COVID-19’s Limited Impact on Drug Shortages in Canada

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Using data from the Drug Shortages Canada website, we ask whether the first months of the coronavirus disease 2019 (COVID-19) pandemic were associated with a significant increase in drug shortages in Canada. We find an increase of 147 shortages (32 percent) reported by manufacturers during March and April 2020 relative to the same months in previous years. The upsurge was concentrated during the two-week period from 25 March to 7 April 2020, after which report counts returned to usual levels. Excess reports cite both supply-side and demand-side causes for shortages. Increases were noted in therapeutic classes associated with COVID-19 care.

Keywords: drug shortages, public health shocks, pharmaceutical supply chain, pharmaceutical demand

Introduction

On 5 March 2020, just as the first case of community transmission of coronavirus disease 2019 (COVID-19) was identified in Canada, Health Canada officials reported engaging with industry stakeholders to monitor and mitigate the impact of the pandemic on drug shortages (Harris 2020; Slaughter 2020). Drug shortages negatively affect patients and care teams in many ways, creating anxiety and worsening outcomes by causing delays and changes in treatment regimens (Donelle et al. 2018; Drug Shortages Task Force 2019).

Policy responses at multiple levels quickly followed. By 23 March, the Canadian Pharmacists Association (2020) encouraged its members to limit patients to 30-day supplies of their prescriptions. Then on 30 March, the federal government signed the Interim Order Respecting Drugs, Medical Devices and Foods for a Special Dietary Purpose in Relation to COVID-19 (Canada 2020b), allowing designated drugs that may not fully meet regulatory requirements to be imported to and sold in Canada. The same day, Health Canada published a web page listing prospective and actual shortages with the greatest potential impact on Canada’s health care system; the list included many drugs used in the treatment of COVID-19 (Canada 2020a). In addition, specific efforts were undertaken by many parties to ration limited supplies. For example, the Canadian Association of Emergency Physicians asked its members to avoid using medications needed for patients on ventilators (Osman 2020).

There are two main channels through which a global public health crisis such as COVID-19 can impede a country’s access to drugs. The first is by triggering a surge in the demand for medicines. The demand for drugs can increase because specific drugs are needed in higher quantities to respond to the public health crisis or, as was observed with ordinary household products, because individuals attempt to stockpile medicines in anticipation of shortages. The second is by disrupting the pharmaceutical supply chain. Recent government reports on the problem of drug shortages have highlighted the increasingly outsourced
and opaque nature of the supply chain as a driver of shortages, notably with regard to the outsourcing of active pharmaceutical ingredients, product manufacturing, and packaging (Drug Shortages Task Force 2019; Multi-Stakeholder Steering Committee on Drug Shortages 2017).

As of the writing of this article, the effect of COVID-19 on drug shortages has been documented only by anecdotal news media reports and is largely unknown. To fill this gap, we use data from the Drug Shortages Canada website and ask whether the first months of the pandemic saw a significant increase in drug shortages in comparison with previous years. We then use the website data and Health Canada’s Drug Product Database (DPD) to investigate whether both supply and demand factors contributed to additional shortages and compare shortages reported during the pandemic with those reported in previous years.

**Methods**

The primary data source used for this article is the Drug Shortages Canada website (Drug Shortages Canada n.d.), operated under contract with Health Canada. Since the website’s launch on 14 March 2017, Canadian manufacturers have been mandated to report shortages and discontinuations to it. Shortages are defined as a situation in which “the manufacturer to whom a document was issued under subsection C.01.014.2(1) of the Food and Drug Regulations that sets out the drug identification number assigned for the drug is unable to meet the demand for the drug” (Drug Shortages Canada, n.d.). Reports include detailed drug information, including the drug identification number (DIN), brand name, common name, company name, active ingredients, strength, dosage form, route, packaging size, and Anatomical Therapeutic Chemical Classification System code. Information specific to shortages includes the reason for the shortage, shortage status as of the most recent report update, and start and end dates of the shortage. Shortages are reported at the DIN and packaging-size levels, such that each distinct strength, form, of a pharmaceutical ingredient in shortage are reported separately.

For this article, we use the August 2020 monthly website extract covering the period from the website’s launch to 31 July 2020. As noted by Donelle et al. (2018), the period closely following the launch of the website saw a momentary surge in reporting. Because of that initial surge, the number of reports filed in 2017 far outnumbers those in the following years (Table 1). For that reason, our analysis focuses on the 6,987 reports filed since 2018. This information is augmented by matching DINs covered by shortage reports to Health Canada’s DPD, a repository of information on drugs available for sale in Canada. This enables us to find out the age of drugs, defined here as the number of years since a drug was first approved, and the generic or innovator status of drugs. Following Donelle et al. (2018), an innovator status is assigned by ingredient group to the DINs of the innovator company, defined as the company with the first approval within an ingredient group.

