Journal of the American Pharmacists Association 62 (2022) 766–774

Contents lists available at ScienceDirect

Journal of the American Pharmacists Association

journal homepage: www.japha.org

RESEARCH

The global impact of COVID-19 on drug purchases: A cross-sectional time series analysis

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ARTICLE INFO

Article history:
Received 6 October 2021
Accepted 21 December 2021
Available online 24 December 2021

ABSTRACT

Background: The drug supply chain is global and at risk of disruption and subsequent drug shortages, especially during unanticipated events.

Objective: Our objective was to determine the impact of coronavirus disease 2019 (COVID-19) on drug purchases overall, by class, and for specific countries.

Methods: A cross-sectional time series analysis of country-level drug purchase data from August 2014 to August 2020 from IQVIA MIDAS was conducted. Standardized units per 100 population and percentage increase in units purchased were assessed from 68 countries and jurisdictions in March 2020 (when the World Health Organization declared COVID-19 a pandemic). Analyses were compared by United Nations development status and drug class. Autoregressive integrated moving average models tested the significance of changes in purchasing trends.

Results: Before COVID-19, standardized medication units per 100 population ranged from 3990 to 4760 monthly. In March 2020, there was a global 15% increase in units of drugs purchased to 5309.3 units per 100 population compared with the previous year; the increase was greater in developed countries (18.5%; $P < 0.001$) than in developing countries (12.8%; $P < 0.0001$). After the increase in March 2020, there was a correction in the global purchase rate decreasing by 4.7% (April to August 2020 rate, 21,334.6/100 population; $P < 0.001$). Globally, we observed high purchasing rates and large changes for respiratory medicines such as inhalers and systemic adrenergic drugs (March 2020 rate, 892.7/100 population; change from 2019, 28.5%; $P < 0.001$). Purchases for topical dermatologic products also increased substantially (42.2%), although at lower absolute rates (610.0/100 population in March 2020; $P < 0.0001$). Interestingly, purchases for systemic anti-infective agents (including antiviral drugs) increased in developing countries (11.3%; $P < 0.001$), but decreased in developed countries (1.0%; $P = 0.06$).

Conclusion: We observed evidence of global drug stockpiling in the early months of the COVID-19 pandemic, especially among developed countries. Actions toward equitable distribution of medicines through a resilient drug supply chain should be taken to increase global response to future unanticipated events, such as pandemics.

Disclosures: Inmaculada Hernandez is a consultant at Pfizer and BMS. Allen Campbell is an employee at IQVIA. All other authors declare no relevant conflicts of interest or financial relationships.

Funding: This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Transparency declaration: Dr. Suda affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; no important aspects of the study have been omitted; and discrepancies from the originally proposed study methods have been explained.

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https://doi.org/10.1016/j.japh.2021.12.014

Key Points

Background:

- The drug supply chain is global and at risk of disruption especially during unanticipated events such as pandemics.
- During the 2019 novel coronavirus (coronavirus disease 2019 [COVID-19]) pandemic, border closings and countries prohibiting drug export potentially threatened global access to essential medicines.
- Supply disruptions can lead to drug shortages, which are increasingly common and can result in worsened clinical outcomes and increased costs.

Findings:

- A global 15% increase in purchases occurred in March 2020 when COVID-19 was declared a pandemic but before peak global infections; the increase was greater (18%) in developed than developing countries (13%).
- Drug stockpiling occurred globally in the early months of the COVID-19 pandemic, especially among developed countries. Variation in drug purchasing responses to COVID-19 by country and development status suggest an uncoordinated approach to supply chain drug distribution.
- International treaties must ensure access and equitable distribution of medications similar to other resources essential to health. Actions toward a more resilient drug supply chain may increase global response to future unanticipated events, including pandemics.

