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# Drug Shortages in Canada



**PMPRB Researcher Series**

July 16, 2020

Canada 

# Introduction

- **Today's session features three presentations on the topic of drug shortages**
  1. An overview of the causes, reporting, and mitigation strategies in Canada and internationally
  2. An analysis of international prices of medicines and Canadian shortages
  3. A case study revealing the impact of a shortage on the Canadian supply chain



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# Part 1

An overview of the causes, reporting, and mitigation strategies in Canada and internationally

**Allison Carey**

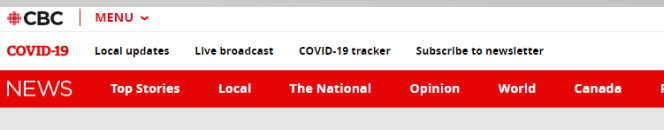
July 16, 2020

# Key Findings

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- 1 Drug shortages have emerged as a serious global issue over the past decade
- 2 The causes of drug shortages are complex and frequently tied to manufacturing and business decisions
- 3 The definition of “drug shortage” as well as reporting requirements and mitigation strategies differ widely among countries

# Increased focus on shortages in the last few years



Montreal

**Ritalin shortage prompts call for Health Canada changes**

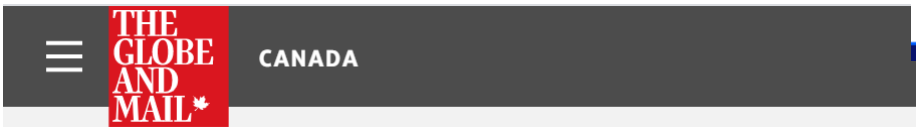


## Le gouvernement lance un site pour suivre les pénuries de médicaments



JACKIE L. LARSON

Plus de JACKIE L. LARSON



## La pénurie persistante de médicaments oblige les pharmacies à s'adapter à la volée, selon l'association



## Prescription Drug Shortages Could Plague The 2020's



## Drug shortages in Canada: Why they happen and what you can do about it



BY MAHAM ABEDI • GLOBAL NEWS

Posted June 12, 2019 4:46 pm

Updated June 12, 2019 4:48 pm

5

## FINANCIAL POST

## Les raisons peu connues pour lesquelles la pénurie de médicaments est devenue un problème chronique au Canada et dans le monde

*Santé Canada répertorie actuellement près de 2 000 médicaments comme étant en pénurie, un problème croissant qui a commencé en 2010*

CTV NEWS

HEALTH

## High-blood pressure drug shortage highlights wider problem in Canada

**RF** Regulatory Focus™

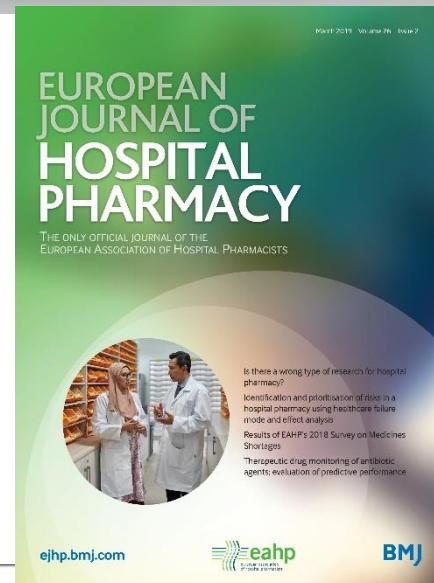
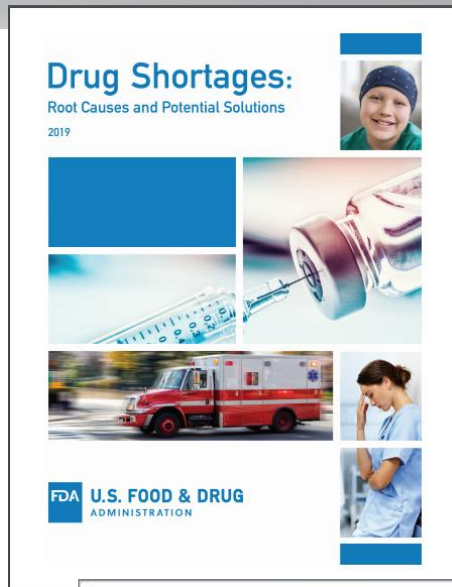
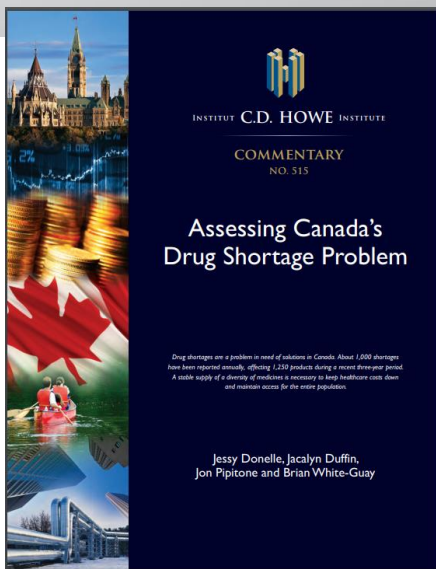
Regulatory Focus™ > News Articles > 2020 > 5 > Drug shortages in Germany – A critical appraisal

## Drug shortages in Germany – A critical appraisal

Posted 28 May 2020 | By Ralf D. Hess, MSc, PhD, Henric Wassmer, Siegfried Schmitt, PhD, Martin Hug, PhD, Anmar Marouf, PhD, Dominik M. Aumer, MBA, Moritz Hauke, MBA, Simon Schulz, MSc, PhD



# National and international organizations are identifying root causes and mitigation strategies



## Guide to reporting drug shortages and discontinuations



Canada



[www.ISPE.org/DrugShortagesPreventionPlan](http://www.ISPE.org/DrugShortagesPreventionPlan)

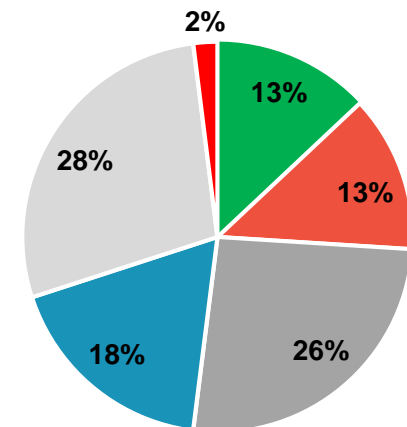


# Drug shortages are a global issue

Industry consolidation and globalization has increased the number of drug shortages internationally

- Drug shortages emerged as a major issue in 2010, and rather than being a local Canadian issue, affect countries worldwide.
- A significant number of mergers and acquisitions in the industry has resulted in fewer options for end users.
- An estimated 80% of the raw ingredients of the world's medicines are made in China and India, which are used to manufacture the active pharmaceutical ingredient (API).

Percentage of API Manufacturing Facilities for All Drugs by Country or Region, August 2019



■ Rest of World ■ China ■ EU ■ India ■ USA ■ Canada

Sources: <https://www.fip.org/files/content/priority-areas/medicines-shortages/fip-summit-on-medicines-shortage.pdf>, [https://www.cadth.ca/media/pdf/Drug\\_Supply\\_Disruptions\\_es-18\\_e.pdf](https://www.cadth.ca/media/pdf/Drug_Supply_Disruptions_es-18_e.pdf)

M&A activity [https://scholarship.law.duke.edu/cgi/viewcontent.cgi?article=6441&context=faculty\\_scholarship](https://scholarship.law.duke.edu/cgi/viewcontent.cgi?article=6441&context=faculty_scholarship)

API facilities <https://www.fda.gov/news-events/congressional-testimony/safeguarding-pharmaceutical-supply-chains-global-economy-10302019>

# Drug shortages are a global issue (continued)

## Factors contributing to shortages around the world

### ➤ Five primary conditions that introduce vulnerabilities in the global supply chain:

1. Globalization of Drug Supply Industry
2. Complexity and Responsiveness
3. Distribution and Inventories
4. Quality and Price
5. Procurement Practices



# Key Findings

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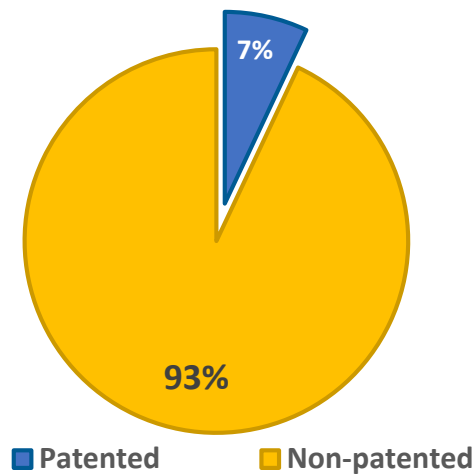
**1** Drug shortages have emerged as a serious global issue over the past decade

**2** The causes of drug shortages are complex and frequently tied to manufacturing and business decisions

**3** The definition of “drug shortage” as well as reporting requirements and mitigation strategies differ widely among countries

# Generic medicines are most vulnerable to shortage

The majority of drug shortages reported in Canada involve non-patented medicines



➤ **Non-patented medicines account for 93% of reported drug shortages in Canada.**

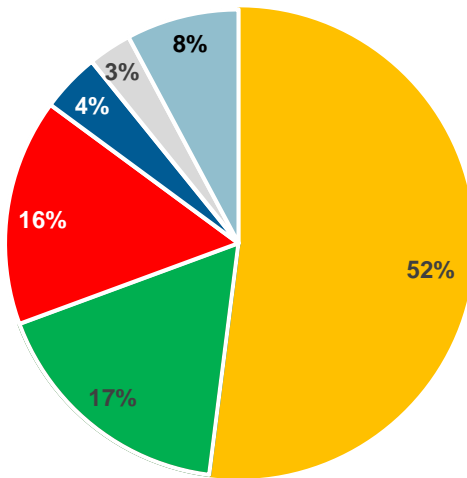
- Sterile injectables are particularly vulnerable to shortages due to their complicated and lengthy manufacturing processes.
- When one or two API manufacturers are the only producer of a particular generic drug, the risk of a shortage increases.

# Causes of drug shortages

- The majority of drug shortages arise as a result of manufacturing and quality issues during production.