We first graphically compare report counts in the first half of 2020, marked by the COVID-19 pandemic, with those of previous years. We determine whether apparent outlier weeks are statistically different from the previous history by comparing observed report counts with those projected after the estimation of an autoregressive integrated moving average (ARIMA) model, which can be used to forecast future values of time series on the basis of the past behaviour of the variable being modeled (Kennedy 2003). We then graphically compare counts of shortage reports broken down by reason cited by manufacturers during the pandemic and in previous years. To account for potential seasonality in reporting patterns, we compare the same period in 2020 and the previous years. Finally, we compare counts of distinct ingredients covered by reports and the distribution of reports by their status at creation, brand status, form, route, and therapeutic class during the pandemic and in previous years.

**Results**

**Number of Shortages Reported**

The number of weekly reports on the Drug Shortages Canada website reveals a two-week spike in reports between 20 March and 7 April 2020 (Figure 1). These two weeks saw 105 and 135 cases reported to the website, whereas the weekly average report count since 2018 is 52.6. Using a time-series approach, we find that the number of reports filed during those weeks is significantly higher than expected on the basis of historical data.\(^1\)

Although weekly report counts reverted to usual levels in the weeks that followed, the two-week spike had a noticeable impact on the report counts for the months of March and April 2020: the two-month count during that period was 604, whereas counts for the same two months were 459 in 2018 and 456 in 2019. The excess shortages for those two months represent a 32 percent increase over the previous years \((N = 148/459\) in 2018 and \(N = 148/456\) in 2019\). In the remainder of this article, we focus our attention on shortages reported during March and April 2020 in comparison with the same months in 2018 and 2019.

**Table 1:** Shortage Reports Filed on the Drug Shortages Canada Website since Its Launch

| Year                  | Reports |
|-----------------------|---------|
| 2017 (Mar.–Dec.)      | 3,707   |
| 2018                  | 2,497   |
| 2019                  | 2,819   |
| 2020 (Jan.–July)      | 1,671   |

Source: Drug Shortages Canada (n.d.).

\(^1\) Canadian Public Policy / Analyse de politiques, October / octobre 2020 doi:10.3138/cpp.2020-107
Reasons Cited for Shortages
Shortage reports filed by manufacturers feature six broad reasons for shortages. In Figure 2, the frequency of shortages during March–April 2020 is contrasted with those in the same months in 2018 and 2019. The frequency of only two reasons increased: “demand increase for the drug,” which increased by 108 percent over the previous year (N = 67/62), and “disruption of the manufacture of the drug,” which increased by 65 percent (N = 130/199). When summing the frequencies of the five supply-related reasons shown in Figure 2 (i.e., all but “demand increase for the drug” and “other”), there was a 25 percent increase in the number of reports citing supply-side reasons (N = 89/438).

Characteristics of Shortages
Table 2 compares characteristics of shortage reports and drugs covered by the reports during March–April 2020 and the same months in 2018 and 2019. The last column presents the difference between the bimonthly counts observed in 2020 and the average of the previous two years.

Two of the five most common therapeutic classes reported saw a substantial increase. The number of reports for antibacterials for systemic use, used to treat patients showing pneumonia symptoms, and analgesics, used to sedate critical COVID-19 patients, increased by 29 and 25 over the averages of previous years, respectively.

A second notable difference between shortage reports of 2020 and those of previous years is the proportion of shortages that had an “actual shortage” status at report creation. A proportion of 86 percent of those filed in March–April 2020 had this status (N = 520/604), compared with 66 percent and 68 percent in 2018 and 2019, respectively (N = 305/459 in 2018; N = 310/456 in 2019).

Other characteristics of drugs in shortage during the pandemic are distributed similarly to previous years. Most reports concern older and generic medicines, consistent with previous analyses of drug shortages in Canada and elsewhere (Drug Shortages Task Force 2019; Donelle et al. 2018; Rinaldi et al. 2017). The form and route distribution of the March–April 2020 shortages also do not differ substantially from previous years.