Introduction

The efficient and resilient performance of the drug supply chain is important because most people worldwide use medications, taking a mean of 1.6 medications daily, with older adults taking 3 medications per day.[1–4] Drug suppliers and manufacturers are most often multinational corporations, providing the drug supply for many countries. Of drugs consumed in most developed countries, 90% of raw active ingredients (active pharmaceutical ingredients) are made in foreign facilities (80% in China and India).[5,6] For 90% of drugs, all active pharmaceutical ingredients are manufactured at a single facility where a single event can disrupt production.[5] Manufacturers then produce finished dosage forms from active pharmaceutical ingredients (i.e., tablet) at a different site. Concerningly, 60% of finished dosage forms are made in a single finished dosage forms manufacturing facility.[5,6]

Disruptions in the drug supply chain can lead to sudden decreases in drug supply, or drug shortages. A drug shortage is defined as a situation where a patient is unable to access an interchangeable version of a medication because of supply limitations.[6] Over the past decade, the number of drug shortages has increased dramatically.[6] Disruption in drug supply may arise from several causes, including manufacturing problems and recalls, sole source contracts, and demand increases. Supply disruptions that lead to shortages are a complex global issue and can be affected by geopolitical issues, trade, civil unrest, weather, and pandemics.[7,8] Drug shortages are concerning because they have a negative impact on patient health outcomes and they result in increased health care costs.[9–12]

The 2019 novel coronavirus (coronavirus disease 2019 [COVID-19]) pandemic, caused by the severe acute respiratory syndrome coronavirus 2, affected drug manufacturing: Chinese active pharmaceutical ingredients manufacturers closed, the European Union and Indian governments prohibited drug export, and finished dosage form disruptions in other countries were reported.[13–16] These issues, combined with news of patients and organizations stockpiling drugs, may have worsened the already strained drug supply chain, especially for inhalers and critical care medications used to treat patients with COVID-19.[16] Before COVID-19, disruptions in the drug supply chain disproportionately affected antimicrobial agents and drugs used for central nervous system and cardiovascular indications,[6] many of which are considered essential medications by the World Health Organization (WHO).[17] However, the impact of the COVID-19 pandemic on purchases of all medications is unknown. Our objective was to determine the extent to which the WHO pandemic declaration affected the global drug supply overall, by class, for specific countries, and new cases of patients infected with COVID-19.

Methods

Setting

We conducted a cross-sectional time series study of global monthly pharmacy sales from August 2014 to August 2020. Data and statistical analysis were conducted in SAS version 9.4 (Cary, NC). This study was approved by the University of Pittsburgh Institutional Review Board and followed the Strengthening the Reporting of Observational Studies in Epidemiology reporting guidelines.

Data source

The current analysis was conducted in IQVIA MIDAS database (Durham, NC), which contains monthly pharmacy sales for 66 countries and 2 geographic regions (Central America [N = 6 countries] and French West Africa [N = 12 countries]) from August 2014 to August 2020. We excluded Venezuela from our analysis because of hyperinflation and unstable purchasing rates (data not indicated). Pharmacy sales are reported in standardized units overall and by sector (retail, hospital). Standardized units are defined as a single tablet/capsule, vial, or 5-mL oral liquid. On average, MIDAS captures 89.5% of all community- and hospital-based pharmacy sales in covered areas. In 2020, 73.3% of the world's population resided in a MIDAS region (Appendix 1). Reported data are internally validated against alternate sources.[18]

Outcomes

Our primary outcome was global changes in monthly drug purchases per 100 population in March 2020, relative to March

2019. March 2020 was selected ex ante to be consistent with the WHO classification of the COVID-19 outbreak as a pandemic on March 11, 2020.[19]

Midyear population sizes were estimated using the United Nations (UN) 2019 Urbanization Prospectus. We examined both overall purchases (including all drugs) and purchases by WHO level-1 Anatomical Therapeutic Chemical (ATC1) class. For each WHO ATC1 class, we listed a sample of subclasses in Appendix 2.

