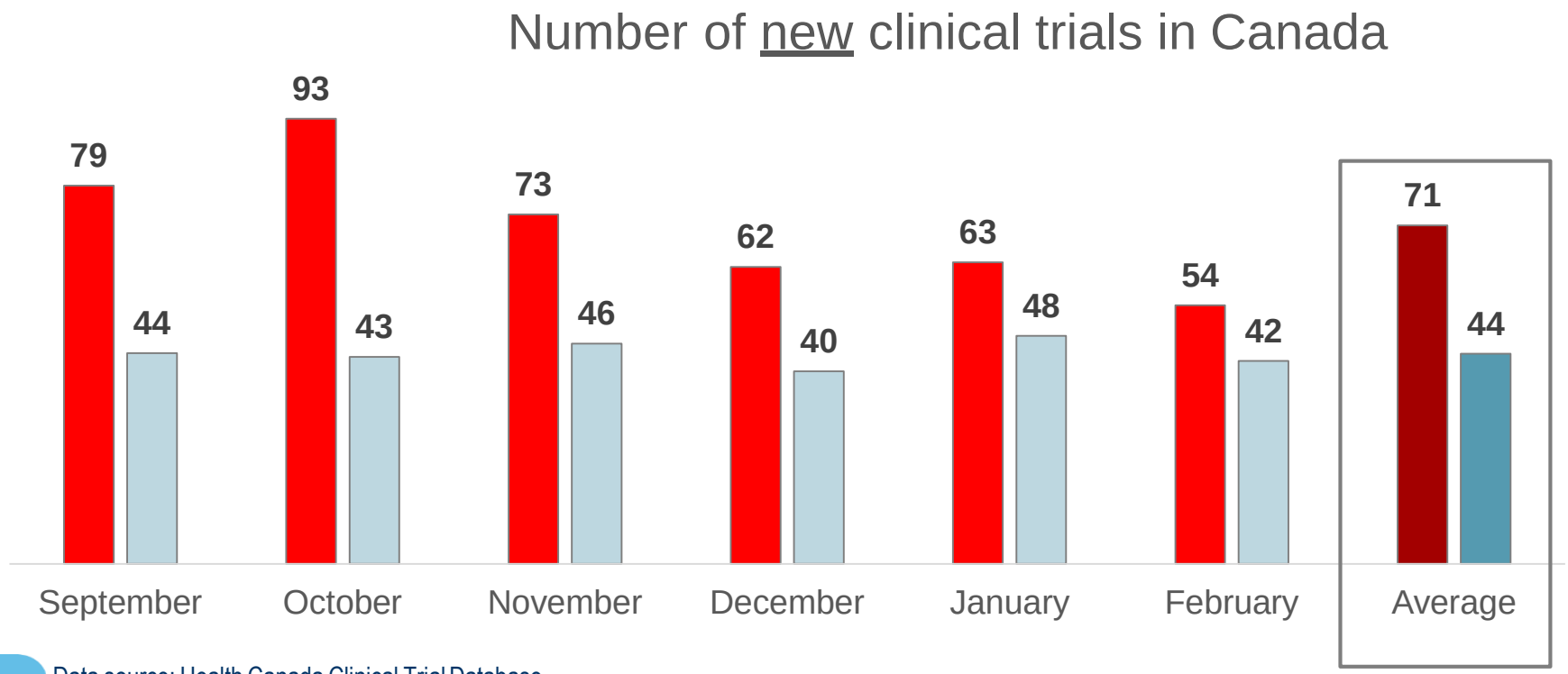
Key Findings

1. The 30-year policy objective to increase R&D investments in Canada by aligning prices with premium-priced countries has not been met
2. Lower prices do not generally result in lower R&D investments, and many countries with lower prices than Canada have higher investments
3. Similarly, lower prices do not generally result in a lower number of clinical trials, and many countries with lower prices than Canada have more clinical trials underway
4. Despite low R&D investments, Canada has a sizable number of clinical trials underway, a minority of which are funded by patentees
5. There are no early signs that patented medicine price reforms are resulting in fewer clinical trials initiated in Canada
6. There are no early signs that patented medicine price reforms are resulting in fewer new medicines being launched in Canada

5 Is the number of new clinical trials started in Canada declining?

Studies that answer yes, are based on information in the Health Canada Clinical Trial Database, which is not appropriate for conducting trend analyses and may not be up to date (e.g. “No Objection Letter”)

In fact, according to the Health Canada Clinical Trial Database the number of new clinical trials being started in Canada has been markedly higher in 2019 compared to the average of previous years.