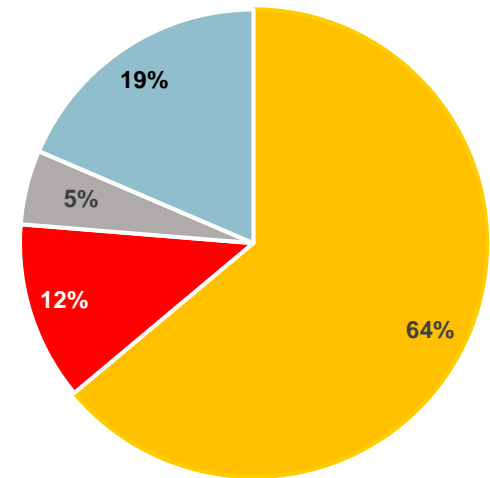
Canada

- Disruption of the manufacture of the drug
- Delay in shipping of the drug
- Demand increase for the drug
- Requirements related to good manufacturing practices
- Shortage of an active or inactive ingredient
- Other



United States

- Manufacturing and quality issues
- Increase in demand
- Natural disaster
- Other



Data source: [drugshortagescanada.ca](http://drugshortagescanada.ca)

Data Source: <https://www.fda.gov/media/131130/download>. Values were adjusted to exclude discontinuations.

# National and international effects of tendering

Tendering can be associated with drug shortages through shifts in demand

- **Issues may arise with production or distribution when single-source tendering is used.**
- **The WHO Fair Pricing Forum, April 2019**
  - Numerous root causes for shortages were discussed, including centralized manufacturing sites and awarding of specific tenders to a small group of companies.
  - The European Society of Medical Oncology (ESMO) convened an international consortium to study the availability of medicines internationally and develop strategic plans to mitigate shortages at global and local levels.
- **In 2018, the pan-Canadian Pharmaceutical Alliance (pCPA), with the Canadian Generic Pharmaceutical Association (CGPA) developed a five-year initiative:**
  - Reduce the prices of nearly 70 of the most commonly prescribed drugs in Canada by 25% – 40%.
  - Tendering is not part of this initiative.

Sources: Dranitsaris, G et al, Drug tendering: drug supply and shortage implications for the uptake of biosimilars. 2017, <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5628685/>

WHO Fair Pricing Forum Report: [https://www.who.int/medicines/access/fair\\_pricing/fair\\_price\\_report\\_2019/en/](https://www.who.int/medicines/access/fair_pricing/fair_price_report_2019/en/)

pCPA-CGPA initiate: <https://canadiangenerics.ca/news-release62/a-joint-statement-from-the-pan-canadian-pharmaceutical-alliance-and-the-canadian-generic-pharmaceutical-association/>

# Key Findings

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- 1 Drug shortages have emerged as a serious global issue over the past decade
- 2 The causes of drug shortages are complex and frequently tied to manufacturing and business decisions
- 3 The definition of “drug shortage” as well as reporting requirements and mitigation strategies differ widely among countries

# Drug Shortages in Canada

## Recent changes to Canadian reporting standards

- **High-profile 2012 shortage led to emergency debate in the House of Commons**
  - Creation of the Multi-Stakeholder Steering Committee on Drug Shortages (MSSC)
  - Creation of a [www.drugshortages.ca](http://www.drugshortages.ca), a website for voluntary shortage reporting managed by IMC
- **On March 14, 2017, reporting became mandatory on a new website overseen by Health Canada, [www.drugshortagescanada.ca](http://www.drugshortagescanada.ca)**
  - Number of reports increased 100% over those on the voluntary website

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CANADA

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# Drug shortages in Canada (continued)

## Reporting strategies

- In Canada, drug shortage is defined as **“a situation in which an authorization holder for a drug is unable to meet the demand for the drug”**.
- Mandatory requirement for manufacturers to report all shortages (anticipated, actual, and discontinuations) on [www.drugshortagescanada.ca](http://www.drugshortagescanada.ca).
  - Nearly 2,000 drugs are currently in shortage in Canada.
- Drug shortages are a multi-stakeholder responsibility, requiring the coordinated involvement of federal, provincial and territorial (P/T) governments, health professional associations and industry associations.
- **The P/T Drug Shortages Task Team coordinates communication requirements, to confirm and assess the status and details of a drug shortage.**
  - **Tier 1:** Anticipated shortages
  - **Tier 2:** Actual shortages
  - **Tier 3:** Shortages with the greatest potential impact

# Drug shortages reporting internationally

## EMA and FDA regulation



EUROPEAN MEDICINES AGENCY  
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- EMA drug shortages catalogue is limited.
- Most shortages are dealt with at the national level.
- The definition of shortages and scope of reporting system is not uniform.
- Causes for drug shortages are under-reported.
- Limited number of countries have publicly available reporting systems.
- FDA drug shortages database covers current and resolved shortages updated regularly.
- Manufacturers are required to report information about a shortage, the reasons and the expected duration of the shortage on the FDA website.
- The American Society of Health System Pharmacists (ASHP) also lists drug shortages and additional information.
- The Center for Drug Evaluation and Research (CDER) was established to address potential or actual shortages of drugs with significant impact on public health.

# Comparison of national reporting systems

Country	Published reports for <u>ALL</u> shortages	Published reports for <u>CRITICAL</u> shortages	Anticipated shortages	Report reason/cause of shortage	Frequency of database updates
Canada	✓	✓	✓	✓	Daily
Australia		✓		✓	Daily
Belgium	✓	✓	✓	✓	Daily
Germany		✓			After each notification
France		✓		✓	
Italy		✓		✓	Weekly
Norway	✓	✓	✓	✓	Weekly
Spain		✓			After each notification
Sweden		✓			Daily
United Kingdom		✓			
Switzerland		✓			After each notification
United States		✓		✓	Daily

# Differences in Reporting Systems

## International comparisons

- Types of medicine shortages reported in national databases greatly differ between countries and data is not necessarily located in one central repository.
- **While MAHs have to report all expected or current shortages in some countries** (e.g. Canada, Belgium, Norway), **in other countries they only have to do so for “essential medicines”** (e.g. Australia, France, Switzerland, United States).
- **Additional online databases held by non-government entities also report shortages in certain countries** (e.g. Australia, France, Switzerland, the United Kingdom and the United States).
- In Europe, MAHs are requested to notify the European Medicines Agency (EMA) for all centrally approved product shortages with a list of all countries impacted.

# Literature to guide the mitigation of drug shortages

## Canada

- Protocol for the Notification and Communication of Drug Shortages
- Guidance Document to Mitigate Drug Shortages through Contracting and Procurement
- Preventing Drug Shortages: Identifying Risks and Strategies to Address Manufacturing-Related Drug Shortages in Canada

## EMA

- Reflection paper on medicinal product supply shortages caused by manufacturing
- Guidance for marketing authorization holders on reporting of shortages in the EU
- Good practice guidance for communication to the public on medicines' availability issues

## United States

- Drug Shortages: Root Causes and Potential Solutions

## Global

- WHO: Medicines shortages Global approaches to addressing shortages of essential medicines in health systems
- WHO: Fair Pricing Forum, 2019
- ISPE: Drug Shortage Assessment and Prevention Tool

# Comparison of national policy on drug shortages

Country	Recommendations on mitigation strategies	Mandatory reporting for <u>ALL</u> drug shortages	Importation from other countries	Alternatives/ Substitutions	Updated policy measures within the last 5 years
Canada	✓	✓	✓		✓
Australia	✓		✓		
Belgium	✓	✓	✓	✓	✓
Germany	✓		✓		✓
France	✓		✓		✓
Italy	✓	✓	✓	✓	✓
Norway	✓	✓	✓	✓	✓
Spain	✓	✓	✓	✓	✓
Sweden	✓	✓	✓	✓	✓
United Kingdom		✓	✓		
Switzerland			✓		
United States	✓		✓		✓

# Differences in Policy Systems

## International comparisons

- In most EU countries, MAHs are legally obligated to report a shortage to national authorities for all medicines at least two months prior to the expected shortage.
- Health Canada requires notification within six months in advance of an expected shortage.
- Some countries require MAHs to adopt risk management plans (e.g. France).
- In Europe, many countries have introduced Public Service Obligations (PSOs).
  - To maintain appropriate and continued supply of a medicinal product to pharmacies to ensure the needs of patients are covered.

# In summary

## The importance of mitigating drug shortages is a global priority

- The main causes of drug shortages are due to complex supply chains that lead to manufacturing and quality issues.
- Canada fares well in comparison to other countries for reporting drug shortages.
- The definition of “drug shortage” as well as reporting requirements, and mitigation strategies differ widely among countries.
- Many countries have made strides in recent years to mitigate shortages through proposing legislative solutions and implementing reporting obligations and sanctions.





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# Part 2

Are Canadian shortages associated with lower prices than in other countries?



Étienne Gaudette, PhD and Yvonne Zhang

July 16, 2020

# Introduction

## Background

- It is well documented that shortages are more prevalent in low-priced older generics, but the role of prices is unclear from an international perspective.
- International supply chains could favor countries with higher prices when there are production disruptions, leading to shortages in countries with lower prices.

## Objective

- Answer the question: “Are Canadian shortages associated with lower prices than in other countries?”

## Methodology

- Use Canadian drug shortages data and international drug sales data to study the relationship between international price ratios and shortage rates.
- Data sources: [www.drugshortagescanada.ca](http://www.drugshortagescanada.ca) and IQVIA MIDAS®.

# Key Findings

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1

Over 90% of drug shortages occur in the non-patented space.

2

There is no clear association between the relative price of medicines and shortages.

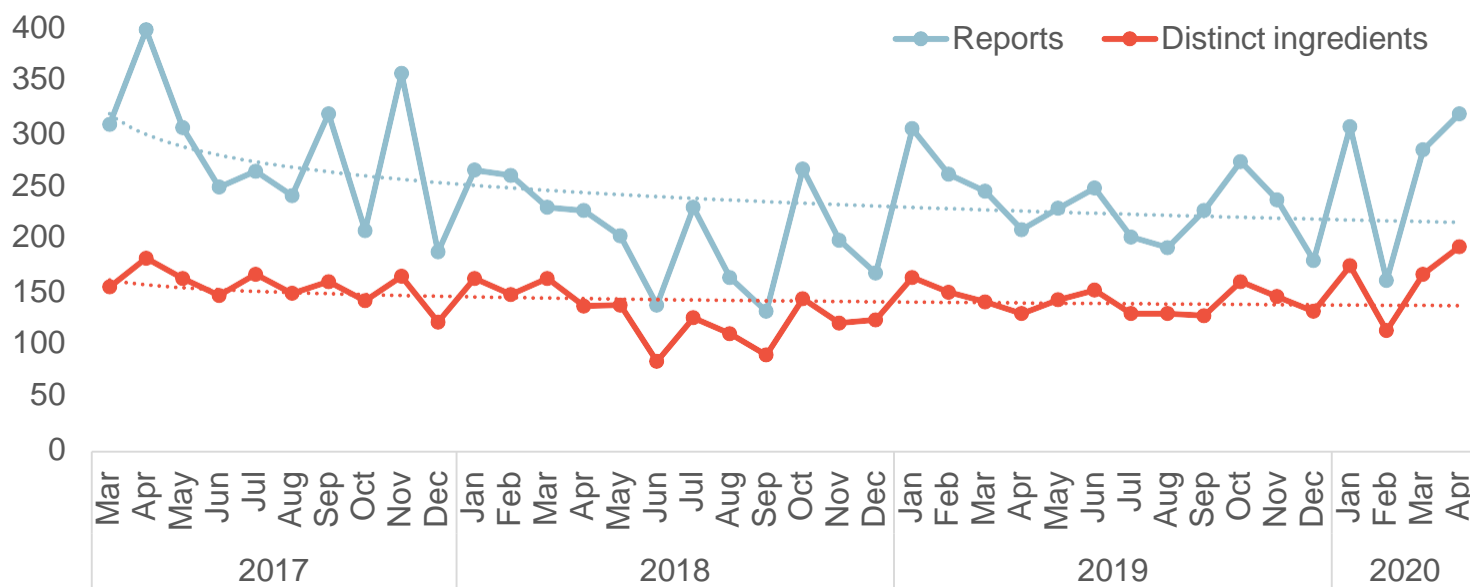
# Recent trends in Canadian shortages

- We use [www.drugshortagescanada.ca](http://www.drugshortagescanada.ca) data to explore Canada's drug shortages from March 2017 to April 2020.
  - Trends in the number of shortage reports filed every month and ingredients going in shortage
  - Shortage outcomes and duration
  - Patented status of medicines in shortage
  