Exposures

To examine whether changes in drug purchasing trends differed by economic development status, we used the UN's 2020 *World Economic Situation Prospectus* to group MIDAS regions into "developed" (N = 33) and "developing" (N = 35) areas. Economies in transition were included in the developing group. This classification accounts for various aspects of a region's total human development, including per capita gross national income, life expectancy, and educational attainment.[20] Because not all regions experienced the start of their epidemics at the same time, we used publicly available data from the COVID-19 Data Repository by the Johns Hopkins University Center for Systems Science and Engineering (compiled by the University of Oxford Our World in Data Group) to calculate new COVID-19 infections per population per month. We compared these epidemic curves with the MIDAS drug purchasing trends.

Statistical analysis

We used interventional autoregressive integrated moving average (ARIMA) models to determine whether global drug purchasing trends changed in March 2020, relative to the previous year. ARIMA models are a type of time series analysis which, unlike other methods (i.e., segmented regression), account for autocorrelation and seasonality, which are common with drug utilization.[21] Thus, ARIMA models can be used to evaluate the impact of interventions or events at the population level where nonlinear trends are observed (such as the impact of the pandemic announcement on drug purchases). We hypothesized that global sales would increase at the start of the pandemic because of individual and regional stockpiling. Therefore, we fit a "pulse" intervention in the first month of the pandemic (March 2020). We also fit a "ramp" intervention to model sustained changes in drug purchases (increase, decrease, or no change) in April 2020 through August 2020. Because drug pricing trends are often autocorrelated and our data demonstrated yearly patterns, we differenced our time series by 12 months to stabilize (smooth) the variability over time. To optimize model fit and meet the assumption of stationarity, we added moving average (q) and autoregressive (p) terms as appropriate based on residual autocorrelation function, partial autocorrelation function, and white noise probability plots. The differenced series demonstrated either a seasonal moving average pattern or autocorrelation at lag 3 or 11 (Appendix 3).

Sensitivity analyses

MIDAS does not capture monthly hospital-based pharmacy sales for 20 regions (N = 3 in the developed group and N = 17 in the developing group) (Appendix 1). In sensitivity analyses, we restricted analyses to the 49 regions with both hospital-based and retail data. To account for decreases (1) in elective inpatient care and (2) initial cases of COVID-19 in China, we repeated our analyses limited to retail medication purchases and removing China, respectively.

Patient and public involvement statement

Before initiation of the research, we engaged partners from health care organizations, drug distributors, regulators, and nongovernmental organizations. These partners' were involved in identifying the research questions and medications for inclusion in our analyses.

Results

Global medication purchases

Globally, the total number of units purchased per month ranged from 217.4 billion to 304.6 billion across the study period (August 2014 to August 2020), with an average (SD) population-standardized rate of 4412.6 units (223.2) per 100 population. Before the WHO pandemic declaration, the global monthly drug purchase rate remained stable, ranging from 3990 to 4760 units per month per 100 population (217.4-271.0 billion total units) (Figure 1). A large increase occurred in March 2020, when COVID-19 was declared a global pandemic but before peak infection rates in the spring and summer (Figure 1). In March 2020, the global purchasing rate for all medications was 5309.3 units per 100 population (304.6 billion total units), a 15.1% increase compared with March 2019 ($P < 0.001$) (Table 1). Drug purchases for most drug classes increased globally, with absolute changes ranging from 1.8% to 42.2%, relative to 2019. Hospital solutions, sensory organ (eye and ear products), and various products (allergens, antidotes, contrast media, and radiopharmaceuticals) experienced nonsignificant decreases. Purchases for genitourinary and sex hormones (contraceptives) did not change relative to 2019 (Table 1).

After the increase in March 2020, there was a correction in the global purchase rate. In April through August 2020, the global purchasing rate for all medications was 21,334.6 units per 100 population, a 4.7% decrease compared with April through August 2019 ($P < 0.001$) (Table 1). With the exception of antiparasitic agents, diagnostic agents, and antineoplastic agents, all other drug classes experienced significant decreases with absolute changes ranging from 0.5% to 18.4% ($P < 0.048$) (Table 1).