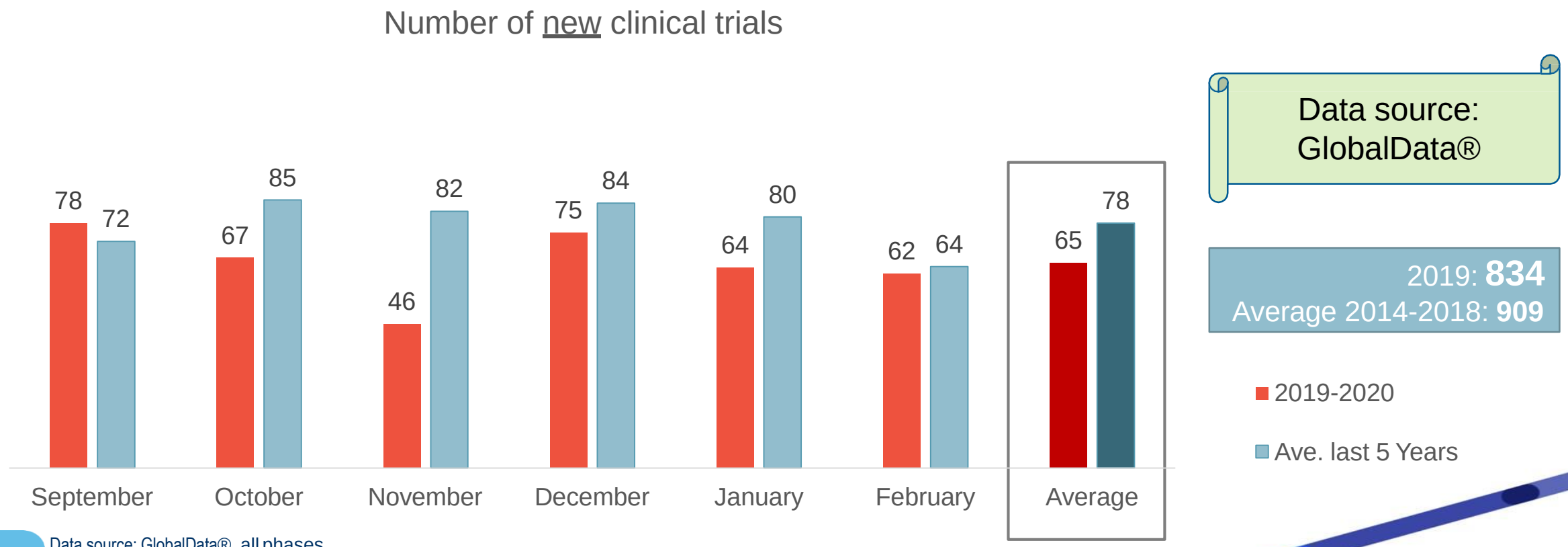
Data source: Health Canada

2019: **707**
Average 2014-2018: **536**

Data source: Health Canada Clinical Trial Database

5 Is the number of new clinical trials started in Canada declining?

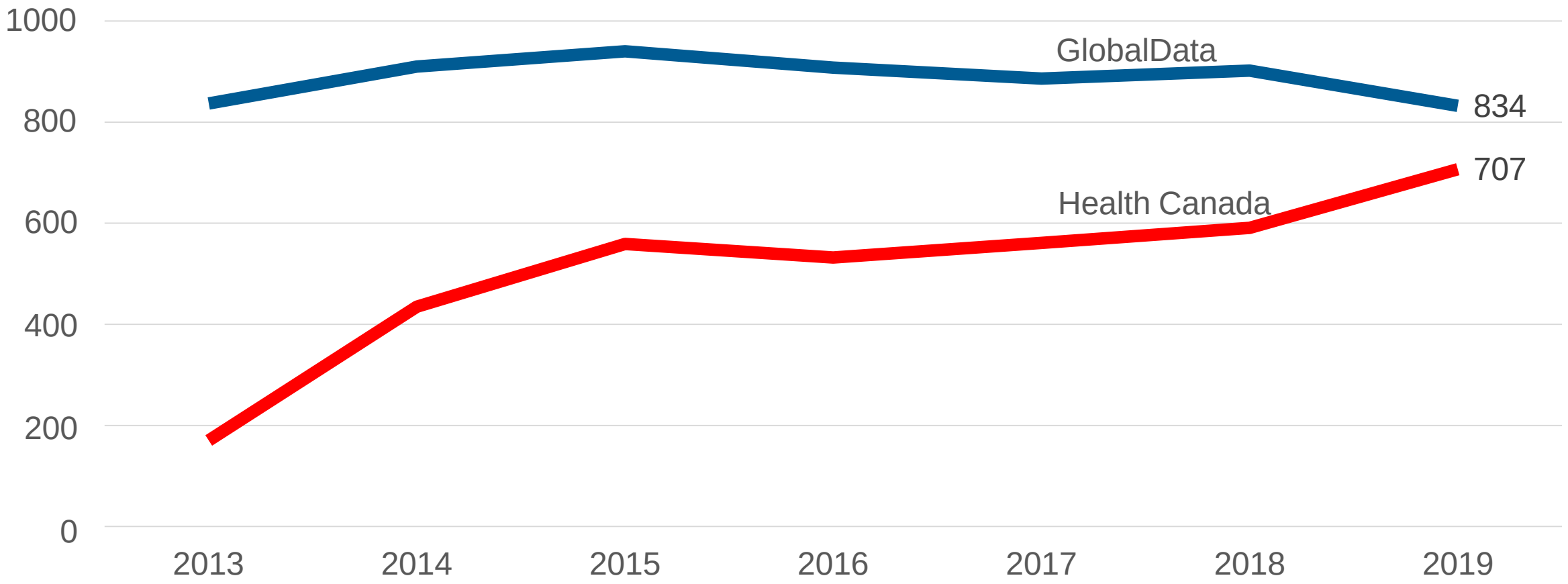
According to GlobalData, the number of new clinical trials being started in Canada has been lower in 2019 compared to the average of previous years.



Data source: GlobalData®, all phases

5 Data source matters

Number of new clinical trials by data source, 2013 to 2019



Data sources: GlobalData ®, Health Canada Clinical Trial Database

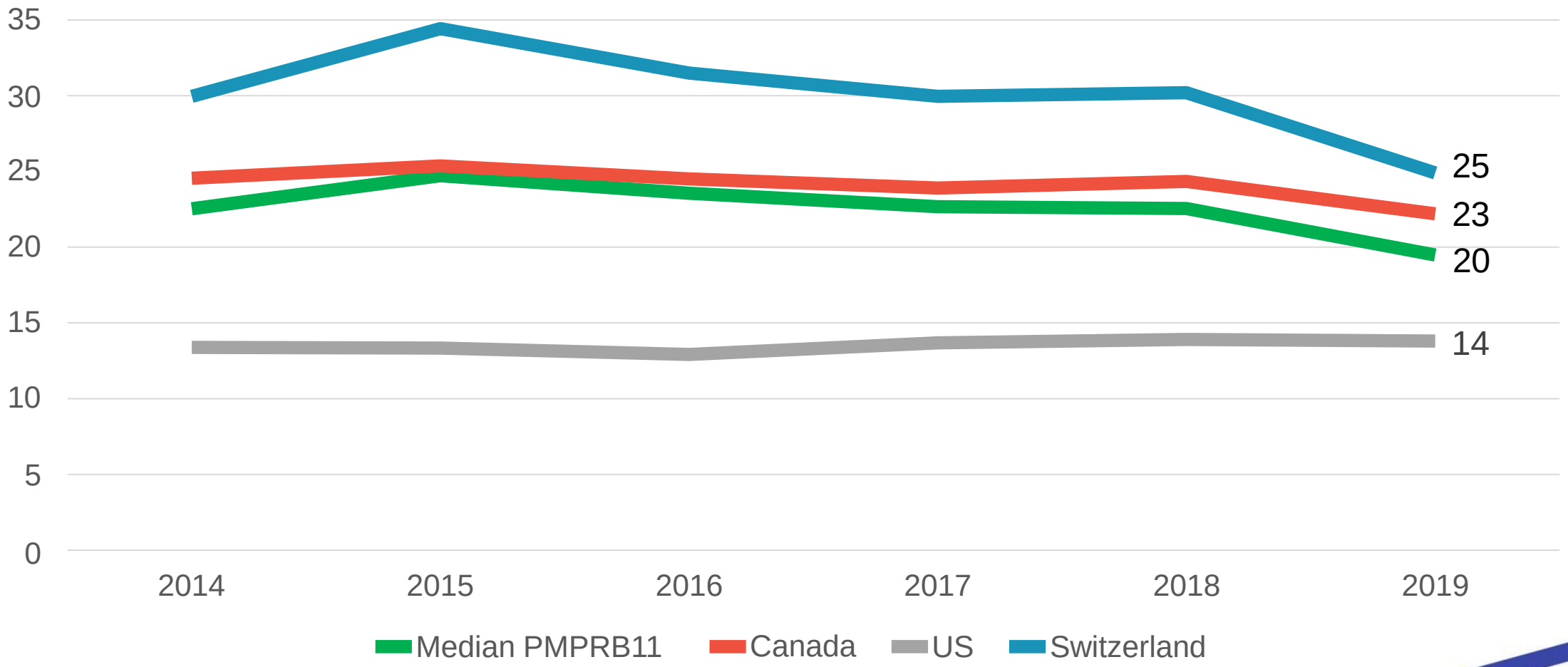
5 Health Canada Clinical Trials Database is not appropriate for conducting trend analyses

- **The Clinical Trials Database is not a registry, and is in fact a subset of all the clinical trials taking place in Canada:**
  - Not all clinical trials underway in Canada are reflected in this database, nor does it contain comprehensive information about each clinical trial.
  - The database only includes trials conducted in patients. In other words, the database does not include Phase I trials conducted in healthy volunteers, bioavailability/bioequivalence studies for generics, or information on single participant trials (for privacy reasons).
- **There are sometimes delays in uploading information into the database, which means that data may not be up to date.**
- **The data in the reports produced by the Health Canada Therapeutic Products Directorate (TPD), and the Biologic and Radiopharmaceutical Drugs Directorate (BRDD) is a more up to date and comprehensive depiction of the clinical trials being submitted to and approved by Health Canada.**

Source: Centre for Regulatory Excellence, Statistics and Trials (CREST), Health Products and Food Branch, Health Canada; TPD and BRDD Drug Submission Performance Reports (Annual and Quarterly) Available at https://www.canada.ca/en/health-canada/services/drugs-health-products/reports-publications/drug-products.html

