

## ORIGINAL ARTICLE

# International trends in prescription opioid sales among developed and developing economies, and the impact of the COVID-19 pandemic: A cross-sectional analysis of 66 countries

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## Abstract

**Purpose:** We sought to compare trends in opioid purchasing between developed and developing economies to understand patterns of opioid consumption, and how they were impacted by the COVID-19 pandemic.

**Methods:** We conducted a retrospective cross-sectional study of retail pharmacy opioid sales from 66 jurisdictions between July 2014 and August 2020. We measured monthly population-adjusted rate of opioid units purchased, stratified by development group and country, and used interventional time series analysis to assess the impact of the COVID-19 pandemic on rates of opioid purchasing among developed and developing economies separately.

**Results:** Rates of opioid purchasing were generally higher among developed economies, although trends differed considerably by development group. Rates of opioid purchasing declined 23.8% (95% confidence interval [CI] –34.7% to 3.6%) in the 5 years prior to the pandemic in developed economies, but rose 15.2% (95% CI 4.6%–35.6%) among developing economies. In March 2020 there was a short-term increase in the rate of opioid purchases in both developing (10.9 units/1000 population increase;  $p < 0.0001$ ) and developed (145.5 units/1000 population;  $p < 0.0001$ ) economies, which was followed immediately by reduced opioid purchasing of a similar scale in April–May 2020 (–14.8 and –171.8 units/1000 population in developing and developed economies, respectively;  $p < 0.0001$ ).

**Conclusion:** The COVID-19 pandemic led to disruptions in opioid purchasing around the world; although the specific impacts varied both between and among developed and developing economies. With global variation in opioid use, there is a need to monitor these trajectories to ensure the safety of opioid use, and adequate access to pain management globally.

## Plain Language Summary

In response to the rising overdose crisis in many developed economies, there have been efforts to promote appropriate opioid prescribing, leading to concerns of increased opioid marketing in developing economies. Furthermore, there have been concerns that the COVID-19 pandemic has led to interruptions in access to opioids

worldwide. We examined retail pharmacy opioid sales from 66 jurisdictions between July 2014 and August 2020 to assess changes over time and the impact of the COVID-19 pandemic. We found that rates of opioid purchasing were generally higher among developed economies, but that rates declined in developed economies, and rose among developing economies. In March 2020, there was an initial increase in opioid purchases across both developed and developing economies, followed by a similar decline over the subsequent 2 months. Global variation in opioid use, and the destabilizing effects of the COVID-19 pandemic suggests a need to monitor these trajectories to ensure the safety of opioid use, and adequate access to pain management around the world.

#### KEYWORDS

drug policy, pain, prescription opioids

#### Key points

- This retrospective study of 66 countries demonstrates considerable variation in opioid trends internationally, with key differences between developing and developed economies.
- In the 5 years prior to the pandemic, rates of opioid purchasing declined 24% in developed economies, but rose 15% among developing economies.
- The COVID-19 pandemic destabilized trends across both developed and developing economies, with initial increases in purchasing in March 2020 being balanced by reduced purchases in April and May.
- There is a need for monitoring of opioid trajectories in many jurisdictions with historically lower opioid use to ensure the safety of opioid use, and adequate access to pain management.

## 1 | INTRODUCTION

The substantial burden of opioid-related harm in North America, particularly in the decade after the introduction of long-acting oxycodone, has been tied, in part, to aggressive opioid marketing strategies and over-prescribing of long-term opioid therapy for chronic noncancer pain (CNCP).<sup>1,2</sup> Specifically, the United States and Canada are among the highest consumers of opioids worldwide, with 143 million opioid prescriptions dispensed in the US in 2020, and approximately 1 out of 8 Canadians being prescribed an opioid in 2017.<sup>3,4</sup> While the rate of opioid prescribing in North America remains unparalleled on a global scale, significant increases in prescribing trends have also been observed in other high-income countries.<sup>5</sup> For example, Blanch et al, reported a 15-fold increase in overall opioid prescription numbers within Australia between 1990 and 2015,<sup>6</sup> and England saw a 127% increase in total volume of opioids prescribed between 1998 and 2016.<sup>7</sup>

While the use of opioid analgesics for chronic cancer pain is supported with evidence, calls have been made for increased opioid stewardship for acute and CNCP.<sup>8</sup> As a result, many countries have released guidelines providing evidence-informed recommendations to support safe opioid prescribing practices for long-term CNCP management.<sup>9,10</sup> Since this time, several national studies have reported a decline in prescription for opioids; from 2017 to 2018, the United States reported a 17% decline in the overall volume of opioids prescribed—the largest single-year drop ever recorded.<sup>11</sup> These

regulatory changes to opioid availability in North America have led to large reductions in profits for manufacturers, who appear to have shifted their marketing efforts to developing economies. For example, in 2017, the US congress informed the World Health Organization (WHO) of Purdue Pharma's global counterpart Mundipharma International, stating Mundipharma was using many of the same “deceptive” and “reckless” practices to sell oxycodone abroad, that they had once used in North America.<sup>12</sup> Additionally, the International Narcotics Control Board (INCB) has reported a significant increase in the non-medical use of tramadol between 2010 and 2019 among developing economies, particularly in West and North Africa, the Middle East, and South Asia.<sup>13</sup> While increased access to opioids to manage pain may be warranted in regions with historically low access to analgesic medication, unfettered expansion of marketing of opioid prescribing in the absence of appropriate opioid prescribing policies and stewardship activities may put developing economies at risk of increased opioid-related harm if patterns similar to those observed in North America were replicated.