Purchases by development status

Across the study period, developed countries purchased more medication units per 100 population than developing countries (mean [SD] of 10,394.4 [631.4] and 3045.9 [184.0], respectively) (Figure 1). Both groups significantly increased their purchasing rates in March 2020, relative to previous years; however, the increase was greater in developed countries (18.5% increase to 13,127.4 units per 100 population; $P < 0.001$) than in developing countries (12.8% increase to 3555.6 units per 100 population; $P < 0.001$). After the increase, there

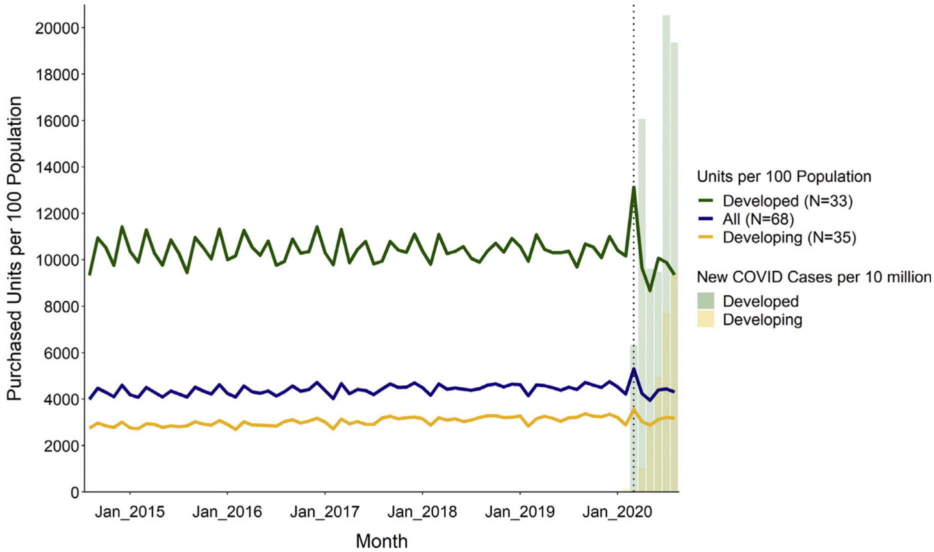

Figure 1. Global purchasing trends per 100 population, all drugs, August 2014 to August 2020. Source: authors' analysis of MIDAS monthly sales data, August 2014 to August 2020; Johns Hopkins COVID-19 database. Note: Dotted black vertical line occurs at March 2020.

was a significant decrease in developed (6.8% decrease) and developing (2.9% decrease) countries in April through August 2020 relative to the previous year. In developed countries, COVID-19 infections peaked in April and July 2020; we did not observe a spring peak in developing countries (Figure 1).

Trends over time by class overall and stratified by development status are shown in Figure 2. Most drug classes had similar trends for developing and developed countries. Classes with agents used to treat patients with COVID-19, such as blood and blood-forming organs (anticoagulants) and anti-infective agents, had significant increases in March 2020 for developed countries whereas developing countries had nonsignificant purchases changes. Respiratory agents experienced increases in March 2020 for developing and developed countries.

Similar decreases from April to August 2020 were observed for most classes for developing and developed countries. However, significant increases occurred from April to August 2020 for alimentary tract, cardiovascular system, dermatologic preparations, blood and blood-forming organs (which include anticoagulants), and systemic hormones (which include steroids) in developing countries, whereas these same classes experienced significant decreases in developed countries.

Purchases by country/jurisdiction

Changes in purchase rates per country in March 2020 relative to March 2019 are shown in Figure 3 and Appendix 1. China experienced the largest decrease (−23.1%), and Central America (130.8%) and Columbia (84.3%) had the largest increases. With the exception of Japan (−6.2%) and Slovenia (2.5%), all other countries that experienced decreases or no change (defined as 10% decrease to 10% increase to account for normal fluctuations in purchase patterns) were developing countries. All other developed countries experienced increases greater than or equal to 10%, with the largest relative changes in small European countries (e.g., Estonia, Hungary, Lithuania, and Bulgaria had increases ≥55%), Australia (62.1%), and New Zealand (46.9%). Canada and the United States had smaller relative increases of 22.5% and 12.1%, respectively (Appendix 4).