5 The number of new clinical trials has been on decline in recent years in all major developed markets

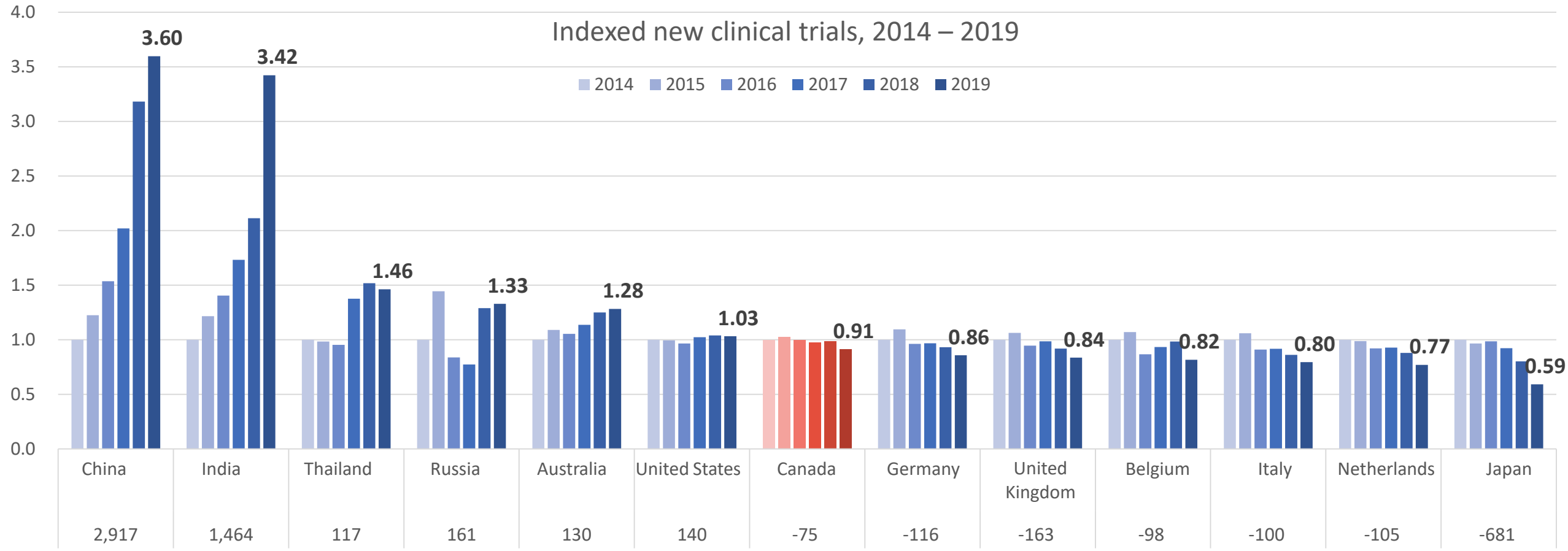
Number of new clinical trials per 1 million people, 2014 – 2019



Data source: GlobalData®

5 The globalization of clinical trials

The number of new clinical trials are on decline in Canada and other developed markets as emerging markets experience substantial growth



6 countries with the largest increases in new clinical trials

6 countries with the largest decreases in new clinical trials

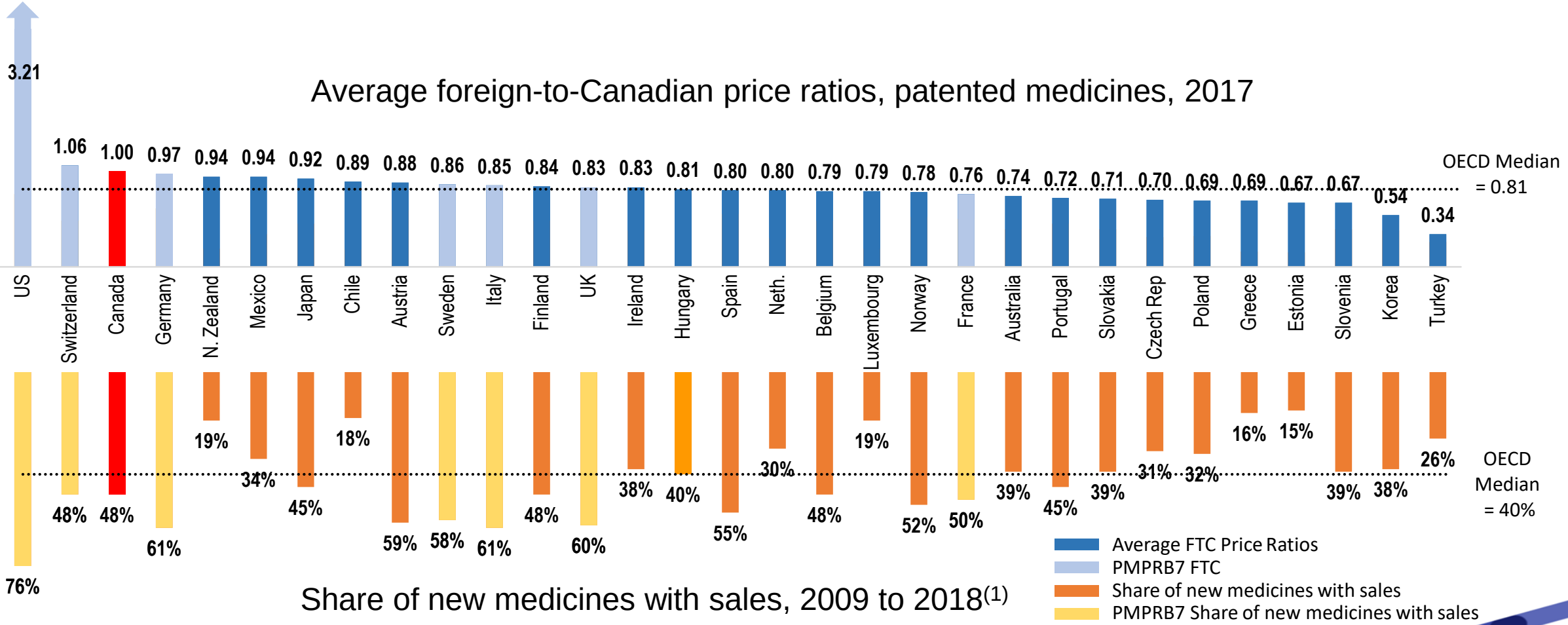
Data sources: GlobalData®, country ranks determined by the difference between 2019 and the 2014 – 2018 median.