- Shortages are reported by manufacturers at the drug identification number (DIN) and package size level
  - Each distinct strength, form, and packaging size of a pharmaceutical ingredient in shortage are reported separately

# 243 new shortages are reported every month on average

Monthly shortage reports filed monthly on the Drug Shortages Canada website, 2018 to 2020

- Monthly shortages reported range between 133 (in Sept. 2018) and 398 (Apr. 2017)
  - Fluctuations in part due to multiple reports for the same ingredient
  - Distinct ingredients in shortage more stable, with a mean of 145/month
- A downward trend in reports is noted until mid-2018

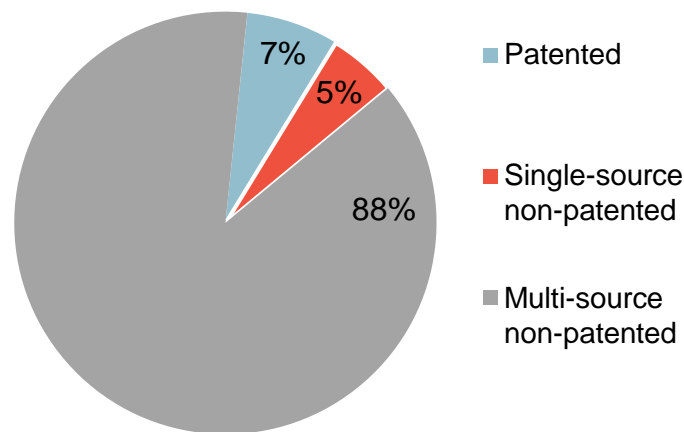


# Non-patented medicines account for most shortages

Distribution of reports by market segment and top five manufacturers by report count, 2017 to 2020

- A vast majority of shortage reports concern non-patented medicines (93%, N=8,577/9,230)
- Manufacturers of generic medicines produce the most reports

**Shortage Reports by Market Status**



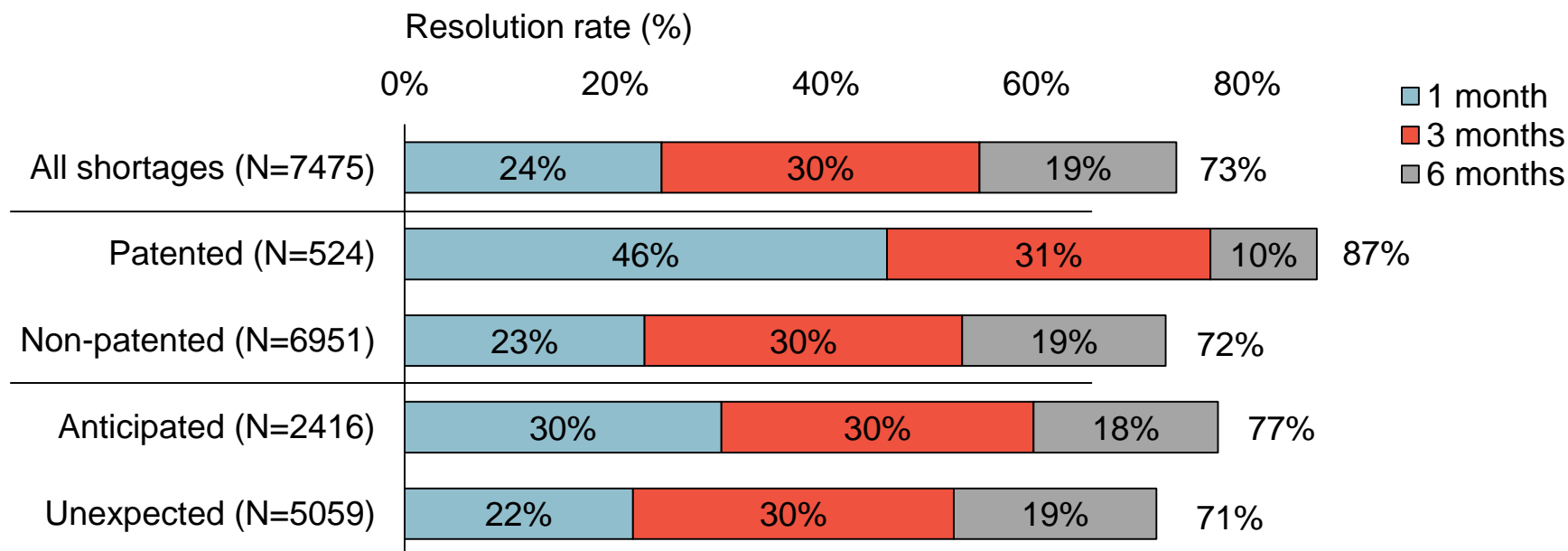
**Generic manufacturers with the Most Reports**

Rank	Reports	% of Total
1	1,247	14%
2	963	10%
3	759	8%
4	686	7%
5	416	5%
<b>Top 5</b>	<b>4,071</b>	<b>44%</b>

# 1 Resolution rates by 1, 3, and 6 months

Resolution rates 1, 3, and 6 months after a shortage report status becomes “actual”, 2017 to 2020

- Only a quarter of shortages are resolved within one month (N= 1,824 / 7,475)
  - 27% still unresolved after 6 months (N=1,997 / 7,475)
- Patented medicines and medicines for which shortages are anticipated have higher resolution rates



Sources: [www.drugshortagescanada.ca](http://www.drugshortagescanada.ca), PMPRB. Note: the figure excludes reports that became actual less than 6 months prior to the data export. A report is “Patented” if the drug identification number (DIN) was patent-protected in the year of the report creation. “Anticipated” and “Unexpected” reports had an “Anticipated shortage” and “Actual shortage” status at creation, respectively.

# Key Findings

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**1** Over 90% of drug shortages occur in the non-patented space.

**2** There is no clear association between the relative price of medicines and shortages.

# 2 Approach

- We link [www.drugshortagescanada.ca](http://www.drugshortagescanada.ca) with international data from IQVIA MIDAS® to study relationships between relative prices and shortage rates
  - We focus on year 2019 and present 2018 as a comparison year
  - A medicine is assigned “In shortage” status if at least one shortage report was filed for the medicine during the year
  - To allow for price comparison consistency, the analysis is restricted to oral solid medicines with at least 3 international price comparisons

# 2 Sample overview, 2019

## Summary statistics of medicines included in the analysis

- Not all medicines sold in Canada have direct equivalents in other countries
- Our analysis includes 19.8% of oral solid medicines (N=1,447 / 7,300), but captures 57.8% of total revenues
- Patented, brand, and high market medicines are overrepresented in our sample
- We conduct subgroup analyses by market segment and market size

	All oral solid medicines		Included in analysis: 3+ international price comparisons	
	N	%	N	%
Total count	7,300	100%	1,447	100%
Market segment				
Patented	717	10%	477	33%
Single-source non patented	726	10%	50	3%
Multiple source non patented	5,857	80%	920	64%
Generic status				
Generic	4,800	66%	699	48%
Brand	1,337	18%	739	51%
Uncategorized	1,163	16%	9	1%
Market size (molecule level)				
Less than \$1M	2,292	31%	267	18%
\$M1 to \$M5	2,435	33%	492	34%
\$M5 to \$M10	1,002	14%	242	17%
\$M10 and over	1,571	22%	446	31%
Form				
Tablet	5,622	77%	1,169	81%
Capsule	1,678	23%	278	19%
Total revenue (\$B)	14.2		8.2	

## 2 Foreign-to-Canadian price ratios (FTC)

- To compare prices of Canadian medicines to international prices, we use Foreign-to-Canadian price ratios (FTC), where the price level in Canada is set to one:

- $\text{FTC of medicine } X = \frac{\text{Price of medicine } X_{\text{Germany}}}{\text{Price of medicine } X_{\text{Canada}}} = 0.9$
- When  $\text{FTC} > 1$ , the Canadian price is *lower* than that of other countries
- When  $\text{FTC} < 1$ , the Canadian price is *higher* than that of other countries
- When  $\text{FTC} = 1$ , the Canadian price is *perfectly aligned* with other countries

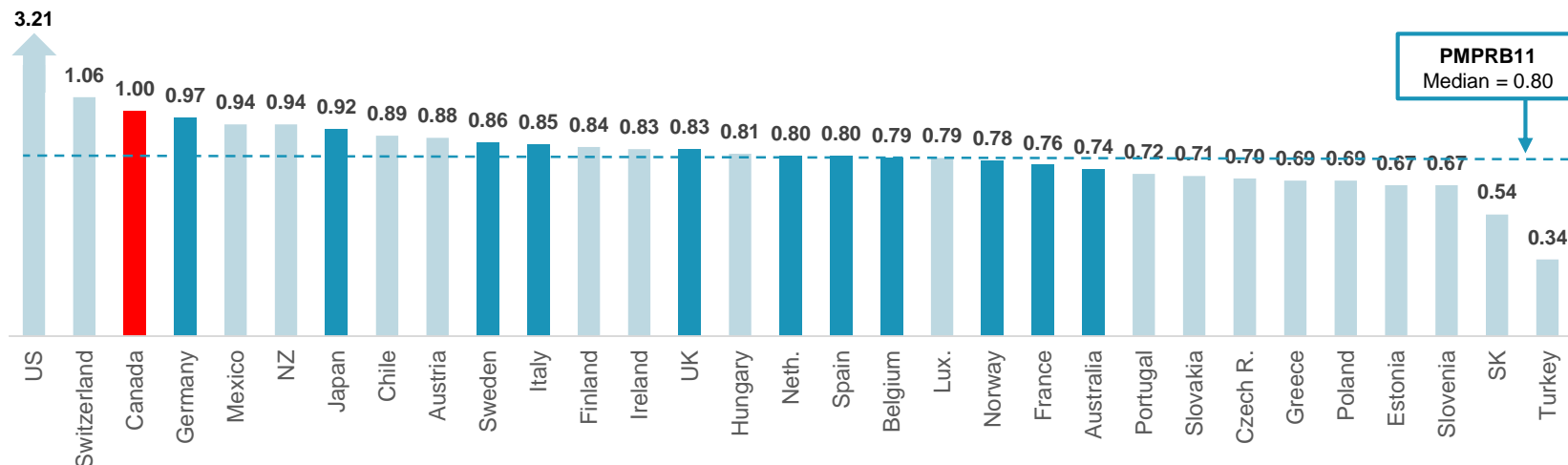
## 2 Canadian prices are higher than those of other countries