Sensitivity analyses

Sensitivity analyses were conducted to assess whether our findings were robust to assumptions of selection criteria within a plausible range.

We first assessed the impact of missing data on our results by restricting our analysis to countries where retail and hospital data were available (N = 49). We observed similar overall and by-class increases in March 2020, globally (14.1% in the sensitivity analysis vs. 15.1% in the primary analysis) and within developed countries (18.3% in the sensitivity vs. 18.5% in the primary analysis) (Appendix 5). However, the overall observed increase in developing countries was lower at 9.9% (vs. 12.8% in the primary analysis).

We next restricted our analysis to retail drugs, to remove the effects of decreased elective inpatient care at the same time as the pandemic on our results. Globally, the relative increase in retail drug purchases in March 2020 was higher than the increase for hospital and retail medicines combined (18.7% in the retail-only analysis vs. 15.1% in primary analysis), especially in developing countries (18.1% vs. 12.8% in the retail-only and primary analyses, respectively) (Appendix 6). Within developing countries, retail purchases for alimentary (gastrointestinal and endocrine drugs), various (allergens antidotes, contrast, radiopharmaceuticals), anti-infective, and genitourinary drugs increased significantly, even though there were no changes for these classes in the combined hospital and retail data. Developing countries also had a substantially larger increase in purchases for antineoplastic/immunomodulating drugs in the retail setting than overall (68.2% in retail-only vs. 28.7% in primary, respectively) (Appendix 6). The trends for developed countries did not change substantially (e.g., overall

Table 1
Changes in purchased units per 100 population, by WHO ATC1 class

ARIMA results testing a pulse intervention in March 2020

WHO ATC1 class	All regions (N = 68)				Developed regions (N = 33)				Developing regions (N = 35)			
	Units per 100 Pop.		% change	*P* value[a]	Units per 100 Pop.		% change	*P* value[a]	Units per 100 Pop.		% change	*P* value[a]
	March 2019	March 2020			March 2019	March 2020			March 2019	March 2020		
All drugs	4611.3	5309.3	15.1	< **0.001**	11081.0	13127.4	18.5	< **0.001**	3151.2	3555.6	12.8	< **0.001**
Alimentary tract and metabolism	755.6	823.0	8.9	**0.008**	1626.0	1840.5	13.2	< **0.001**	559.2	594.7	6.4	**0.402**
Respiratory system	694.7	892.7	28.5	< **0.001**	1553.4	2092.0	34.7	< **0.001**	500.9	623.7	24.5	< **0.001**
Cardiovascular system	621.9	720.4	15.8	< **0.001**	1869.2	2214.2	18.5	< **0.001**	340.4	385.4	13.2	< **0.001**
Nervous system	573.7	710.4	23.8	< **0.001**	1898.3	2370.0	24.8	< **0.001**	274.7	338.1	23.1	< **0.001**
Sensory organs	515.8	485.0	−6.0	0.682	1206.5	1093.1	−9.4	0.47	359.9	348.7	−3.1	0.158
Dermatologic preparations	429.0	610.0	42.2	< **0.001**	956.4	1286.7	34.5	< **0.001**	310.0	458.2	47.8	< **0.001**
Various	267.0	266.5	−0.2	0.419	234.1	273.9	17.0	< **0.001**	274.4	264.8	−3.5	0.988
Musculoskeletal system	220.3	224.1	1.8	**0.043**	516.6	544.1	5.3	**0.003**	153.4	152.3	−0.7	**0.024**
Blood and blood-forming organs	145.1	159.5	10.0	**0.007**	383.5	458.9	19.7	< **0.001**	91.2	92.4	1.2	0.797
Anti-infective agents for systemic use	124.9	127.9	2.4	**0.001**	189.0	210.4	11.3	< **0.001**	110.5	109.4	−1.0	0.06
Systemic hormones[b]	100.8	118.6	17.7	< **0.001**	248.1	303.3	22.3	< **0.001**	67.5	77.2	14.3	< **0.001**
GU system and sex hormones	81.6	85.5	4.8	0.07	200.5	218.9	9.2	**0.009**	54.8	55.6	1.5	0.285
Antiparasitic, insecticides, and repellents	21.8	22.8	4.9	< **0.001**	22.8	25.0	9.8	< **0.001**	21.5	22.3	3.8	< **0.001**
Diagnostic agents[c]	21.2	22.7	7.2	< **0.001**	97.0	106.2	9.5	< **0.001**	4.1	4.0	−2.7	0.716
Antineoplastic and immunomodulators	19.5	24.3	24.3	< **0.001**	53.0	63.8	20.3	< **0.001**	12.0	15.4	28.7	< **0.001**
Hospital solutions[d]	18.6	15.8	−14.8	0.134	26.7	26.7	−0.2	0.281	16.8	13.4	−20.0	**0.043**