Key Findings

1. The 30-year policy objective to increase R&D investments in Canada by aligning prices with premium-priced countries has not been met
2. Lower prices do not generally result in lower R&D investments, and many countries with lower prices than Canada have higher investments
3. Similarly, lower prices do not generally result in a lower number of clinical trials, and many countries with lower prices than Canada have more clinical trials underway
4. Despite low R&D investments, Canada has a sizable number of clinical trials underway, a minority of which are funded by patentees
5. There are no early signs that patented medicine price reforms are resulting in fewer clinical trials initiated in Canada
6. There are no early signs that patented medicine price reforms are resulting in fewer new medicines being launched in Canada

6 Countries with lower patented drug prices than Canada may have greater availability of new medicines

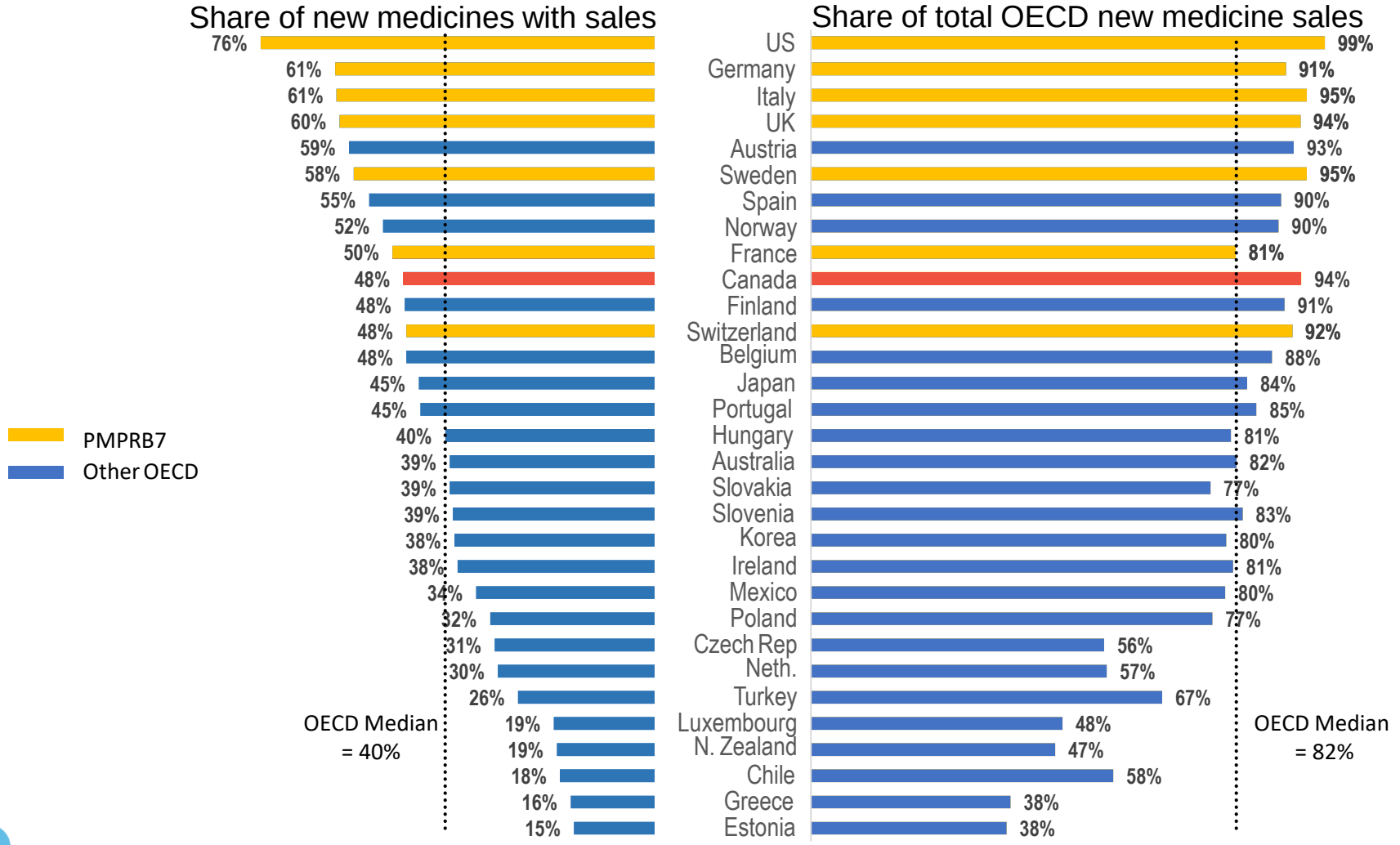
Despite higher drug prices prevailing in Canada, less than half (48%) of all new drugs have sales in Canada, lower than other major markets, many of which have lower average patented drug prices



Data source: PMPRB Annual Report, 2017; PMPRB Meds Entry Watch, 2018.
Note (1): New medicines approved in Canada and the PMPRB7 from 2009 to 2017 with available sales, by country, by Q4-2018. Refer to data source for specifics.

6 New medicines approved in Canada account for 94% of OECD sales for all new medicines

While Canada's share of new medicines launched in Canada and the PMPRB7 is 48%, these medicines do account for a much larger share of OECD sales (94%)

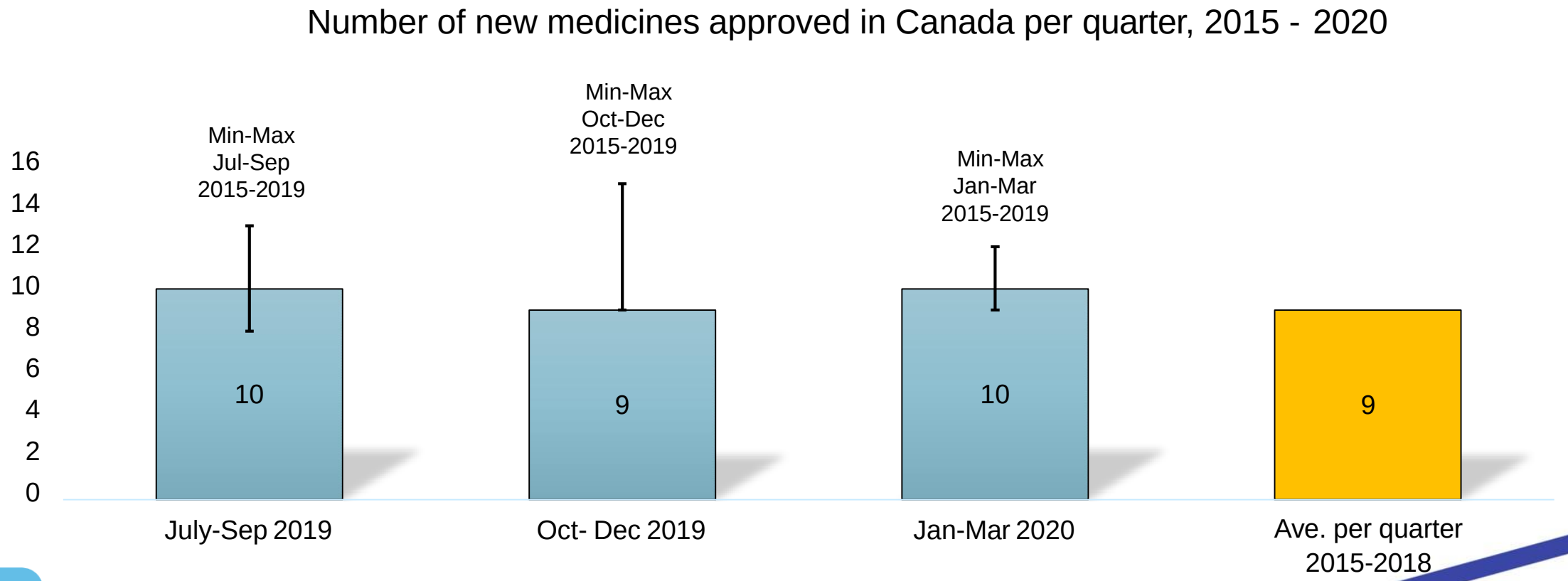


Data source: PMPRB Meds Entry Watch, 2018.

6 Is the number of new drugs being launched in Canada declining?

Reports that answer yes, are based on sales data, which offer a partial and delayed picture of the drugs being launched in Canada and internationally.

The number of new medicines approved by Health Canada over the most recent three quarters is in line with past trends.