Multilateral foreign-to-Canadian price ratio (FTC), OECD, 2017

➤ For each medicine, we find the median FTC across the PMPRB11 comparator countries:

- Australia, Belgium, France, Germany, Italy, Japan, the Netherlands, Norway, Spain, Sweden and the United Kingdom

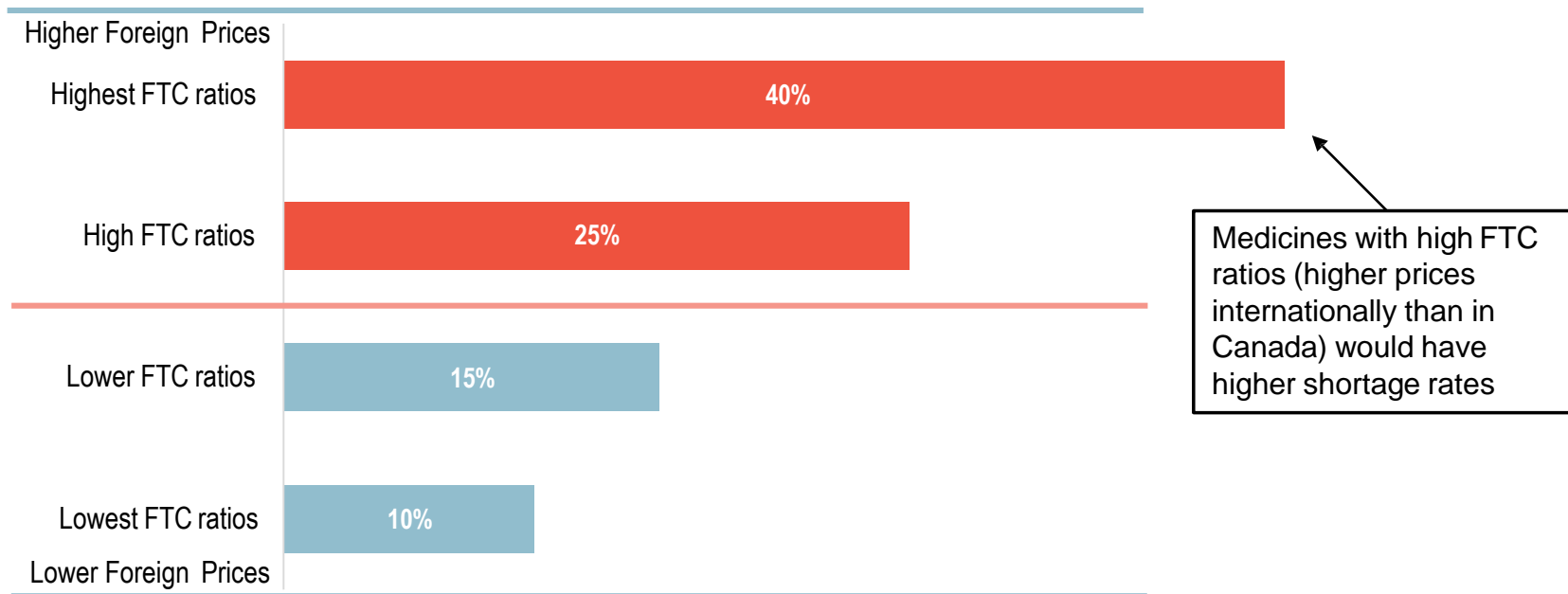
➤ Prices of medicines in most OECD countries are lower than in Canada, such that most FTCs are below 1:



## 2 Shortage rates by price ratio

### Hypothesis to test

- We graph shortage rates by Foreign-to-Canadian price ratio (FTC) range
- If lower Canadian prices were associated with more shortages, we would find higher shortage rates in medicines with high FTCs, for example:

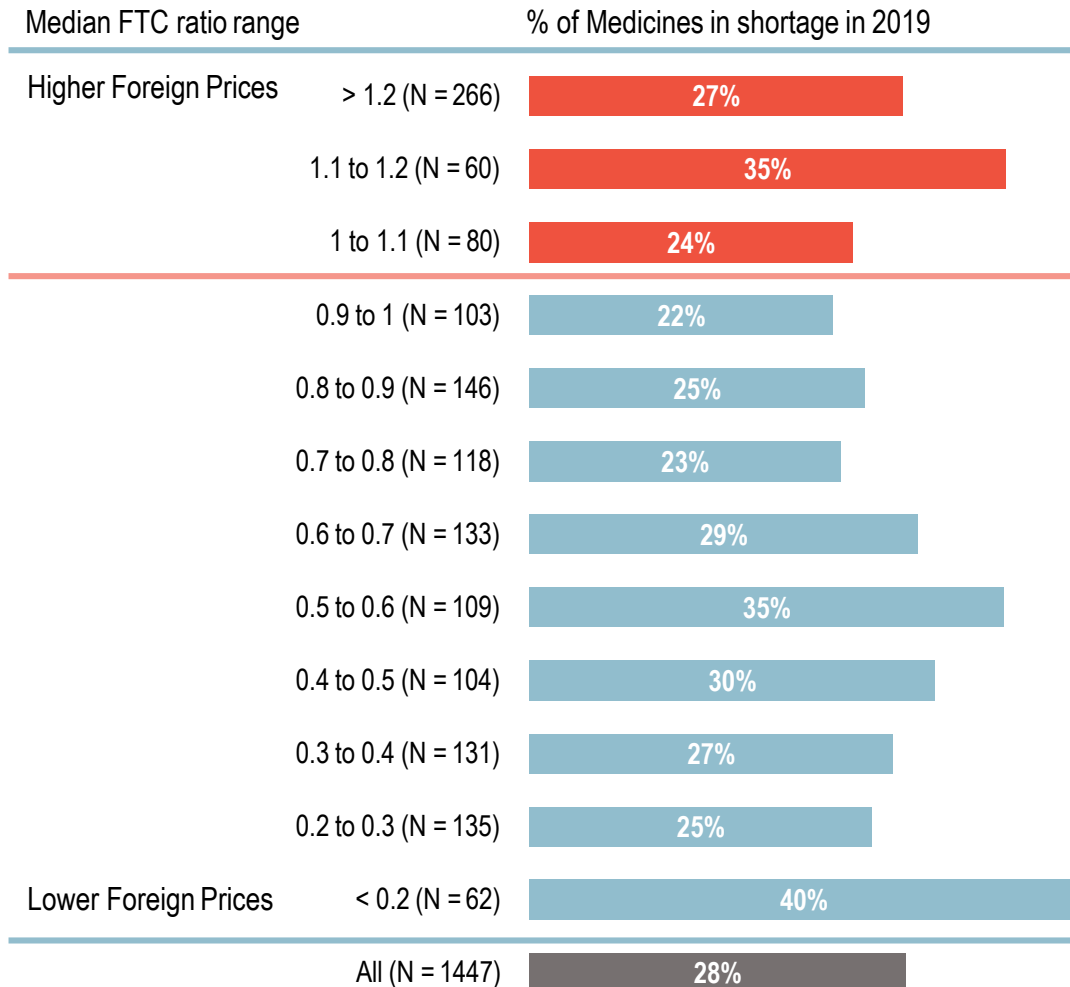


# 2 No clear association between FTC ratio and shortage rates

Proportion of medicines in shortage by median FTC, PMPRB11, 2019

- No clear association is observed between higher foreign prices and rates of shortages

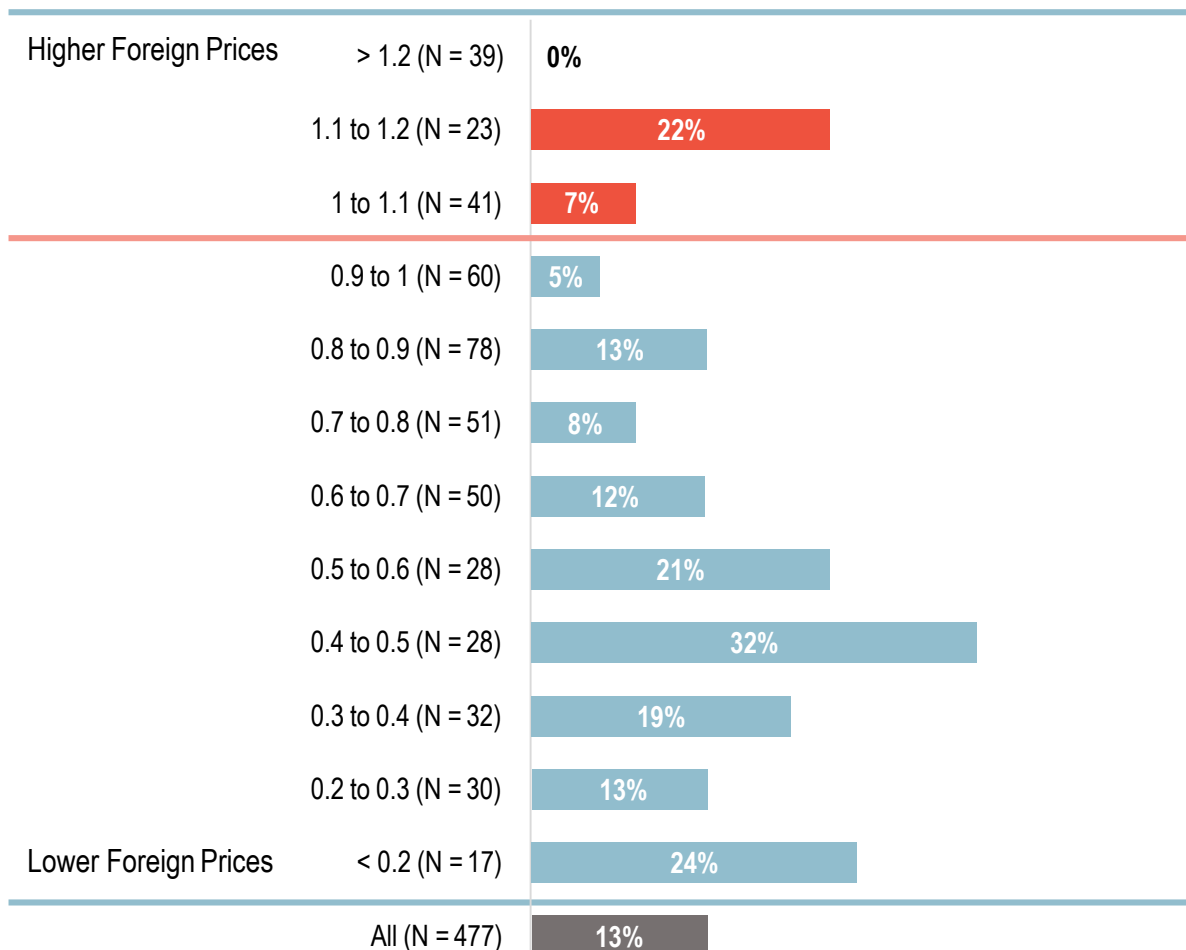
- Medicines within four of the six lowest FTC ratio ranges have higher shortage rates than the average (28%)
  - Medicines with significantly *higher* Canadian prices