More recently, the arrival of the COVID-19 pandemic has introduced interruptions into the supply of pharmaceuticals worldwide, leading to concerns related to drug shortages, and changes in the ways chronic medications are made available.<sup>14</sup> For example, both the US and Canada have reported substantial reductions in opioid prescribing in the months following March 2020,<sup>15,16</sup> likely reflecting a combination of COVID-mandated changes in policy, and fewer

surgeries and dental procedures during the pandemic. Despite documented trends in North America, there is little information on the impacts of the ongoing pandemic on access to pharmaceutical opioids in other developed economies. Therefore, we conducted a study to compare trends in the rate of opioid purchasing between developed and developing economies around the world, to understand shifting patterns of opioid consumption over time, and to evaluate the impact of the COVID-19 pandemic on these trajectories.

## 2 | METHODS

### 2.1 | Study design and data source

We conducted a monthly, cross-sectional study of national retail prescription opioid sales data from 66 countries and jurisdictions between July 2014 and August 2020 using IQVIA's Multinational Integrated Data Analysis (MIDAS) database (Parsippany, NJ, USA), which contains opioid purchasing data from 69 countries/regions. Specifically, data is obtained from annual transactions from pharmaceutical manufacturers to wholesaler distribution centers and represents a national survey of prescription drug sales. We excluded data from hospital and long-term care settings, from countries with no opioid data ( $N = 2$ ) and from Venezuela where the economic crisis led to a highly irregular pattern of drug purchasing. The 66 countries in our final sample comprised approximately 72.6% of the world's population in 2019 (Table S1 in supplement). Data in the MIDAS database is reported as the number of total standardized drug units purchased, with a unit defined as a single tablet/capsule, patch, vial or 5 ml oral liquid. Data are internally validated each year through a standardized quality assurance program which validates sales data for each product against alternate sources by comparing estimated sales volumes against clients' actual sales volumes.<sup>17,18</sup> Medication sales data is projected to represent national pharmacy sales across all jurisdictions, regardless of payer.<sup>17</sup> Among the 66 countries in the current analysis, MIDAS captured an average of 89.5% of national sales. Data capture was 100% in 21 countries, 80%–99% in 27 countries, and 60%–79% in 10 countries. Only Kuwait and the United Arab Emirates had coverage <50%.

Among the 66 included jurisdictions, 64 were countries, and two were jurisdictions that combined purchases from multiple countries (Central America and French West Africa). We grouped included jurisdictions into “developed” ( $N = 33$ ) and “developing” ( $N = 33$ ) economies (including economies in transition) using the United Nations (UN) 2020 World Economic Prospectus. This classification uses the Human Development Index (HDI) to account for life expectancy and educational attainment in addition to national income. This study was approved by the University of Pittsburgh Institutional Review Board.

### 2.2 | Included opioid formulations

We identified opioid and opioid-combination products within eight classes of opioids that are currently marketed and indicated to

manage pain (Table S2): (1) codeine, (2) tramadol, (3) oxycodone, (4) hydrocodone, (5) morphine, (6) hydromorphone, (7) fentanyl, and (8) other opioids (butorphanol, dihydrocodeine, levorphanol, opium, oxymorphone, pentazocine, ketobemidone, buprenorphine, and tapentadol). We excluded methadone and buprenorphine/naloxone as they are most commonly used to treat opioid use disorder.

### 2.3 | Measures of opioid use

Our primary measure was the rate of opioid units purchased per 1000 population from July 2014 to August 2020. For each month, we summed the total number of purchased opioids internationally ( $N = 66$  countries) and by development group ( $N = 33$  each). Rates were standardized using mid-year population sizes from the United Nations 2019 Population Prospectus. We report overall opioid purchasing, as well as purchasing by drug class. We first estimated changes in the rate of opioid units purchased over time both prior to and during the COVID-19 pandemic. Specifically, we calculated the relative change in international opioid purchasing rates using the last 6 months of each calendar year (July–December) and reported the difference between the July and December purchasing rate in 2019, relative to that in 2014 (i.e.,  $[\text{rate in 2019} - \text{rate in 2014}] / \text{rate in 2014}$ ). We then calculated the relative change in rate between the months of March to August 2020 (defined as the “pandemic period”) compared to the same timeframe the year prior (March to August 2019; “pre-pandemic period”) to capture broad shifts in purchasing rates in the early months of the pandemic. We quantified the variability around all estimates using bootstrap-based confidence intervals on 10 000 samples. Analyses were conducted overall within each development group, and stratified across each of the 66 individual jurisdictions.