ARIMA results testing a ramp intervention in April 2020 through August 2020

WHO ATC1 class	All regions (N = 68)				Developed regions (N = 33)				Developing regions (N = 35)			
	Units per 100 Pop.		% change	*P* value[a]	Units per 100 Pop.		% change	*P* value[a]	Units per 100 Pop.		% change	*P* value[a]
	April to August 2019	Apr-Aug 2020			April to August 2019	Apr-Aug 2020			April to August 2019	Apr-Aug 2020		
All drugs	22389.9	21334.6	−4.7	< **0.001**	51129.2	47632.4	−6.8	< **0.001**	15903.6	15435.7	−2.9	< **0.001**
Alimentary tract and metabolism	3797.5	3734.1	−1.7	**0.048**	7787.1	7327.4	−5.9	**0.048**	2897.1	2928.0	1.1	**0.048**
Respiratory system	3002.8	2595.5	−13.6	< **0.001**	6198.2	5305.1	−14.4	< **0.001**	2281.6	1987.8	−12.9	< **0.001**
Cardiovascular system	3046.0	3029.3	−0.5	< **0.001**	9050.1	8841.6	−2.3	< **0.001**	1690.9	1725.5	2.0	< **0.001**
Nervous system	2730.6	2636.7	−3.4	< **0.001**	8708.7	8277.5	−5.0	< **0.001**	1381.4	1371.3	−0.7	< **0.001**
Sensory organs	2474.5	2159.6	−12.7	< **0.001**	5139.2	4452.2	−13.4	< **0.001**	1873.0	1645.3	−12.2	< **0.001**
Dermatologic preparations	2265.2	2471.5	9.1	< **0.001**	4841.1	4795.3	−0.9	< **0.001**	1683.8	1950.2	15.8	< **0.001**
Various	1357.6	1254.4	−7.6	**0.031**	1154.2	1093.8	−5.2	**0.031**	1403.5	1290.4	−8.1	**0.031**
Musculoskeletal system	1086.0	996.7	−8.2	< **0.001**	2505.0	2279.8	−9.0	< **0.001**	765.7	708.9	−7.4	< **0.001**
Blood and blood-forming organs	721.5	711.6	−1.4	**0.023**	1865.6	1802.0	−3.4	**0.023**	463.3	467.0	0.8	**0.023**
Anti-infective agents for systemic use	603.0	492.3	−18.4	< **0.001**	803.3	608.6	−24.2	< **0.001**	557.8	466.2	−16.4	< **0.001**
Systemic hormones[b]	508.5	499.5	−1.8	< **0.001**	1174.4	1079.0	−8.1	< **0.001**	358.2	369.5	3.2	< **0.001**
GU system and sex hormones	405.7	380.2	−6.3	< **0.001**	972.0	925.0	−4.8	< **0.001**	278.0	258.0	−7.2	< **0.001**
Antiparasitic, insecticides, and repellents	107.9	103.0	−4.5	0.309	98.9	78.3	−20.8	0.309	109.9	108.6	−1.2	0.309