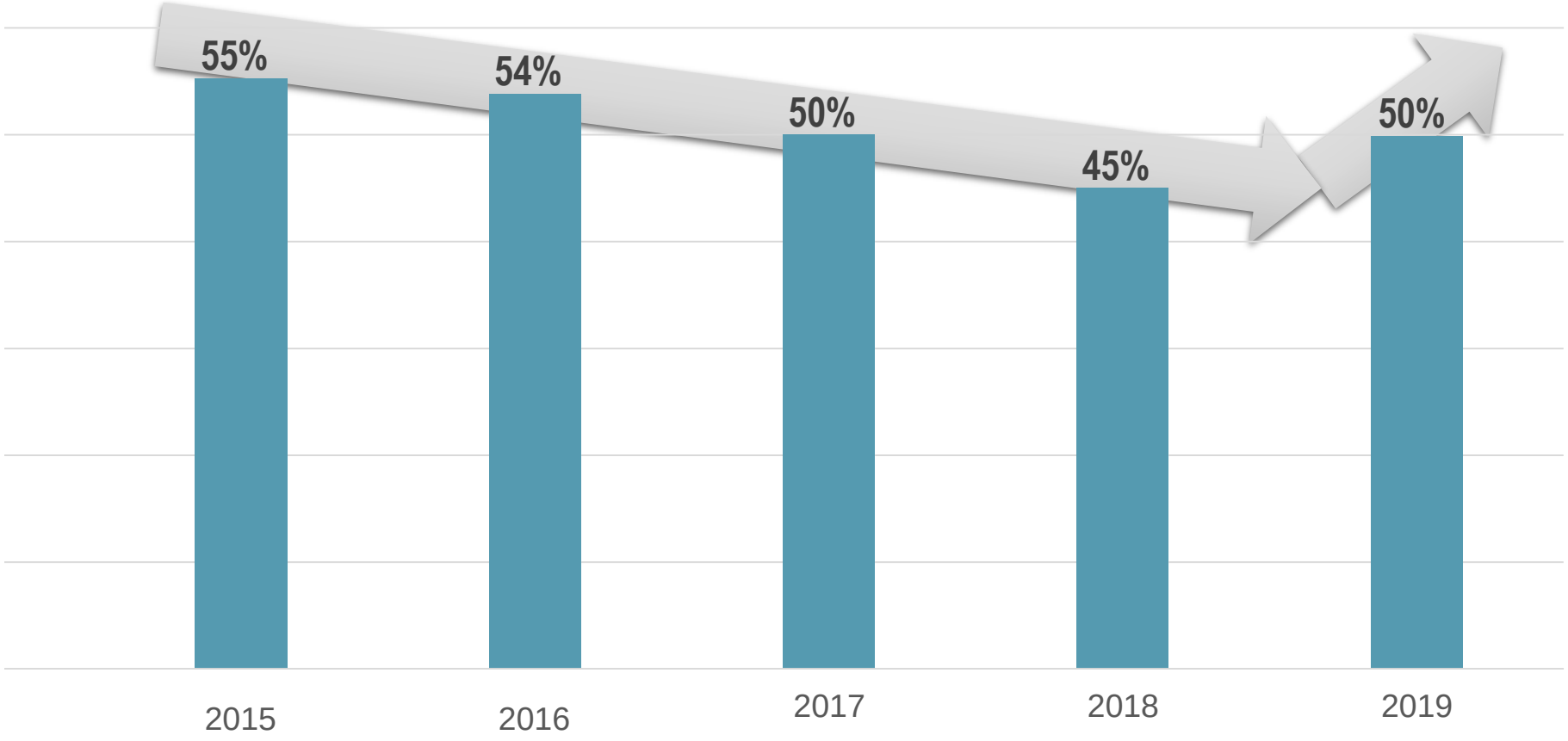


Data source: Health Canada Drug Product Database

6 Is the number of new drugs being launched in Canada declining?

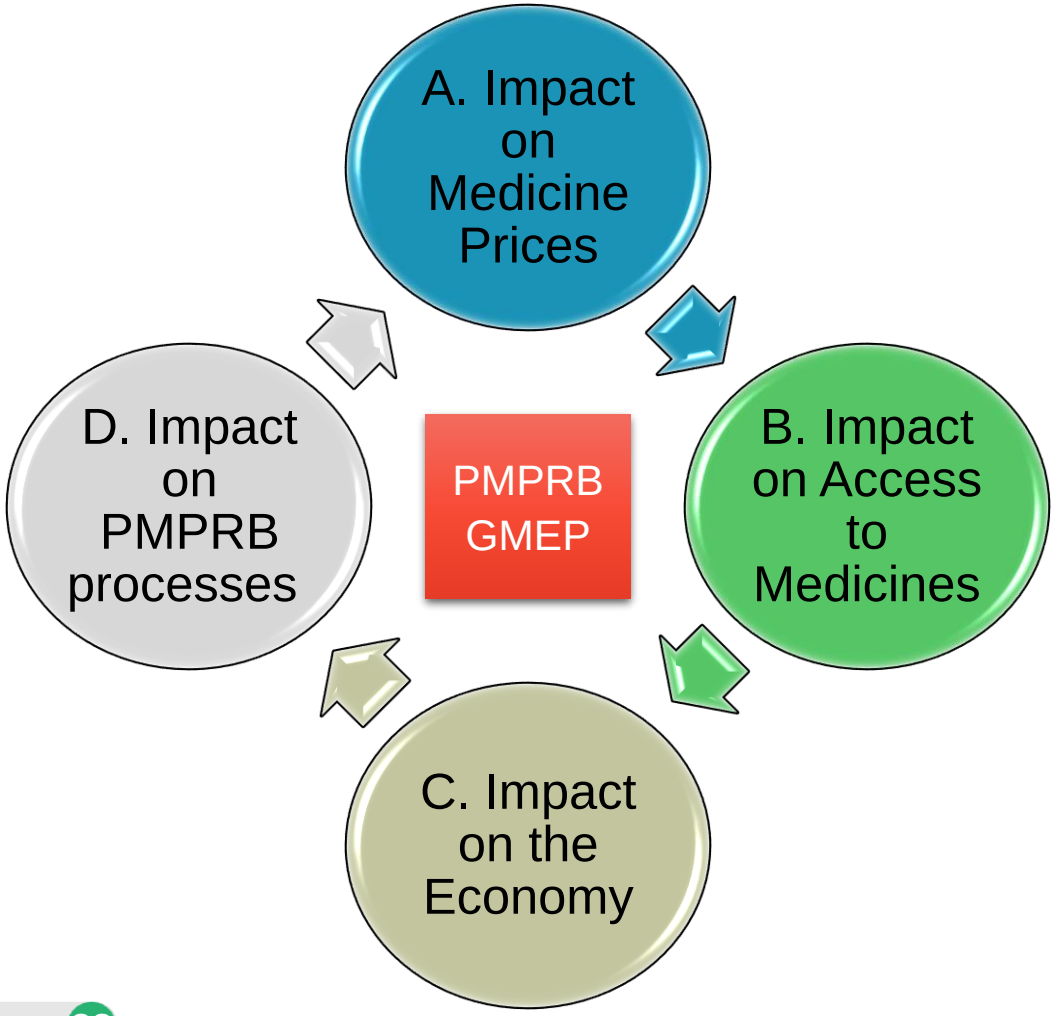
Half of new medicines approved in Canada in 2019 received approval within one year of United States approval, higher than in 2018

Share of new medicines approved by Health Canada within one year of FDA approval



Data sources: FDA and Health Canada Drug Product Database

Guideline Monitoring and Evaluation Plan (GMEP)



- The PMPRB is committed to the development and execution of an extensive GMEP to assess their impact and inform any future enhancements.
- The new GMEP is the most comprehensive to date, aiming for an in-depth assessment of four key impact areas (shown in the graphic).
- Discussions with interested stakeholders, expected to shape the GMEP development.
- Both qualitative and quantitative indicators will be employed, and various administrative, commercial, international, domestic and internal data sources will be consulted.
- Trends prior and post framework implementation will be compared and reported regularly (i.e. baseline results versus post implementation).
- Some impacts are expected to be immediate, while others may take longer to materialize. Also, some impacts may be directly attributable to the PMPRB, while other may also be impacted by factors outside the PMPRB purview.