To further understand the impact of the COVID-19 pandemic (defined as starting in March 2020, when the WHO declared COVID-19 a pandemic) on rates of opioid use, we used autoregressive integrated moving average (ARIMA) models to assess changes in the opioid purchasing rates in developed and developing economies separately using two pulse transfer functions (March 2020 and April–May 2020) to test for short-term disruption in rates. We confirmed stationarity using the augmented Dickey-Fuller test and selected model parameters using the residual autocorrelation function (ACF), partial autocorrelation function (PACF), and inverse autocorrelation function (IACF) correlograms. The final model specification was determined using autocorrelation plots and the Ljung-Box chi-square test for white noise.

## 3 | RESULTS

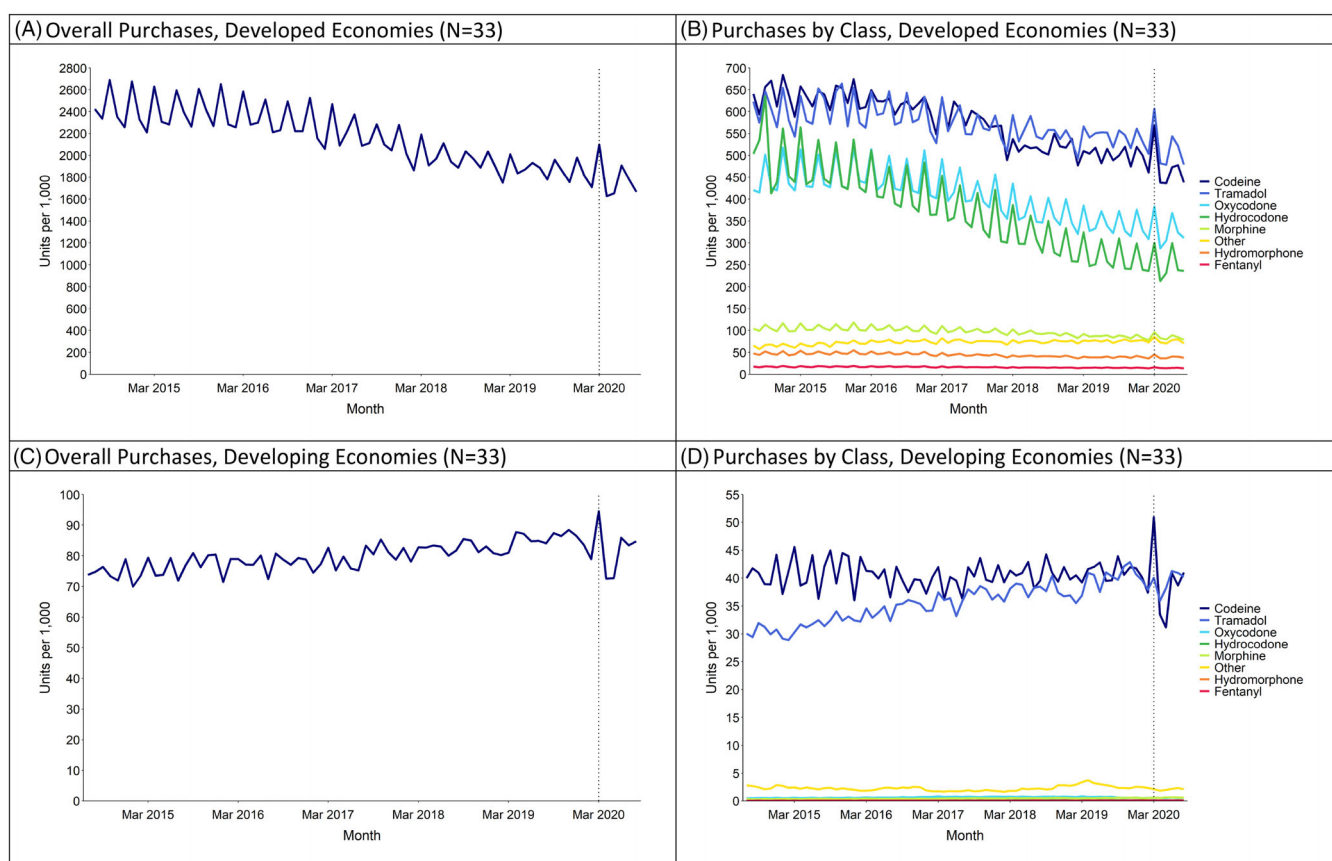
### 3.1 | Opioid purchasing rates prior to the COVID-19 pandemic

Overall, a total of 3195.6 units of opioids were purchased per 1000 population in the last 6 months of 2014, lowering 21.1% (95%

**TABLE 1** Changes in rates of retail opioid purchases (units per 1000 population), by development status and class, 2019 versus 2014