## 2 No clear association for patented medicines...

Proportion of patented medicines in shortage by median FTC, PMPRB11, 2019

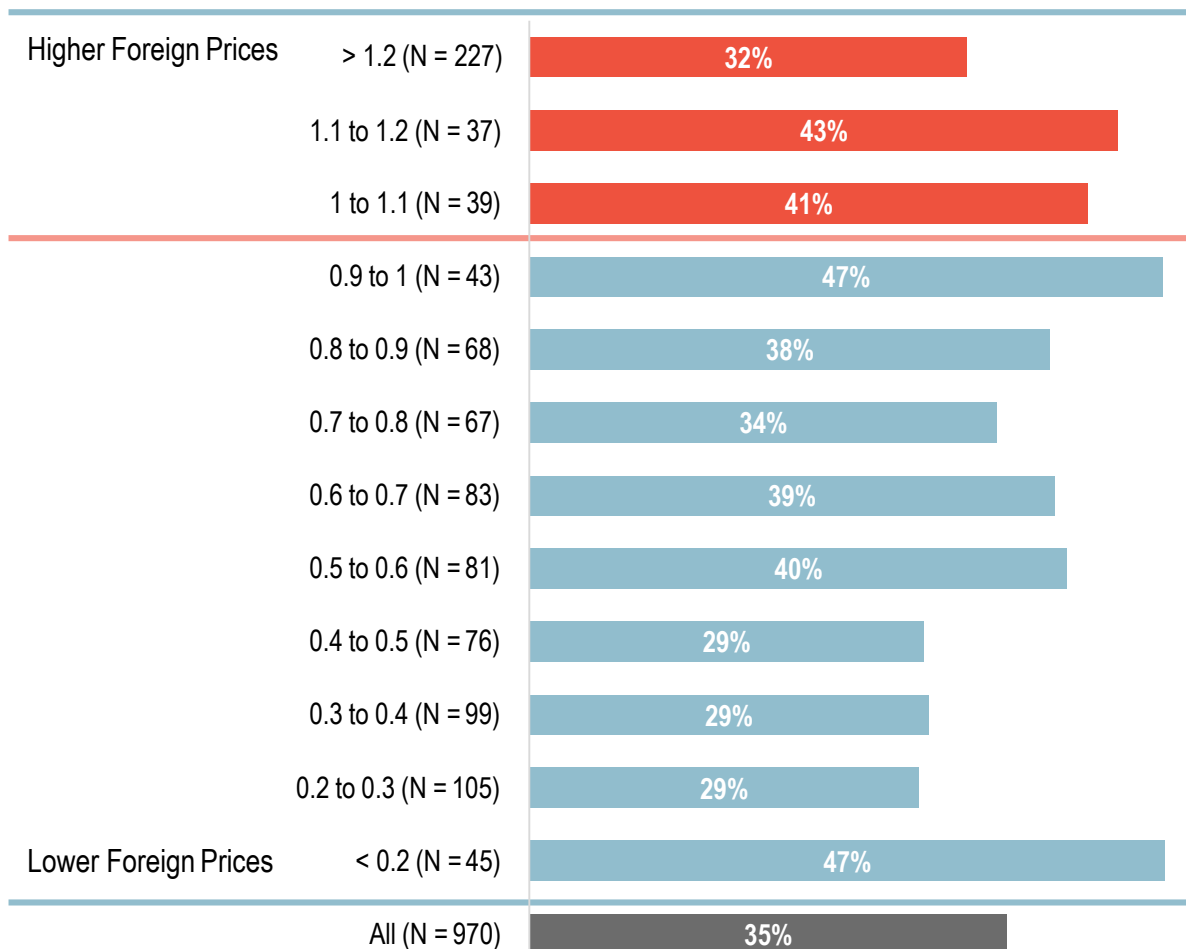
- No clear association is observed in this segment
- Highest shortage rates are observed for lower FTC bins
  - Medicines with significantly *higher* Canadian prices



## 2 ... and non-patented medicines

Proportion of non-patented medicines in shortage by median FTC, PMPRB11, 2019

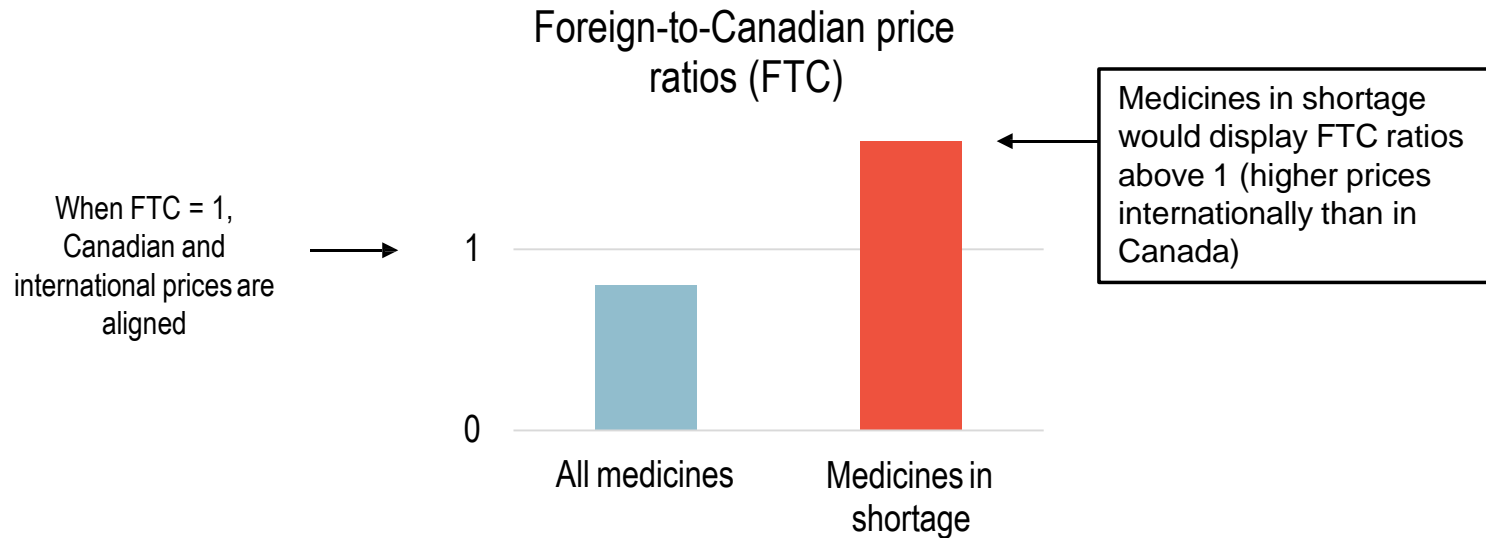
- There is also no clear association observed in this segment
- Shortage rates are mostly uniform across FTC ranges
- Most medicines shown here are multi-source non-patented (N=920)



## 2 Price ratios of medicines in shortage

### Hypothesis to test

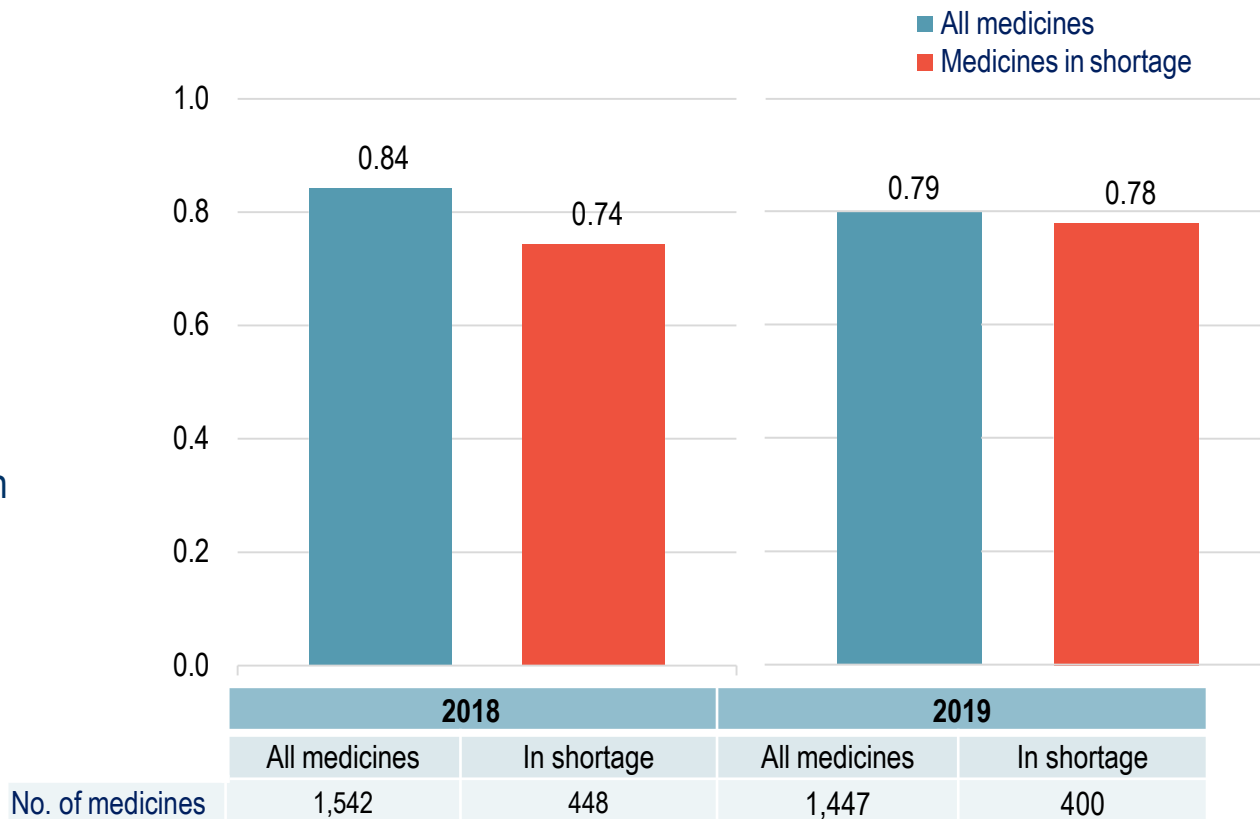
- If lower Canadian prices than in other countries were associated with more shortages, we would find many FTCs above 1 among drugs in shortages, for example:



## 2 Medicines in shortage in Canada are priced *higher* than in comparator countries

Median FTC of medicines by shortage status, PMPRB11, 2018 and 2019

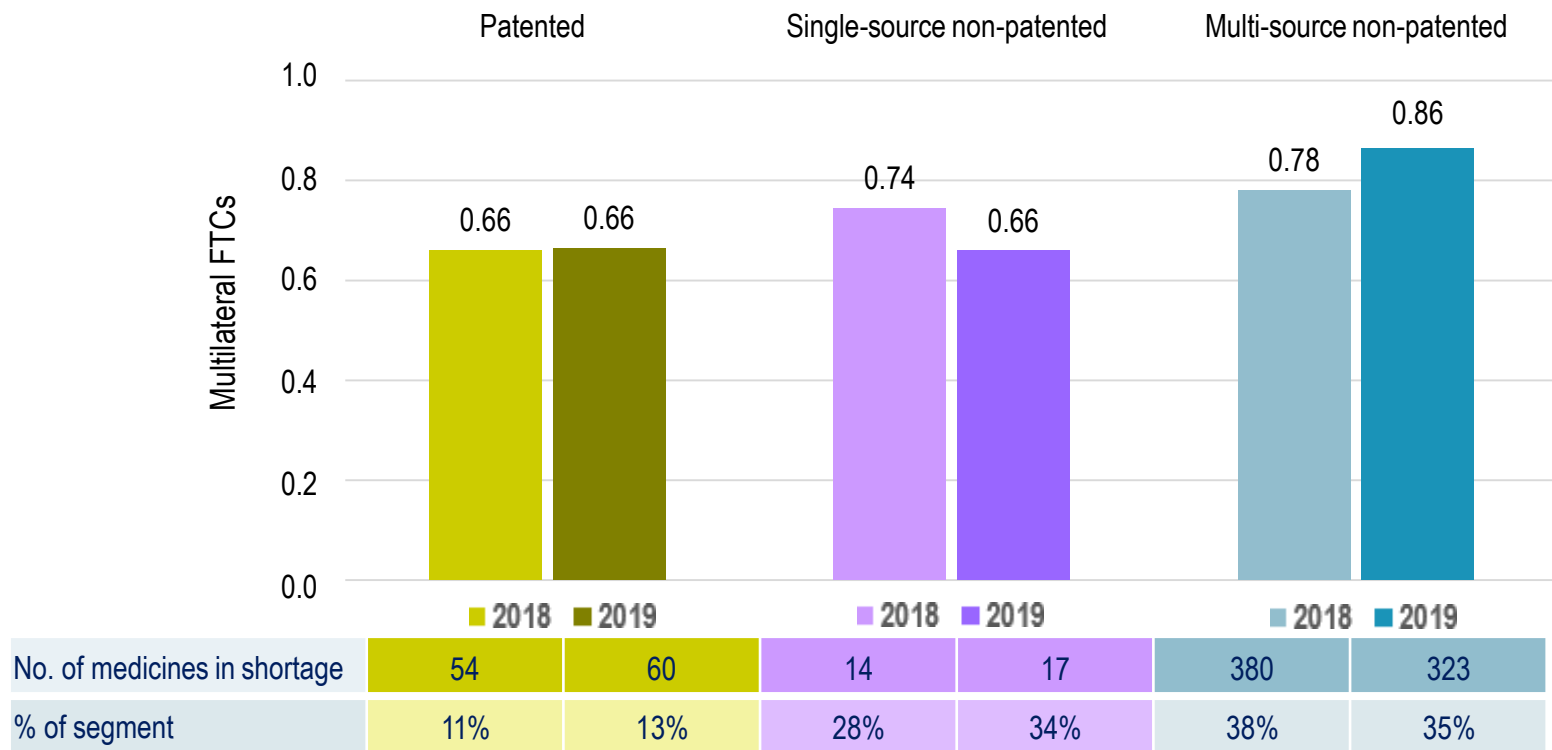
- The median FTCs of medicines in shortage in Canada are below 1
  - Prices in comparator countries are lower than in Canada
- Price ratios of medicines in shortage are slightly lower or about equal to those of the overall sample



# 2 Canadian prices of medicines in shortage are *higher* than comparator countries for all market segments...

Median FTC of medicines in shortage by market segment, PMPRB11, 2018 and 2019

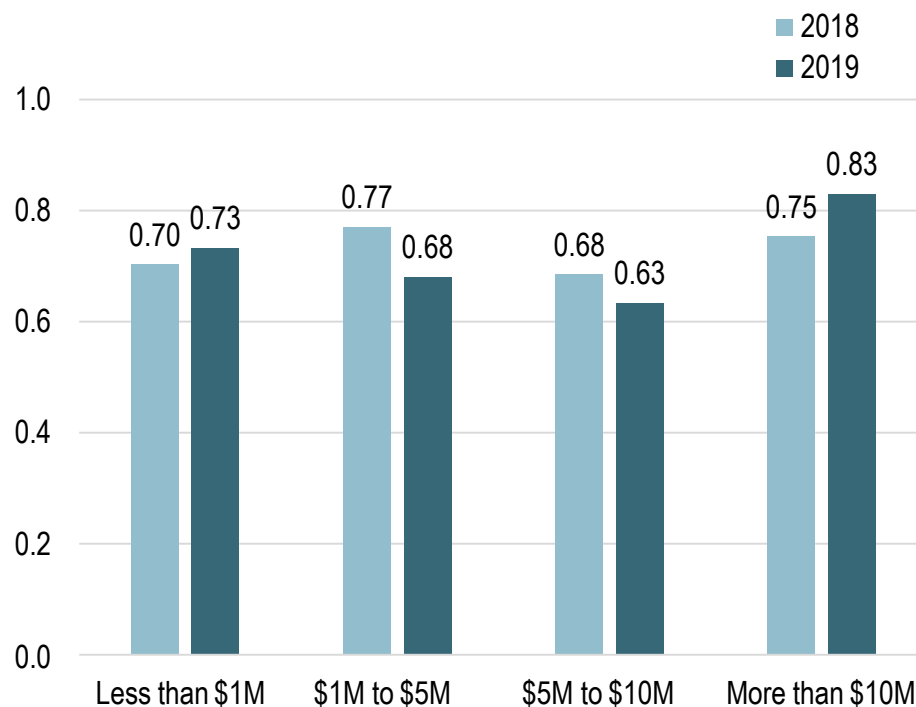
- The median FTCs of medicines in shortage in Canada are below 1 for all market segments
  - Prices in comparator countries are lower than in Canada



## 2 ... and all market sizes

### Median FTC of medicines in shortage by market size, PMPRB11, 2019

- Prices of medicines in shortage in Canada are higher than foreign prices for all market size categories



	2018	2019	2018	2019	2018	2019	2018	2019
No. of medicines in shortage	51	49	148	147	103	78	146	126
% of segment	19%	18%	29%	30%	35%	32%	32%	28%

# Conclusion

- **We do not find an association between lower prices in Canada and drug shortages**
- **More work is needed to confirm and clarify our findings**
  - Conduct multivariate statistical analysis of the factors contributing to shortages
  - Analyze price dynamics before and after shortages using quarterly data
    - During a shortage, the supply contraction is expected to lead to higher prices
- **Next steps will feature collaboration with stakeholders**
  - Health Canada and public insurers



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# Part 3

A Canadian drug shortage case study with  
international price comparisons



**Brian O'Shea**

July 16, 2020

# Amantadine case study: objectives and methods

## ➤ Objectives:

1. Illustrate how the impact of a drug shortage in Canada can be seen across a variety of data sources throughout the supply chain
2. Compare the Canadian experience with price levels and unit volume changes in other countries

## ➤ Data sources used:

- **Reports** filed to Drug Shortages Canada website
- **Wholesaler sales:** IQVIA Canadian Drug Store and Hospital Purchases Audit (CDH)
- **Retail sales:** IQVIA Payer Insights database
- **Public drug plan claims:** NPDUIS Database from the Canadian Institute for Health Information (CIHI)
- **International comparisons:** IQVIA MIDAS® Database

# Amantadine background information

- Used in treatment of Parkinson's Syndrome, and in the short-term management of drug-induced extrapyramidal symptoms [e.g. from antipsychotics].
- A single manufacturer in Canada produces both the cap and syrup forms of amantadine.
  - Last competitor effectively ceased sales prior to 2016
- Due to a drug shortage caused by “disruption of manufacture of drug”, amantadine wholesaler cap sales ceased in Canada for most of 2017
  - Shortage received some media attention at the time: [Apr 2017 CBC article](#) ‘You cannot just stop these medications’: no end in sight for Parkinson's drug shortage
  - Syrup shortages reported later on due to “demand increase for drug”, as cap patients switched to the syrup form

Product	Form / strength	Patent status	2018 Sales (CDH)
Amantadine	cap 100mg	generic	\$2.3M
	syrup 50mg/500mL	generic	\$1.6M

# Shortage reports imply a shift to amantadine syrup due to shortage of the cap form

## ➤ Amantadine cap shortage (447 days):

- Nov 2016 to Feb 2018
- Reason for shortage: “Disruption of the manufacture of the drug.”
- Company comments on drug shortage report include “NOTE: limited stock available”

## ➤ Subsequent amantadine syrup shortages due to “Demand increase for the drug”:

1) Apr 18, 2017 to May 24, 2017 (36 days)

- Occurred a few months after cap shortage began, and was likely due to patients switching to the syrup from the cap