THANK YOU

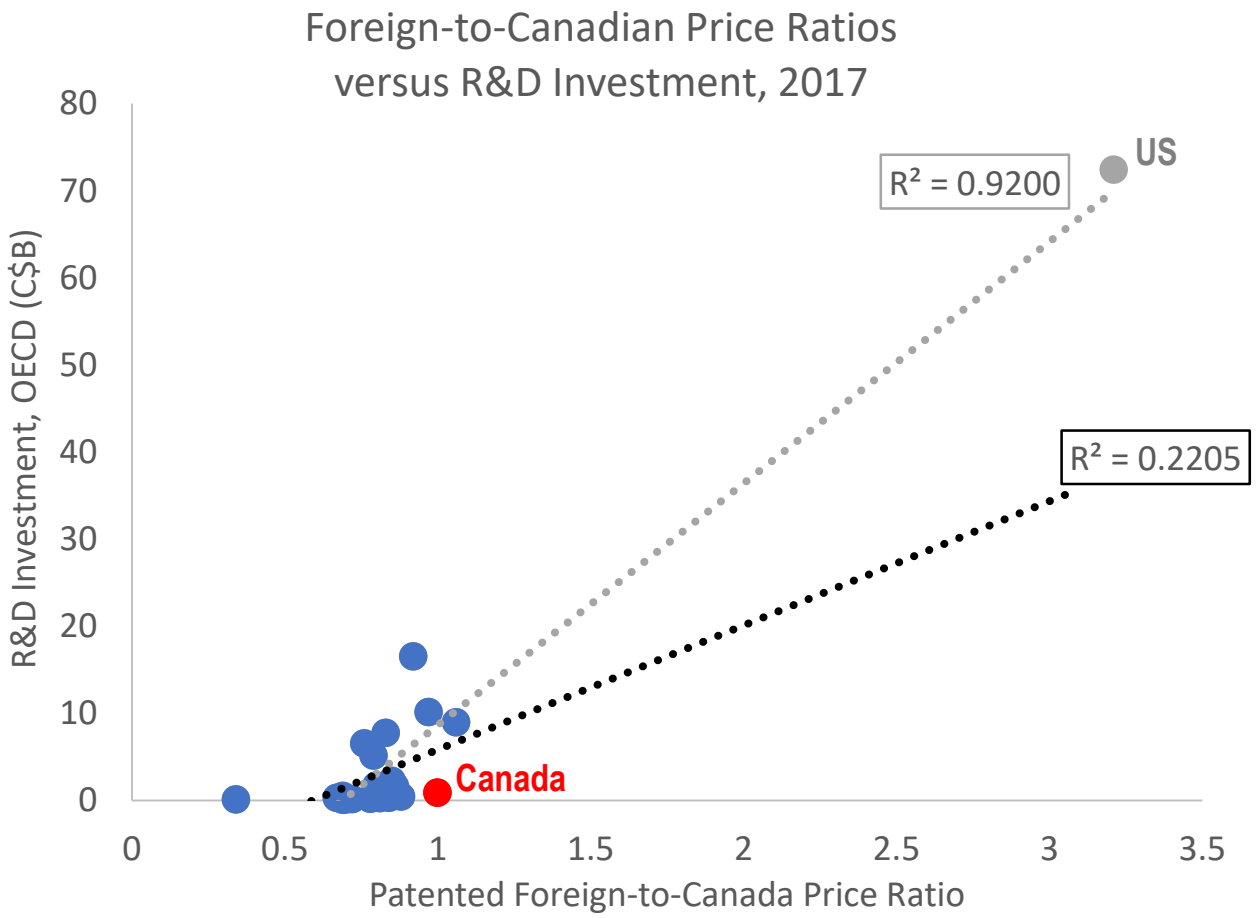
Patented Medicine Prices Review Board

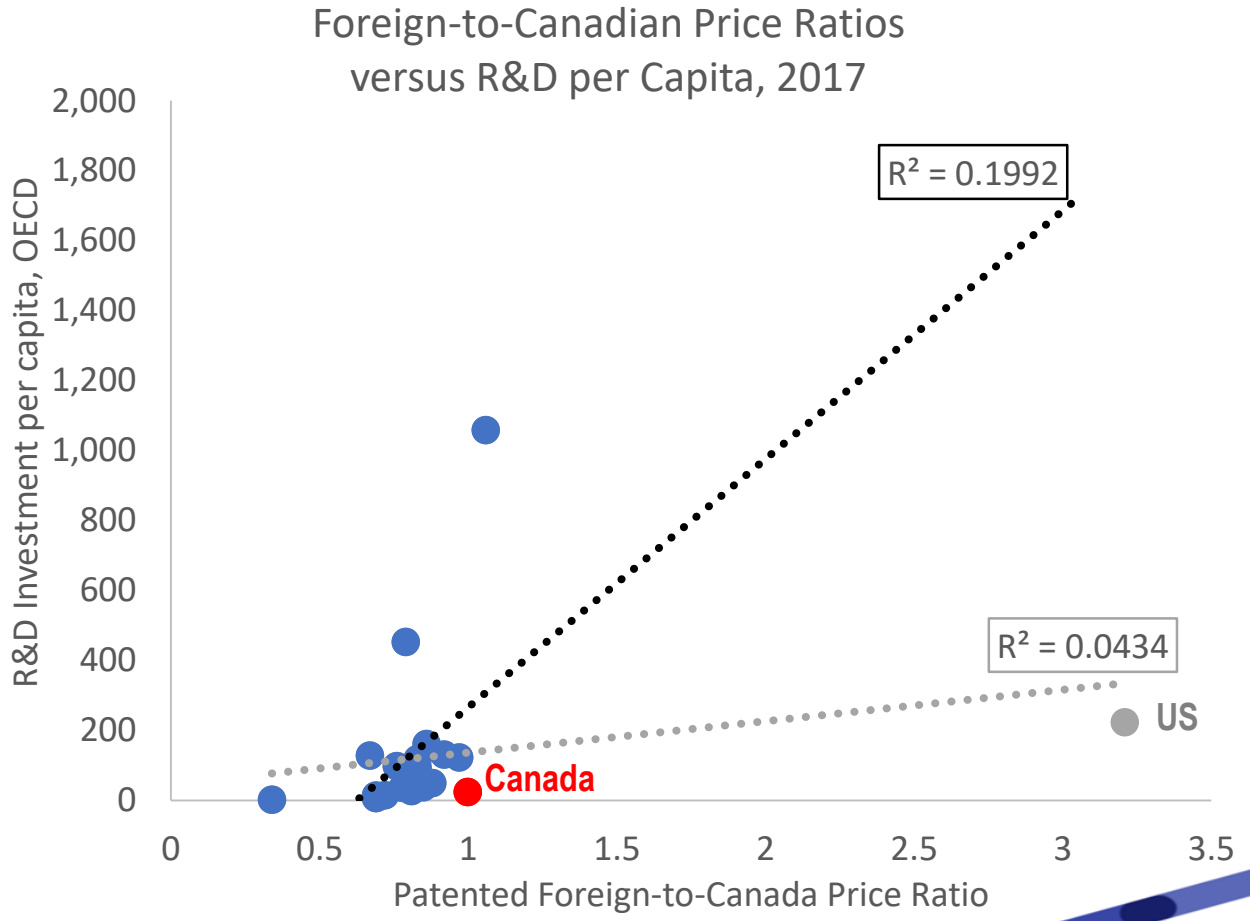
Annex

References

- Jayasundara K, Hollis A, Krahn M, et al., *Estimating the clinical cost of drug development for orphan versus non-orphan drugs.* Orphanet Journal of Rare Diseases, 2019. 14(1): p. 12.
- Hoen E, *Global Access to Medicines Challenge. Time for a new approach?* , in *4th International PPRI Conference: Medicines access challenge – The value of pricing and reimbursement policies.* . 2019, Journal of Pharmaceutical Policy and Practice: Netherlands. p. k1.
- Leoni P and Sandroni A, *Can patent duration hinder medical innovation.* International Journal of Health Economics and Management, 2016. 16(4): p. 397-406.
- Golec J, Hegde S, and Vernon JA, *Pharmaceutical R&D Spending and Threats of Price Regulation.* The Journal of Financial and Quantitative Analysis, 2010. 45(1): p. 239-264.