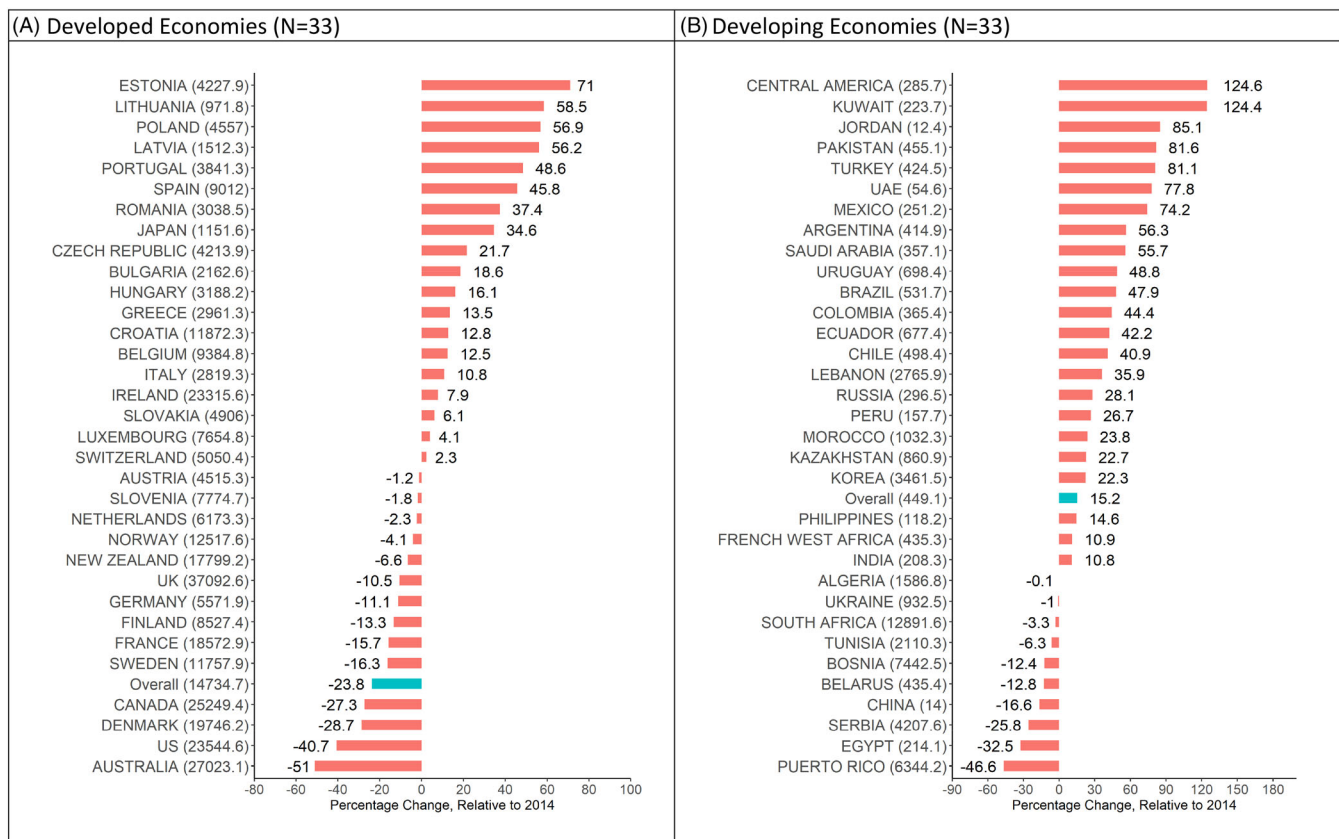
Variable	All countries (N = 66)			Developed economies (N = 33)			Developing economies (N = 33)		
	Units per 1000 in July–December			Units per 1000 in July–December			Units per 1000 in July–December		
	2014	2019	% Change (95% CI)	2014	2019	% Change (95% CI)	2014	2019	% Change (95% CI)
All Opioids	3195.6	2521.4	−21.1 (−32.6, 4.6)	14734.7	11221.1	−23.8 (−34.7, 3.6)	449.1	517.6	15.2 (4.6, 35.6)
Codeine	939.3	766.1	−18.4 (−35.1, −8.0)	3857.7	3018.4	−21.8 (−42.8, −9.7)	244.7	247.3	1.1 (−9.6, 23.3)
Tramadol	853.5	809.2	−5.2 (−18.3, 22.2)	3668.7	3251.5	−11.4 (−23.7, 19.4)	183.5	246.7	34.5 (18.2, 66.4)
Oxycodone	521.9	387.4	−25.8 (−32.9, 25.7)	2701.4	2052.6	−24 (−31.4, 30.1)	3.1	3.8	23.7 (−14.9, 144.5)
Hydrocodone	593.9	298.8	−49.7 (−54.9, 124.4)	3086.9	1592.6	−48.4 (−48.9, −48.1)	0.53	0.82	55.8 (−71.9, 447.5)
Morphine	123.7	100.1	−19.0 (−36.3, 6.5)	635.2	519.9	−18.2 (−35.9, 8.1)	1.9	3.4	79.3 (46.1, 164.3)
Other	87.3	97.9	12.0 (−16.1, 79.0)	391.1	457.9	17.1 (−16.5, 113.2)	15.1	14.9	−0.7 (−18.0, 145.2)
Hydromorphone	55.7	44.7	−19.7 (−46.8, 38.9)	289.0	238.4	−17.5 (−45.2, 44.7)	0.12	0.06	−50.4 (−83.2, −10.1)
Fentanyl	20.3	17.2	−15.3 (−40.3, 15.9)	104.7	89.9	−14.1 (−40.4, 18.7)	0.24	0.48	96.4 (11.7, 322.3)

Source: Authors' analysis of MIDAS drug purchases, July 2014–December 2019.