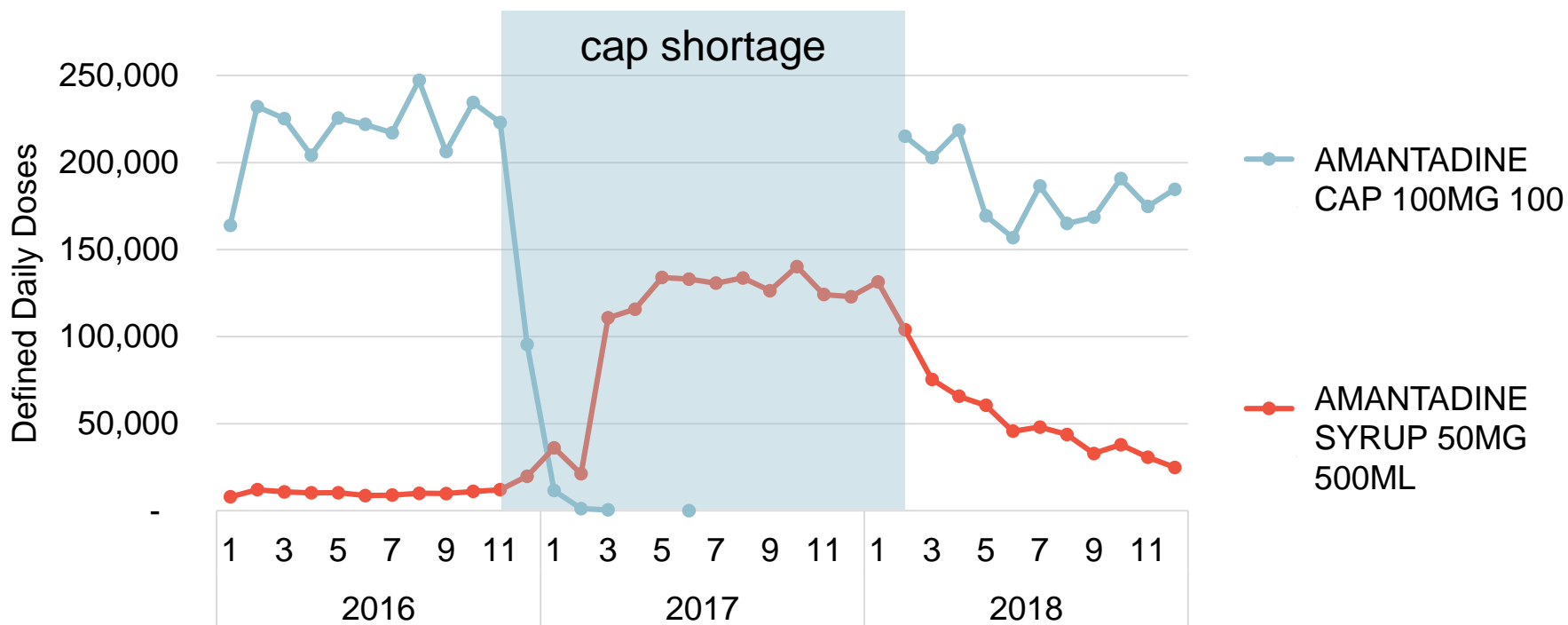
2) Nov 23, 2018 to Jan 7, 2019 (45 days)

- This shortage occurred months after the cap shortage was resolved in Feb 2018
- Company comments for this report: “AMANTADINE HCl 100mg CAPS 100 remain available.”

# Drug shortage effects on supply chain start with wholesaler purchases of amantadine caps and syrup

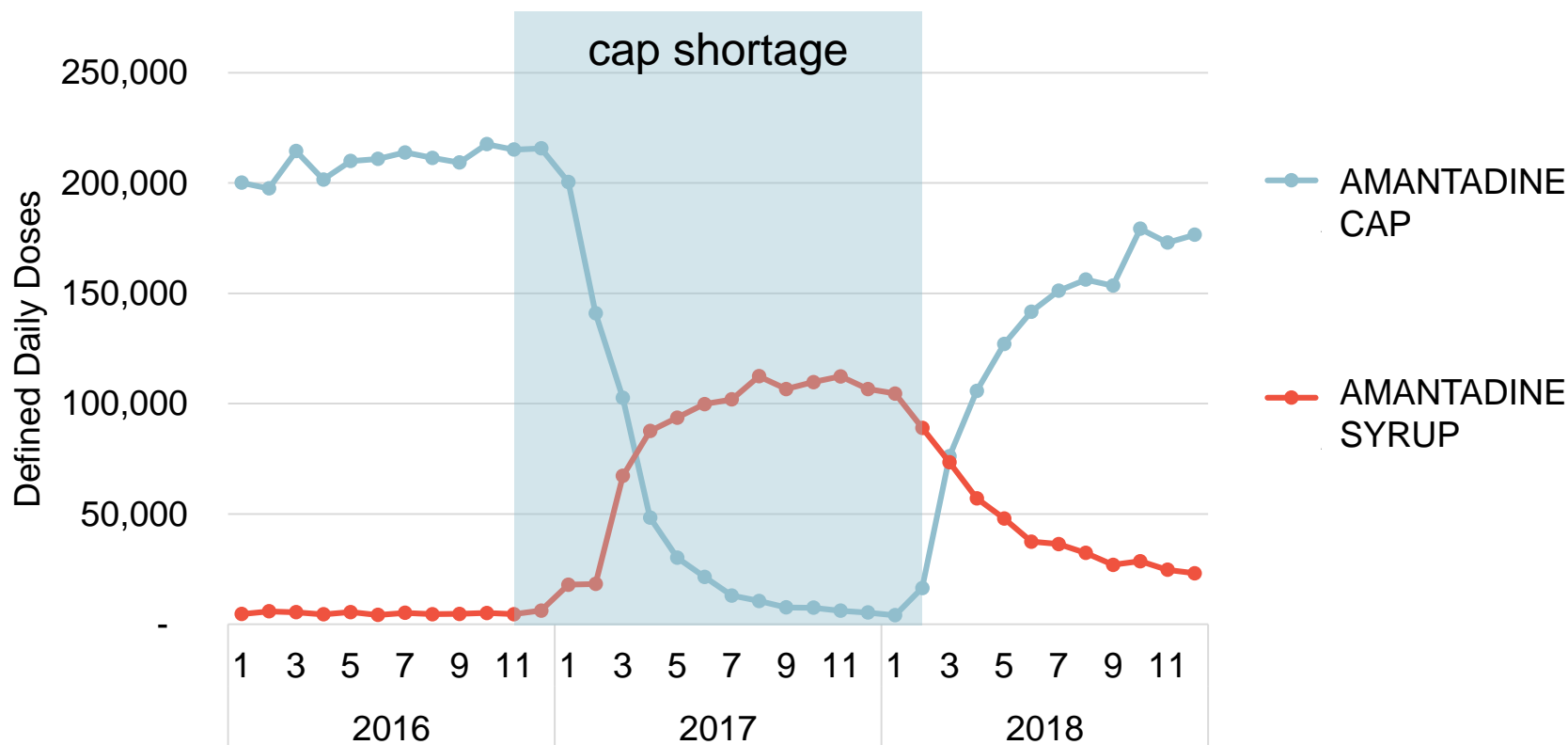
Unit volumes standardized to 200mg defined daily dose for long-term Parkinsons treatment

- Monthly wholesaler unit volumes show drop-off in cap sales and corresponding increase in syrup units for the duration of the cap shortage



# Pharmacy sales of amantadine show a similar switch to syrup as cap volumes run low

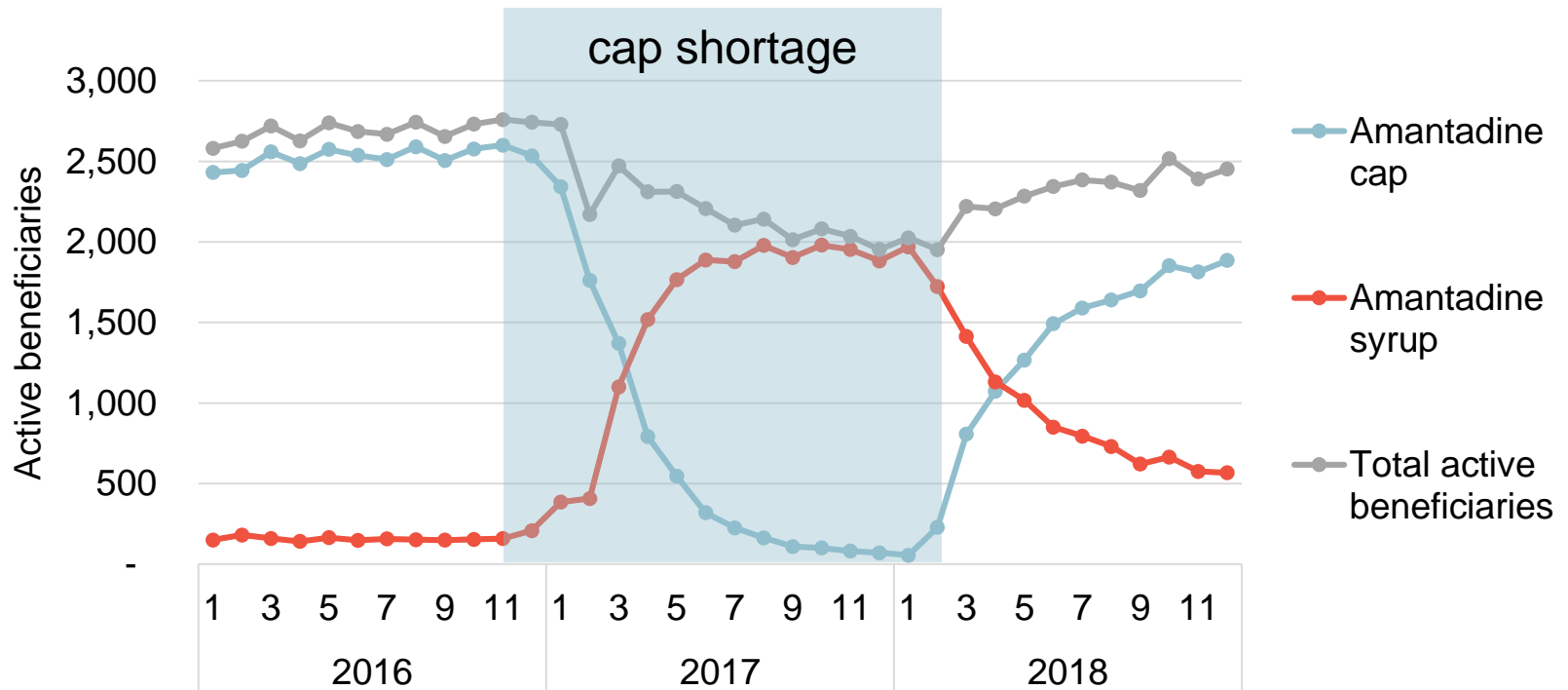
Unit volumes standardized to 200mg defined daily dose for long-term Parkinsons treatment



- Cap retail sales start declining in Jan 2017, about one month after wholesaler units
- Avg monthly DDD in 2017 was 39% lower than Oct 2016, before cap shortage began

# Public plan data indicate not all cap patients switched to syrup

Total active beneficiary population declined despite increase in syrup prescriptions