Discussion
In this article, our primary aim is to determine whether the COVID-19 pandemic has thus far been associated with an increase in drug shortages in Canada. We find that it has. The number of shortages reported by manufacturers increased by 147 (32 percent) during March and April 2020 relative to the same months in the previous two years. The upsurge was concentrated during the two-week period from 25 March to 7 April 2020, during which 240 shortage reports were filed on the Drug Shortages Canada website. Increases were noted in therapeutic classes associated with COVID-19 care. If the increase in shortages experienced during those weeks is significant, we note that it is modest relative to the number of reports filed every year. For instance, the 147 excess reports over the two-month period represent 5 percent of the number of reports filed in 2019 (N = 147/2,819). After the two-week surge, weekly and monthly report counts returned to usual levels.

Despite the finding that the excess shortages in the early months of the pandemic were modest, our results suggest that Canada’s access to medicines is vulnerable.
to some extent to major public health events. This vulnerability is noted for both the demand- and the supply-side channels discussed in the introduction, given that excess reports cited both increases in demand and supply disruptions as reasons for the shortages.

Most policies introduced since the beginning of the pandemic, such as limiting prescriptions to 30-day supplies and efforts to ration medicines needed by COVID-19 patients, aimed to prevent and manage demand-side shortages. With Canadian new infections steadily declining as of the writing of this article, there is hope for fewer rationing efforts, although experts warn of renewed spread of the disease (Davidson 2020).

Supply-side shortages, which accounted for more than half (60 percent; \( N = 89/148 \)) of the excess shortages in recent months, are more challenging to anticipate and contain. The only policy implemented so far to that effect is the interim order to facilitate importing medicines in Canada (Canada 2020b), but its impact was probably mitigated by opposite efforts from other countries: since the beginning of the pandemic, 38 countries have implemented temporary export restrictions on critical medical supplies, including a variety of medicines and active pharmaceutical ingredients (World Customs Organization, n.d.). With global COVID-19 infections on the rise, Canada’s access to medicines may be further tested by supply chain disruptions in the near future.

Thankfully, the impact of COVID-19 on Canada’s drug shortages has so far been limited. But how can unpredictable supply chain shortages best be handled if COVID-19 causes further disruptions? In the short term, it will be essential to attentively monitor shortages beyond those of medicines used for COVID-19 care. Of greatest focus should be shortages reported for patented medicines and single-source non-patented medicines, which do not have direct substitutes and shortages of which can have the greatest impact on patients. When shortages are noted in these segments, stakeholders should work together to re-establish supply chains when possible, arrange for the importation of medicines, and ration stocks.

In the longer term, several policy options could be considered to further strengthen Canada’s resilience in the face of global shocks. A first step could be to establish an essential medicines list for Canada, as advised by multiple academics and stakeholders (Canada 2018; Eom, Grootendorst, and Dufﬁn 2016; Jarvis et al. 2019). Many avenues could then be adopted for the medicines deemed essential. For example, contracts could be drawn with suppliers to store and rotate medicines in the event of a health emergency, following the example of the United Kingdom’s Essential Medicines Buffer Stockpile (Bidstats 2019), or they could be covered by contracts requiring a certain supply maturity rating, as recommended by a US task force (Drug Shortages Task Force 2019).

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**Figure 2:** Reasons Cited for Shortage Reports Filed in the Months of March–April 2018–2020

Source: Drug Shortages Canada (n.d.).

| Reason                                | March–April 2018 | March–April 2019 | March–April 2020 |
|---------------------------------------|------------------|------------------|------------------|
| Demand increase for the drug          | 45               | 62               | 129              |
| Disruption of the manufacture of the drug | 199             | 237              | 329              |
| Delay in shipping of the drug         | 87               | 89               | 92               |
| Requirements related to complying with good manufacturing practices | 11               | 16               | 18               |
| Shortage of an active ingredient      | 36               | 7                | 6                |
| Shortage of an inactive ingredient or component | 0               | 7                | 0                |
| Other                                 | 37               | 32               | 45               |
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Limitations

We note three limitations to our study. First, our methods are observational and cannot inform about the causal impact of the pandemic on shortages. Second, although shortage reporting is mandatory in Canada, compliance has not yet been assessed, and the true number of shortages may have been greater than reported, both during the pandemic and during the comparison period. Finally, shortage reports do not provide direct insight into severity of shortages and their impact on patients. Manufacturers are mandated to report shortages when they cannot meet the demand, which usually comes from wholesalers. Such shortages may not have a direct impact on patients, for instance when supply lines are re-established before hospital and pharmacy stocks are depleted. At the other end of the spectrum, measures put in place to ration medications in anticipation of shortages and localized shortages at the pharmacy level may have great impact on patients and not translate in new shortage reports by manufacturers.