**FIGURE 1** Rates of retail opioid purchases (units per 1000 population), July 2014–August 2020, by development status and class.

confidence interval [CI] −32.6% to 4.6%) to 2521.4 units per 1000 population in the last half of 2019 (Table 1; Figure 1). However, this effect differed considerably by development group, with opioid rates lowering in developed economies (23.8% reduction [95% CI −34.7% to

3.6%] from 14734.7 to 11221.1 units per 1000 population), and rising in developing economies (15.2% increase [95% CI 4.6% to 35.6%] from 449.1 to 517.6 units per 1000 population). Among developed economies, the rate of opioid use lowered across nearly all opioid



**FIGURE 2** Percentage change in population-adjusted rates of retail opioid purchases by jurisdiction, July–December 2019 versus July–December 2014.

**TABLE 2** Changes in rates of retail opioid purchases (units per 1000 population) during the first stage of the COVID-19 pandemic, by development status and class

Variable	All countries (N = 66)			Developed economies (N = 33)			Developing economies (N = 33)		
	Units per 1000 in March–August			Units per 1000 in March–August			Units per 1000 in March–August		
	2019	2020	% Change (95% CI)	2019	2020	% Change (95% CI)	2019	2020	% Change (95% CI)
All opioids	2532.9	2401.0	−5.2 (−6.7, −2.8)	11317.6	10733.5	−5.2 (−6.6, −2.7)	509.5	493.8	−3.1 (−8.2, 0.9)
Codeine	764.0	719.6	−5.8 (−10.6, −3.6)	3018.4	2831.3	−6.2 (−12.2, −3.8)	244.7	236.2	−3.5 (−13.2, −0.3)
Tramadol	807.1	772.2	−4.3 (−6.3, −1.0)	3281.2	3111.8	−5.2 (−7.0, −1.8)	237.3	236.6	−0.3 (−4.9, 4.5)
Oxycodone	392.9	371.6	−5.4 (−6.3, −2.0)	2079.5	1980.1	−4.8 (−5.7, −1.0)	4.4	3.5	−20.6 (−54.8, 14.6)
Hydrocodone	306.3	283.4	−7.5 (−42.5, −0.5)	1632.8	1518.3	−7.0 (−7.2, −6.9)	0.8	0.73	−9.2 (−48.5, 21.8)
Morphine	100.9	98.1	−2.7 (−6.5, 4.7)	525.6	510.8	−2.8 (−6.6, 4.1)	3.1	3.7	19.5 (2.7, 40.5)
Other	100.5	95.2	−5.3 (−18.7, 2.3)	455.4	456.7	0.3 (−3.9, 5.3)	18.8	12.5	−33.4 (−45.0, 7.4)
Hydromorphone	44.0	44.2	0.4 (−6.1, 7.0)	234.7	236.8	0.9 (−5.7, 7.7)	0.061	0.065	6.5 (−22.2, 23.4)
Fentanyl	17.3	16.8	−2.7 (−7.6, 1.0)	90.2	87.7	−2.7 (−7.9, 1.0)	0.45	0.54	19.0 (−6.5, 42.0)

Source: Authors' analysis of MIDAS drug purchases, March 2019–August 2020.

classes over the 5 year study period. This decline was most dramatic for hydrocodone and oxycodone (48.4% reduction from 3086.9 to 1592.6 per 1000 population and 24.0% reduction from 2701.4 to 2052.6 per 1000 population, respectively) between the last 6 months of 2014 and 2019. In contrast, growth in opioid use occurred across almost all opioid

drug classes studied in developing economies, but was driven by rising rates of tramadol use which increased by 34.5% (95% CI 18.2% to 66.4%) from 183.5 to 246.7 units per 1000 population.

Country-level changes in the rate of opioid prescribing varied considerably by development status and by jurisdiction (Figure 2 and



**TABLE 3** Results of time series analysis of impact of COVID-19 pandemic on rates of retail opioid purchases

Outcome	ARIMA model	March 2020 pulse intervention			April to May 2020 pulse intervention		
		Estimate	95% Confidence Interval	p-Value	Estimate	95% Confidence Interval	p-Value
Developing economies							
Opioid units purchased	(2,1,0) (0,1,0) <sub>12</sub> no intercept	10.9 units/ 1000	6.1 to 15.6 units/1000	<b>&lt;0.0001</b>	-14.8 units/1000	-17.9 to -11.7 units/1000	<b>&lt;0.0001</b>
Developed economies							
Opioid units purchased	(2,1,0) (0,1,1) <sub>12</sub> no intercept	145.5 units/ 1000	83.4 to 207.6 units/1000	<b>&lt;0.0001</b>	-129.2 units/1000	-171.8 to 86.6 units/1000	<b>&lt;0.0001</b>

Note: Boldface indicates statistical significance ( $p < 0.05$ ).