- Mahlich JC and Roediger-Schluga T, *The Determinants of Pharmaceutical R&D Expenditures: Evidence from Japan.* Review of Industrial Organization, 2006. 28(2): p. 145-164.
- Vernon JA, *Examining the link between price regulation and pharmaceutical R&D investment.* Health Econ, 2005. 14(1): p. 1-16.
- Vernon JA, *Drug research and price controls.* Health & Medicine, 2003: p. 22-25.
- Giaccotto C SR, Vernon J, *Explaining Pharmaceutical R&D Growth Rates at the Industry Level: New Perspectives and Insights*. 2003.
- Green DG, *Is price regulation necessary: a summary of arguments* PharmacoEconomics, 1998. 14(Suppl 1): p. 137- 142.
- Scherer FM, *Pricing, profits, and technological progress in the pharmaceutical industry* Journal of Economic Perspectives, 1993. 7(3): p. 97- 115.

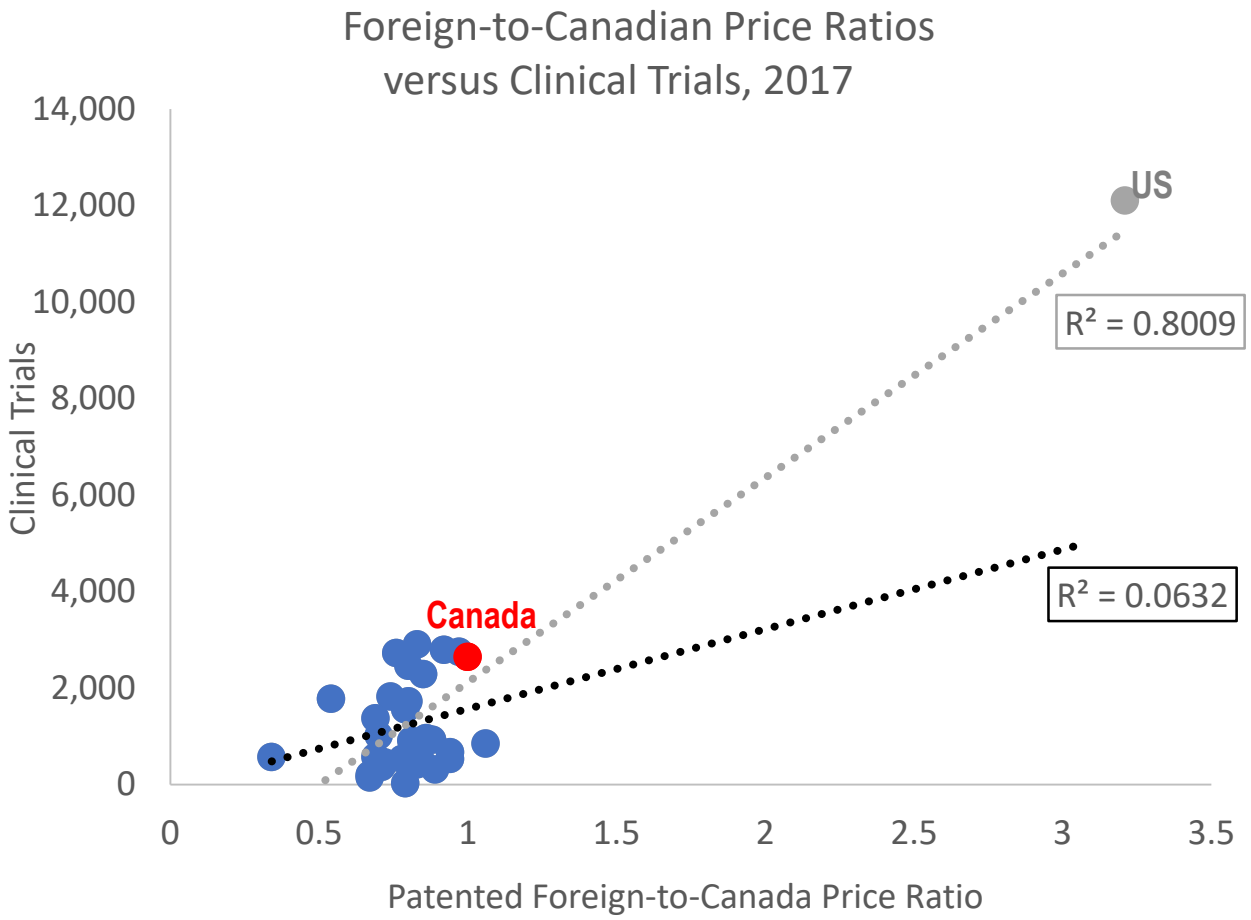
2 Higher prices do not result in greater R&D investments