Table 2: Characteristics of Shortage Reports Filed in March–April 2018–2020

| Group or Characteristic                          | 2018   | 2019   | 2020   | Difference from 2018–2019 Average (N) |
|-----------------------------------------------|--------|--------|--------|--------------------------------------|
| Reports                                       | 459 (100) | 456 (100) | 604 (100) | 147                                  |
| Ingredients with a report                      | 239    | 220    | 288    | 59                                   |
| Report status at creation                      |        |        |        |                                      |
| Anticipated shortage                           | 154 (34) | 146 (32) | 84 (14) | −66                                  |
| Actual shortage                               | 305 (66) | 310 (68) | 520 (86) | 213                                  |
| Age of drugs, y, M (SD)                        | 15.8 (14.2) | 13.5 (11.8) | 16.5 (12.9) | 1.9 (−0.1)                           |
| Brand status                                  |        |        |        |                                      |
| Generic                                       | 369 (80) | 380 (83) | 512 (85) | 138                                  |
| Innovator                                     | 89 (19) | 73 (16) | 91 (15) | 10                                   |
| Unknown                                       | 1 (0)  | 3 (1)  | 1 (0)  | −1                                   |
| Form                                          |        |        |        |                                      |
| Tablet                                        | 270 (59) | 262 (57) | 329 (54) | 63                                   |
| Capsule                                       | 59 (13) | 63 (14) | 78 (13) | 17                                   |
| Solution                                      | 64 (14) | 60 (13) | 86 (14) | 24                                   |
| Other                                         | 66 (14) | 71 (16) | 111 (18) | 43                                  |
| Route                                         |        |        |        |                                      |
| Oral                                          | 336 (73) | 333 (73) | 423 (70) | 89                                   |
| Intravenous                                   | 37 (8)  | 44 (10) | 75 (12) | 48                                   |
| Topical                                       | 16 (3)  | 25 (5)  | 40 (7)  | 26                                   |
| Other                                         | 70 (15) | 54 (12) | 66 (11) | 25                                   |
| Top 5 therapeutic classes (ATC2)               |        |        |        |                                      |
| C09—Agents acting on the renin–angiotensin system | 32 (7) | 80 (18) | 68 (11) | 12                                   |
| J01—Antibacterials for systemic use           | 21 (5)  | 12 (3)  | 45 (7)  | 29                                   |
| N02—Analgesics                                | 19 (4)  | 12 (3)  | 40 (7)  | 25                                   |
| N06—Psychoanaleptics                          | 50 (11) | 37 (8)  | 39 (6)  | −5                                   |
| N05—Psycholeptics                             | 49 (11) | 29 (6)  | 36 (6)  | −3                                   |

Notes: The age of drugs is defined on the basis of the year of first approval of the DIN identified by the shortage report in DPD. Following Donelle et al. (2018), an innovator status is assigned by ingredient group to the DINs of the innovator company, defined as the company with a first approval within the group. Therapeutic classes are defined on the basis of the second level of the ATC Classification System code. The top 5 therapeutic classes are based on March–April 2020 report counts. Differences with 2018–2019 average are rounded to the nearest integer. ATC2 = second level of the Anatomical Therapeutic Chemical classification system code; DIN = drug identification number; DPD = Drug Product Database.

a Unless otherwise indicated.

Sources: Drug Shortages Canada (n.d.) and Health Canada (2015).
Medicine Prices Review Board (PMPRB), but the views expressed in the article are his alone and do not represent official views of the PMPRB or the Government of Canada.

Note
1 To test whether report counts for those weeks significantly differ from the previous history, we use an ARIMA modeling approach. Using weekly data from 1 January 2018 to 24 March 2020 (i.e., the period preceding the weeks of the spike), we conduct an Augmented Dickey–Fuller test and reject the null hypothesis of a unit root process in the weekly number of reports filed on the website (Z[1] = -9.500, approximate p = 0.0000). Using the likelihood maximization technique of conducting five Berndt–Hall–Hall–Hausman algorithms followed by ten Broyden–Fletcher–Goldfarb–Shanno algorithms, we find that the autoregressive moving average (1,1) specification maximizes likelihood. Using this specification, we conduct out-of-sample forecasts for the weeks of 25 March–31 March 2020 and 1 April–7 April 2020. We estimate confidence intervals around these forecasts as the point estimate plus or minus 1.96 times the square root of the mean standard error of the forecasts. The forecast values are 50.9 reports (95% CI: 10.6–91.2) for the week of 25 March–31 March 2020 and 54.3 reports (95% CI: 14.0–94.6) for the week of 1 April–7 April 2020. In both cases, the observed number of reports for the week exceeds the upper bound of the confidence interval. Stata Version 14.2 (StataCorp LLC, College Station, TX) was used for this analysis.

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