Figure S1). Consistent with the overall results, opioid rates decreased in 14 out of 33 developed economies (42.4%) between the last 6 months of 2019 and 2014. Jurisdictions with the most dramatic reductions in the rate of opioid use generally had higher overall rates of opioid use compared to the international average, and included countries in North America (United States and Canada), Australia, and Denmark (Figure 2). One exception to this trend in developed economies was Ireland. Specifically, Ireland had a rate of opioid purchasing above the international average in 2014 (23315.6 units per 1000 population in Ireland vs. 14734.7 units per 1000 population overall), but also reported a small growth in opioid use over the 5 year study period (7.9% relative increase from last half of 2014 compared to 2019). Despite an overall reduction in opioid purchases across all developed economies, 19 of 33 (57.6%) jurisdictions recorded increases in country-level sales. The highest growth occurred among the Baltic countries (Estonia, Lithuania and Latvia) and Poland (range 56.2% to 71.0% growth between last 6 months of 2014 vs. 2019), all of which had lower-than-average rates of opioid purchasing in 2014.

Among developing economies, 23 of 33 (69.7%) jurisdictions demonstrated growth in opioid purchasing over the 5-year study period. The highest growth occurred in Central America (124.6% increase) and Kuwait (124.4% increase; Figure 2 and Figure S1). Consistent with the findings in developed economies, in general, countries experiencing growth in opioid purchases had lower-than-average rates of opioid use in 2014, and those countries with the largest reductions had higher rates. For example, Puerto Rico purchased 6344.2 opioid units per 1000 population in 2014 (compared to international rate in developing economies of 449.1 units per 1000 population), which fell by 46.6% over the next 5 years. Exceptions to these patterns were Uruguay, Brazil, Ecuador, Lebanon, Morocco, Kazakhstan, and Korea which all experienced growth in their rate of opioid purchasing despite being above the international average in 2014. Similarly, rates of opioid use lowered in both China and Egypt despite low opioid use rates overall (14 per 1000 population and 214.1 per 1000 population in 2014, respectively).

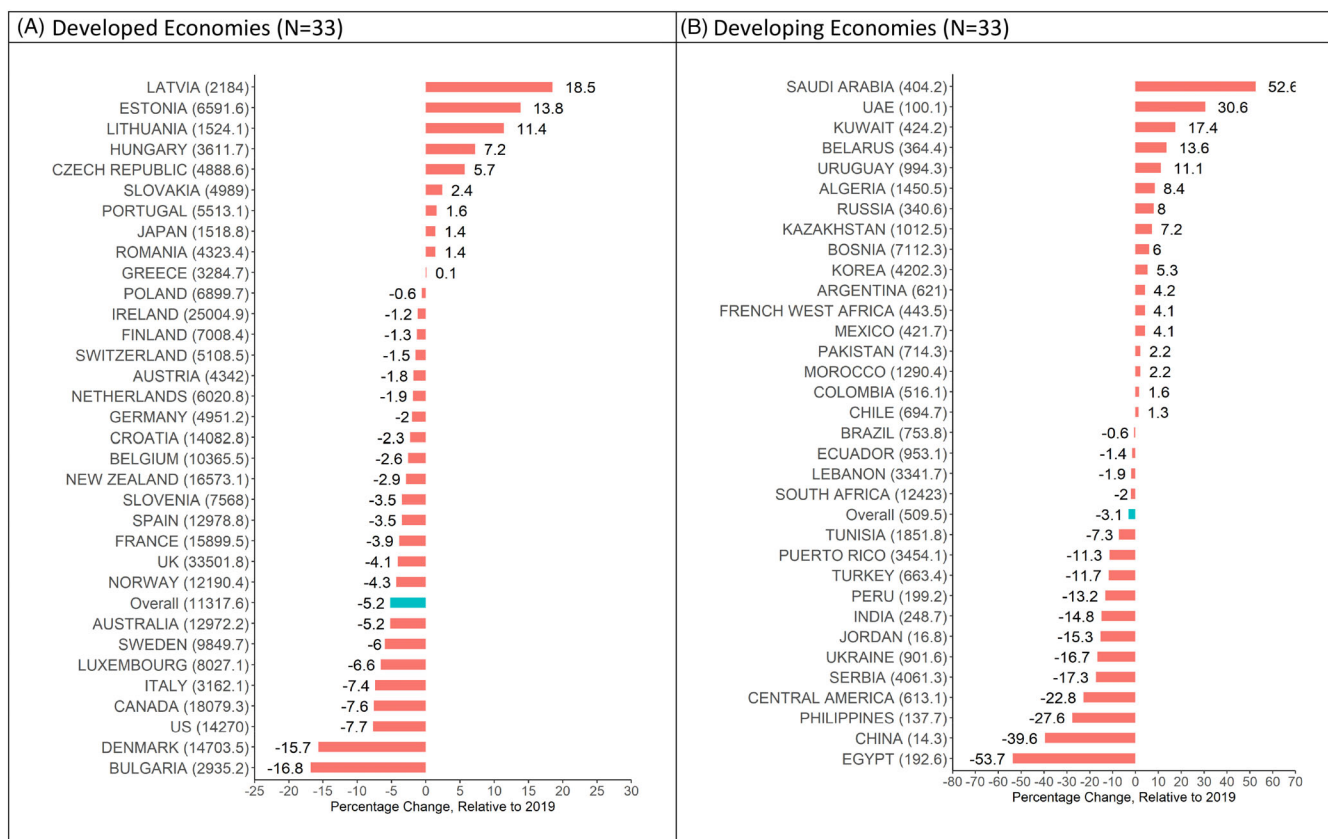
### 3.2 | Impacts of the COVID-19 pandemic