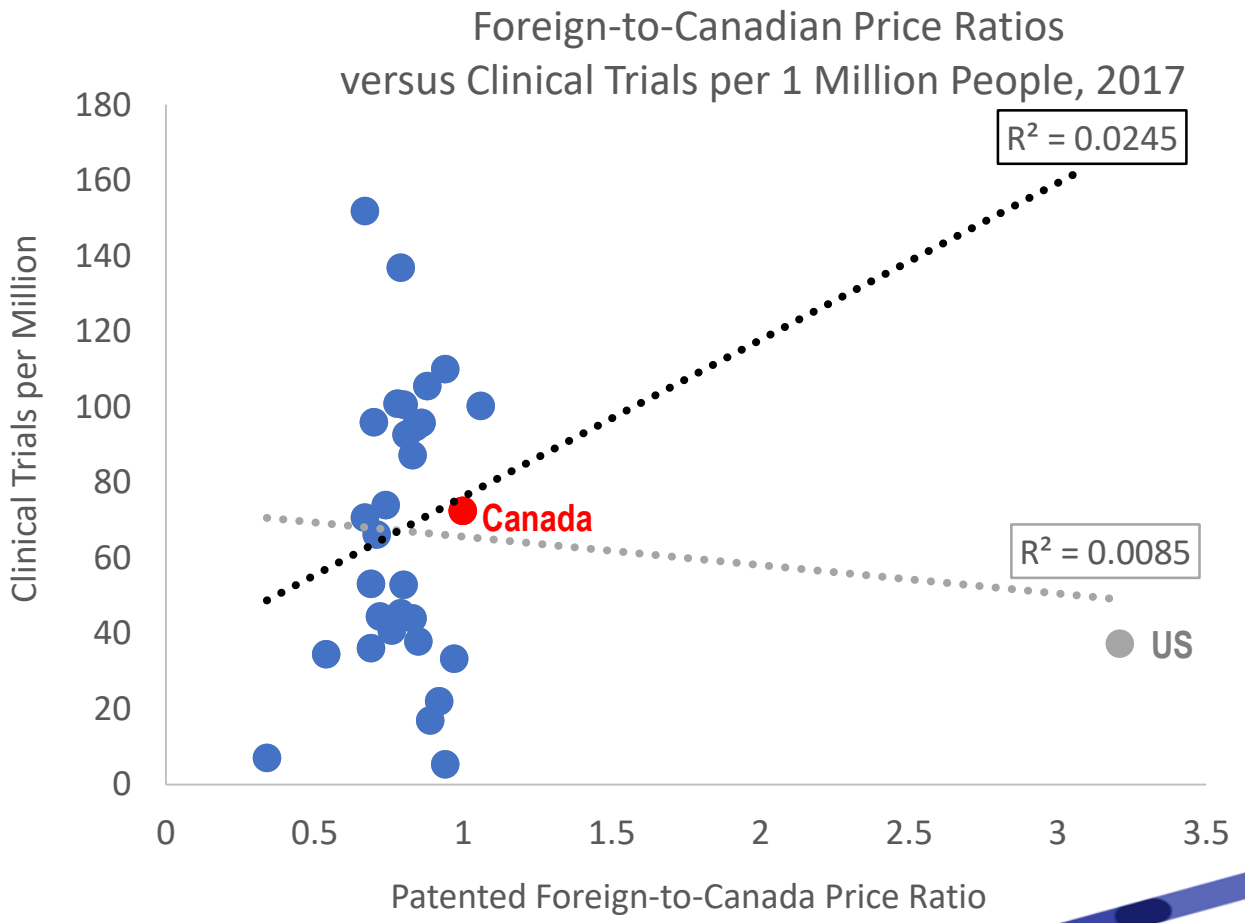




Data sources: PMPRB Annual Report, 2017 (FTC, R&D); OECD (population).
R^2 is the percentage of the response variable variation that is explained by a linear model.
As a significant outlier the United States has a disproportionate effect on the R^2

3 Higher prices do not result in more clinical trials





Data sources: PMPRB Annual Report, 2017; GlobalData®; OECD (population).
R^2 is the percentage of the response variable variation that is explained by a linear model.
As a significant outlier the United States has a disproportionate effect on the R^2

6 List of new medicines approved by Health Canada per quarter 2019- 2020

Jul-Sep 19		
	Trade Name	NOC date
1	Netspot	03-Jul-19
2	Esperoct	04-Jul-19
3	Vitrakvi	10-Jul-19
4	Dacogen	11-Jul-19
5	Nerlynx	16-Jul-19
6	Lokelma	25-Jul-19
7	Emgality	30-Jul-19
8	Ultomiris	28-Aug-19
9	Calquence	23-Aug-19
10	Talzenna	06-Sep-19

Oct-Dec 19		
	Trade Name	NOC date
1	Trulance	10-Oct-19
2	Balversa	25-Oct-19
3	Intrarosa	01-Nov-19
4	Galli Eo	13-Nov-19
5	Aklief	25-Nov-19
6	Mylotarg	28-Nov-19
7	Xospata	23-Dec-19
8	Rinvoq	23-Dec-19
9	Vascepa	30-Dec-19

Jan-Mar 20		
	Trade Name	NOC date
1	Vyndaqel	20-Jan-20
2	Rozlytrek	10-Feb-20
3	Cablivi	28-Feb-20
4	Nubeqa	20-Feb-20
5	Xofluza	19-Feb-20
6	Mayzent	20-Feb-20
7	Beovu	12-Mar-20
8	Piqray	11-Mar-20
9	Cabenuva	18-Mar-20
10	Vocabria	18-Mar-20

Note: List contains all trade names approved by Health Canada in 2019- 2020 (1st quarter) under the submission of a NAS (New Active Substance) and Priority- NAS.
Data sources: Health Canada Drug Product Database

6 List of new medicines approved by Health Canada in 2019

Trade Name (medicinal ingredient)	NOC Date	FDA Approval Date	Lag in years
Lutathera (lutetium (177lu) oxodotreotide)	2019-01-09	2018-01-26	1.0
Onstryv (safinamide)	2019-01-10	2017-03-21	1.8
Symdeko (ivacaftor, tezacaftor)	2019-06-27	2018-02-12	1.4
Vonvendi (von willebrand factor (recombinant), vonicog alfa)	2019-01-10	2015-12-08	3.1
Rinvoq (upadacitinib)	2019-12-23	2019-08-16	0.4
Mylotarg (gemtuzumab ozogamicin)	2019-11-28	2017-09-01	2.2
Aklief (trifarotene)	2019-11-25	2019-10-04	0.1
Gallieo (gallium (68ga) chloride)	2019-11-13	2019-08-21	0.2
Intrarosa (prasterone)	2019-11-06	2016-11-16	3.0
Balversa (erdafitinib)	2019-10-25	2019-04-12	0.5
Trulance (plecanatide)	2019-10-10	2017-01-19	2.7
Talzenna (talazoparib)	2019-09-06	2018-10-16	0.9
Ultomiris (ravulizumab)	2019-08-28	2018-12-21	0.7
Calquence (acalabrutinib)	2019-08-23	2017-10-31	1.8
Emgality (galcanezumab)	2019-07-30	2018-09-27	0.8
Lokelma (sodium zirconium cyclosilicate)	2019-07-25	2018-05-18	1.2
Nerlynx (neratinib maleate)	2019-07-16	2017-07-17	2.0
Dacogen (decitabine)	2019-07-11	2006-05-02	13.2

Trade Name (medicinal ingredient)	NOC Date	FDA Approval Date	Lag in years
Vitrakvi (larotrectinib)	2019-07-10	2018-11-26	0.6
Esperoct (antihemophilic factor viii [recombinant, b-domain truncated], pegylated)	2019-07-04	2019-02-19	0.4
Netspot (oxodotreotide)	2019-07-03	2016-06-01	3.1
Zejula (niraparib)	2019-06-27	2017-03-27	2.3
Evenity (romosozumab)	2019-06-17	2019-04-09	0.2
Tibella (tibolone)	2019-05-10	Not approved	
Skyrizi (risankizumab)	2019-04-17	2019-04-23	0.0
Libtayo (cemiplimab)	2019-04-10	2018-09-28	0.5
Verzenio (abemaciclib)	2019-04-05	2017-09-28	1.5
Vizimpro (dacomitinib)	2019-02-26	2018-09-27	0.4
Lorbrena (lorlatinib)	2019-02-22	2018-11-02	0.3
Demylocan (decitabine)	2019-01-21	2006-05-02	12.7
Vascepa (icosapent ethyl)	2019-12-30	2012-07-26	7.4
Xospata (gilteritinib fumarate)	2019-12-23	2018-11-28	1.1
Onpattro (patisiran sodium)	2019-06-07	2018-08-10	0.8
Yescarta (axicabtagene ciloleucel)	2019-02-13	2017-10-18	1.3
Oxervate (cenegermin)	2019-02-08	2018-08-22	0.5
Idhifa (enasidenib mesylate)	2019-02-06	2017-08-01	1.5

Approved by Health Canada within one year of FDA approval

Note: List contains all trade names approved by Health Canada in 2019 under the submission of a NAS (New Active Substance).
Data sources: FDA and Health Canada Drug Product Database