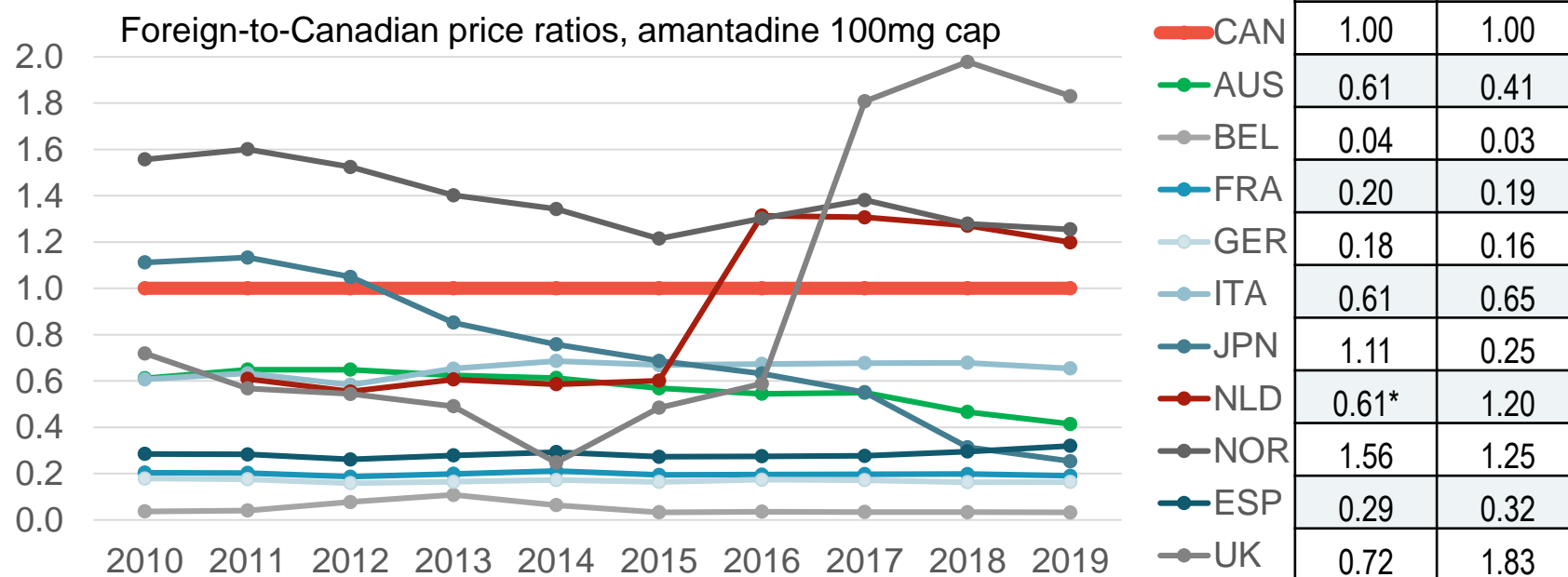
- Public plan claim data shows a shift from cap to syrup, but total active beneficiaries still declined
- Total monthly active beneficiaries in 2017 were 20% lower on average than in Oct 2016, but total annual beneficiaries for all amantadine products only declined 7% in 2017

Source: National Prescription Drug Utilization Information System Database, Canadian Institute for Health Information, 2016 to 2018. Plans included: British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador, Yukon, and the Non-Insured Health Benefits Program.

# Canadian amantadine capsule prices have been among the highest in the PMPRB11 over the past decade

2017 Canadian shortage does not appear to be due to lower pricing than in comparator countries

- Foreign-to-Canadian price ratios have increased for the UK and Netherlands, but stayed relatively consistent or declined in other PMPRB11 countries over the past decade
  - Canadian amantadine shortage occurred in 2016-17, when Canadian prices were 4<sup>th</sup> – highest after the UK, Norway, and the Netherlands
  - PMPRB11 median price ratio fell from 0.61 in 2010 to 0.37 in 2019

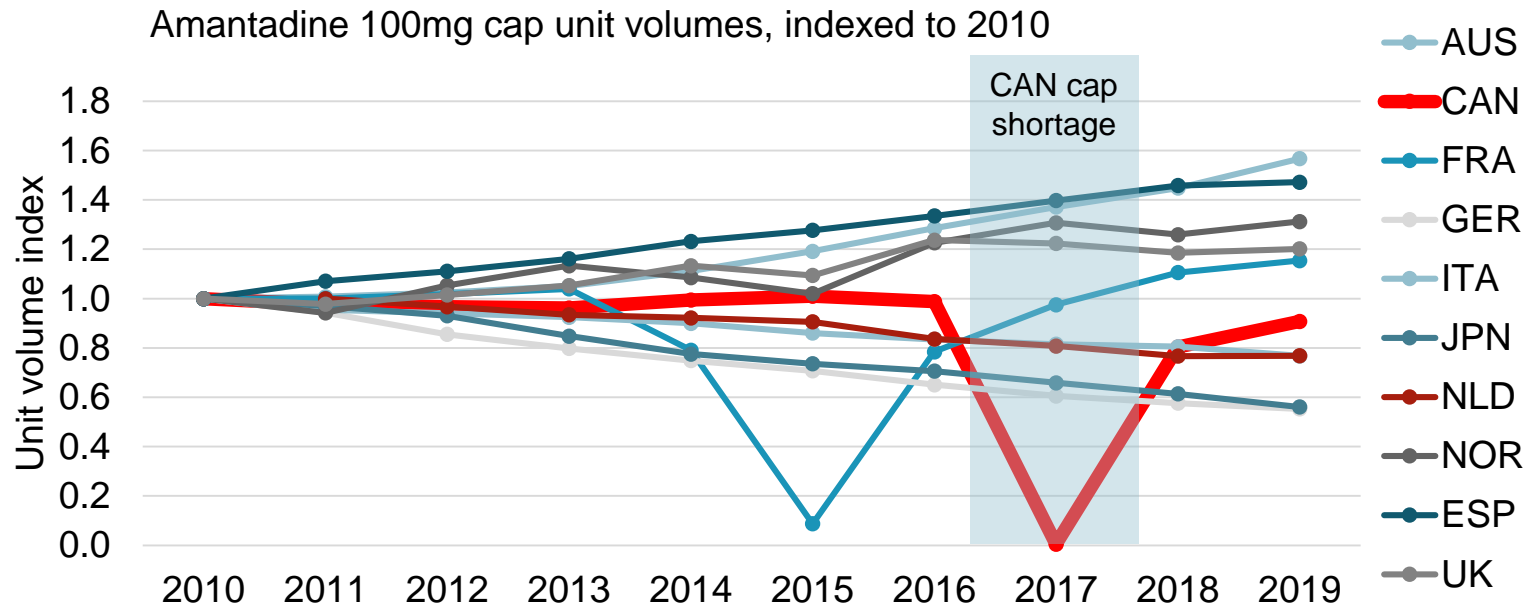


\* 2011 price ratio. 2010 Netherlands data unavailable.

Source: IQVIA MIDAS® Database, prescription retail and hospital markets, 2010 to 2019. All rights reserved.

# France is the only other PMPRB11 country with an amantadine sales disruption similar to Canada

Other amantadine markets with 1 manufacturer did not have similar experience as CAN and FRA



- In Australia, Canada, France, Italy, and Spain, a single manufacturer has accounted for over 99% of the amantadine oral solid market since 2014
- Canada and France are the only PMPRB11 countries where amantadine cap sales underwent a steep decline in one year before recovering

Sources: IQVIA MIDAS® Database, prescription retail and hospital markets, 2010 to 2019. All rights reserved.

UK NHS. [A Guide to Managing Medicines Supply and Shortages, 2019.](#)

# Amantadine case study shows how shortages impact the Canadian supply chain and affect patient therapy

Impact of drug shortage seen throughout the supply chain

- Duration of drug shortage report for amantadine caps was closely mirrored by monthly wholesaler unit volumes
- Retail pharmacy sales of the cap begin to decline about a month after the first drop in wholesaler units
- Public plan claims imply cap patients switched to syrup, but total beneficiary population still declines throughout 2017
  - Unknown to what extent patients discontinued amantadine therapy or took lower doses to stretch out their prescriptions
- International price comparison shows Canadian prices were near the top of the PMPRB11 over the past decade
  - Four other PMPRB11 countries had amantadine markets dominated by a single manufacturer
  - France is the only other PMPRB11 country that experienced a similar amantadine sales disruption

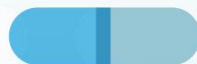


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# Drug Shortages in Canada

Overall conclusion



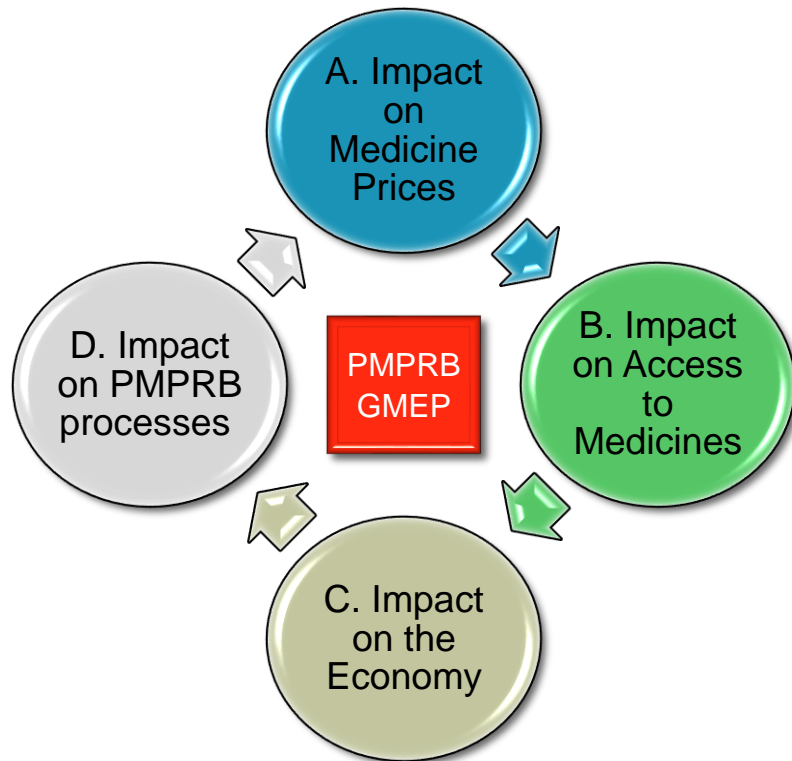
**PMPRB Researcher Series**

July 16, 2020

# Five takeaways from today's session

1. Drug shortages are an important international issue.
2. Multiple countries, including Canada, implemented strategies to monitor shortages and mitigate their impact.
3. There is no clear association between shortages and the price of medicines in Canada relative to other countries.
4. The Amantadine case study shows that shortages can have long-lasting effects on patient care in Canada.
5. When the Amantadine shortage struck Canada, capsule prices were 4<sup>th</sup> highest among PMPRB11 comparator countries.

# 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.



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Questions

&

Answers