Early in the COVID-19 pandemic, there was a temporary disruption in opioid prescribing, which was apparent in both developed and developing economies among all frequently prescribed opioids (Figure 1). In March 2020, there was a statistically significant short-term increase in the rate opioid purchases in both developing (10.9 units/1000 population increase;  $p < 0.0001$ ) and developed (145.5 units/1000 population;  $p < 0.0001$ ) economies (Table 3; Figure 1). This was followed immediately by a rapid reduction in opioid purchases of similar scale in April and May 2020 in both economies (-14.8/1000 population in developing economies and -171.8 units/1000 population in developed economies;  $p < 0.0001$ ), after which rates of opioid purchases stabilized. As a result of these changes, the rate of opioid purchasing declined slightly in both developed (5.2% reduction, 95% CI [-6.6% to -2.7%]) and developing economies (3.1% reduction, 95% CI [-8.2% to 0.9%]) when comparing March to August 2020 against the same months in 2019 (Table 2).

Most developed economies observed less than a 10% change in retail opioid purchases in the first 6 months of the COVID-19 pandemic (Figure S2). Exceptions to this among developed economies were Latvia (18.5% increase), Estonia (13.8% increase), Lithuania (11.4% increase), Denmark (15.7% decrease) and Bulgaria (16.8% decrease; Figure 3). Among developing economies, the rate of opioid use increased by more than 10% among 5 jurisdictions (Saudi Arabia, United Arab Emirates, Kuwait, Belarus and Uruguay), but decreased considerably (>10% reduction) in 11 jurisdictions, most dramatically in Central America, Philippines, China and Egypt (Figure 3).

## 4 | DISCUSSION

In this large study of across 66 international jurisdictions representing three-quarters of the global population, we observed important differences in patterns of opioid use over time between developing and developed economies, as well as considerable variation within each of the development groups. While per capita rates of opioid use are generally much higher among developed economies, they have declined



**FIGURE 3** Percent changes in population-adjusted rates of retail opioid purchases (units per 1000 population) by jurisdiction, July–December 2019 versus July–December 2014.

over the past 5 years, in contrast to developing economies where rates are generally lower, but have been climbing over this same period. The impact of the COVID-19 pandemic can be observed in all jurisdictions, with opioid purchases being destabilized early in the pandemic, leading to declines in rates of opioid use across most jurisdictions.

During the COVID-19 pandemic, we observed disruptions in opioid supplies in both developed and developing economies, and across all of the most commonly prescribed opioid formulations. This is likely explained by two pandemic-related factors. First, there is clear evidence of widespread interruptions in global supply chains for pharmaceuticals, which led to threats of shortages in many countries, particularly early in the pandemic.<sup>14,19,20</sup> As a result, many countries introduced limits on the duration of chronic medications, including opioids, which could be dispensed to protect unstable drug supplies and prevent gaps in access for patients.<sup>19,21</sup> Second, as public health restrictions were introduced around the world, many people experienced challenges accessing healthcare providers, and there was a reduction in surgeries and dental services which as often associated with opioid use. Therefore, our findings suggest that gaps in accessing care and pharmacy services may have also led to interruptions in opioid therapy. It is impossible to disentangle these two phenomena with this data, and it is likely that each jurisdiction was impacted differently by drug shortages and pandemic-related public health measures.

However, these findings demonstrate the important impact of the COVID-19 pandemic on dynamics of opioid use around the world, and highlight a need to evaluate their influence on patient outcomes, as it relates to both pain management and unsafe transitions to unregulated drug supplies.

Outside of the pandemic, we also observed several changes in patterns of opioid purchasing among developed and developing economies. Reduced opioid purchasing among developed economies is not unexpected as this was driven by large reductions in opioid use among the United States, Canada, and Denmark, three jurisdictions where considerable attention has been paid to historically high opioid prescribing, leading to changing clinical practice guidelines and drug policy over the past 5 years.<sup>9,10,22</sup> Furthermore, the large reduction in rate observed in Australia is important because, despite policies such as rescheduling of codeine that were designed to promote appropriate opioid prescribing, previous research has not demonstrated a large reduction in the volume of opioids prescribed,<sup>23</sup> with a recent meta-analysis suggesting a plateauing of rates between 2014 and 2017.<sup>24</sup> Therefore, our findings may be reflective of reductions in opioid use in Australia following broad consultation and implementation of regulatory changes designed to safe and appropriate opioid use between 2018 and 2020.<sup>25</sup> Among developing economies with higher opioid prescribing rates in 2014, we observed similar patterns, with these countries tending to have reductions in the rate opioid use in 2019. In

particular, there was a large reduction in the rate of opioid prescribing in Puerto Rico (46.6%), which may be influenced by trends in the United States, and the recent introduction of a prescription drug monitoring program.<sup>26</sup> Importantly, although these reductions in opioid prescribing are likely reflective of broad approaches to promote opioid stewardship and safer prescribing in these jurisdictions, there is evidence emerging that rapidly lowering opioid doses among chronic opioid recipients can lead to patient harm and transitions to the unregulated opioid supply.<sup>27</sup> This speaks to the need to consider carefully the interconnectedness of the regulated and unregulated drug supplies when introducing and adapting opioid-related policies in regions with historically high opioid prescribing rates.

In contrast to the findings from developed economies, this study demonstrated that, in general, opioid prescribing rates are lower among developing economies, but have been rising in most countries. However, these patterns also differ by individual jurisdictions, with developing countries with historically lower rates exhibiting growth in opioid use. It is important to contrast this against opioid policies implemented in countries with historically high rates of prescribing which have largely focused on opioid stewardship since 2015. In particular, as opioid manufacturers have seen their profits lower in North America, Australia, and parts of Europe, there is evidence of increased marketing of opioids in other parts of the world.<sup>2,12,28</sup> With these changes, it is crucial to understand whether this rising opioid use is filling a gap in access to pain management that has been identified in many developing economies, or whether it is indicative of misleading marketing practices similar to approaches taken in North America early in the 21st century. Therefore, rising trends must continue to be monitored to ensure the safety and appropriateness of opioid use around the world, learning from the experiences of other jurisdictions that are now grappling with a worsening overdose crisis, being driven by the unregulated opioid supply.

One country that warrants further discussion is Ireland, which had one of the highest rates of opioid sales among the jurisdictions studied in 2014 (23 316 units per 1000 population), but reported a 7.9% increase in opioid use between 2014 and 2019 and only a small reduction in opioid use during the pandemic. This overall growth aligns with reports using prescription claims data in Ireland,<sup>29</sup> and has occurred in parallel with evidence of high rates of opioid-related harms, which rose to 43.5 deaths per million in 2016.<sup>30</sup> This suggests a need to further understand the dynamics of prescription and non-prescription opioid use in Ireland to support the development of drug policies designed to promote safe opioid use and harm reduction.

#### 4.1 | Limitations

Several limitations of this study merit discussion. First, we relied on data on retail prescription opioid sales and cannot capture patient level data. Therefore, we are unable to ascertain individual-level impacts of changing drug policies over time, or the COVID-19 pandemic. Second, we do not have data available on measures of pain or opioid-related harm. Third, we selected our primary measure to be rate of units purchased, which does not account for varying potency of different opioid classes. However, due

to our inclusion of various non-oral formulations and less commonly prescribed opioids with poorly established morphine equivalence ratios, we were unable to report our data using milligrams of morphine equivalents. Fourth, we have discussed several potential factors related to jurisdiction-specific trends in opioid sales over time; however, given the large number of policy responses that have been implemented by governments over the past decade, it is difficult to definitively link ecological trends to specific interventions. More detailed, jurisdiction-specific analyses are required to better understand the dynamics within each of these markets. Finally, it is important to note that reductions in opioid prescribing are not always reflective of higher quality care, with jurisdictions with historically high opioid rates reporting increased transitions away from prescription opioids and toward the unpredictable, unregulated drug supply after changing clinical guidelines and restrictive opioid policies.<sup>31</sup> Therefore, while these data provide important international context and comparisons to inform future work, research within individual jurisdictions is needed to understand shifting dynamics in opioid use and drivers of opioid-related harm to ensure that responses are safe, appropriate and do not unintentionally put patients at risk harm.

## 5 | CONCLUSION

Although rates of opioid use vary considerably around the world, with differing dynamics within and between developmental groups, the COVID-19 pandemic led to considerable interruptions in opioid purchasing in nearly all jurisdictions studied. As we can anticipate that rates of opioid purchasing will continue to climb in many developing economies as drug supplies are re-established during the COVID-19 pandemic, it is important to work proactively to determine the appropriateness of pharmaceutical marketing practices and changing opioid prescribing to support the safe use of opioids while also addressing needs for pain management.

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### CONFLICT OF INTEREST

The authors declare no conflict of interest.

### AUTHOR CONTRIBUTIONS

**Tara Gomes:** Literature search, study design, data interpretation, writing. **Katherine Callaway:** Study design, data collection, data analysis, data interpretation, critical revision of manuscript. **Katie Suda:** project administration, study design, data interpretation, critical revision of manuscript. **Ria Garg:** Literature search, data interpretation, critical



revision of manuscript. **Mina Tadrous:** Project administration, study design, data interpretation, critical revision of manuscript.

## ETHICS STATEMENT

This study was approved by the University of Pittsburgh Institutional Review Board.

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## DATA AVAILABILITY STATEMENT

Due to its proprietary nature, data from this study cannot be shared by the authors. The data that support the findings of this study are available (at a cost) from IQVIA. Restrictions apply to the availability of these data, which were used under license for this study. Data are available from IQVIA ([www.iqvia.com](http://www.iqvia.com)) with the permission of IQVIA.

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## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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