Diagnostic agents[c]	95.4	88.1	−7.6	0.082	440.0	396.0	−10.0	0.082	17.7	19.1	8.1	0.082
Antineoplastic and immunomodulators	94.6	100.2	6.0	0.309	257.7	254.8	−1.1	0.309	57.8	65.6	13.5	0.309
Hospital solutions[d]	93.3	82.1	−12.1	< **0.001**	134.8	116.8	−13.4	< **0.001**	84.0	74.3	−11.6	< **0.001**

Abbreviations used: ARIMA, autoregressive integrated moving average; ATC1, level-1 Anatomical Therapeutic Chemical; GU, genitourinary; Pop., population; GU, genitourinary; WHO, World Health Organization.
Source: Authors' analysis of MIDAS monthly sales data, August 2014 to August 2020.
[a] Reported *P* values are for an ARIMA pulse intervention in March 2020 (top) and ARIMA ramp intervention (bottom). Bold denotes $P < 0.05$.
[b] Excludes sex hormones and insulins.
[c] There were no available data for diagnostic agents in Luxembourg for 92% of the study period. Peru has missing data for this class in 7 months.
[d] There were no available data for hospital solutions in Switzerland across the study period. Algeria has missing data for this class in 21 months.

increase of 19.7% vs. 18.5% in retail-only vs. primary analysis, respectively).

Our final sensitivity analysis excluded China, where drug purchase patterns likely differed because most COVID-19 cases occurred before the WHO declaration. Excluding China from the analysis demonstrated a 19.4% global increase (vs. 15.1%) in drug units purchased per 100 population (Appendix 7). This sensitivity analysis especially moderated the increase for developing countries (20.8% increase vs. 12.8% increase in our primary analysis).

Discussion

Statement of principal findings

We observed a striking global increase in drug purchases in March 2020 as the pandemic was declared. After this increase, there was a rapid decrease in April through August 2020. The March 2020 increase in drug purchases was larger in developed than developing countries and resulted in a greater subsequent decrease for developed countries. Differences in drug class trends for developing and developed countries may be due to limits in drug supply and tendency of manufacturers to sell medications to economically advantaged countries. Therefore, developing nations may be more vulnerable to disruptions because of their already-limited supply.[22] Countries with drug stockpiles may have needed limited additional drug purchases for a pandemic and may explain large increases in respiratory agents and anti-infective agents. Large percentage increases in drug purchases may also be due to limited health care infrastructure. However, developed countries with well-established health care systems (e.g., Australia, Scandinavia) experienced increases greater than 50% in units purchased.

Strengths and weaknesses of the study

The IQVIA MIDAS dataset provides an unprecedented view of drug purchases from most of the world's population, including developing and developed countries from each continent. MIDAS provides standardized sales data that allows for unique country-level comparisons over time. The data are also recent and internally validated. Although drug purchases may not reflect consumption, MIDAS is reconciled for returns and likely reflects patient use after the drug purchase date. The MIDAS dataset does not include all drug purchases for each country, and hospital data were only available for 49 countries. However, sensitivity analyses limited to countries with both hospital and retail data available did not change our overall conclusions. Although the primary analysis (excluding China because of earlier COVID occurrence) demonstrated significantly greater purchases by developed countries, including China resulted in a larger increase in developing countries (although smaller in magnitude). Our data do not account for medication supplies accessed from stockpiles, investigational products, or drugs available through emergency use authorizations, including remdesivir. Therefore, our results for medications needed to treat patients with COVID-19 (i.e., respiratory and anti-infective agents) may be underestimated.

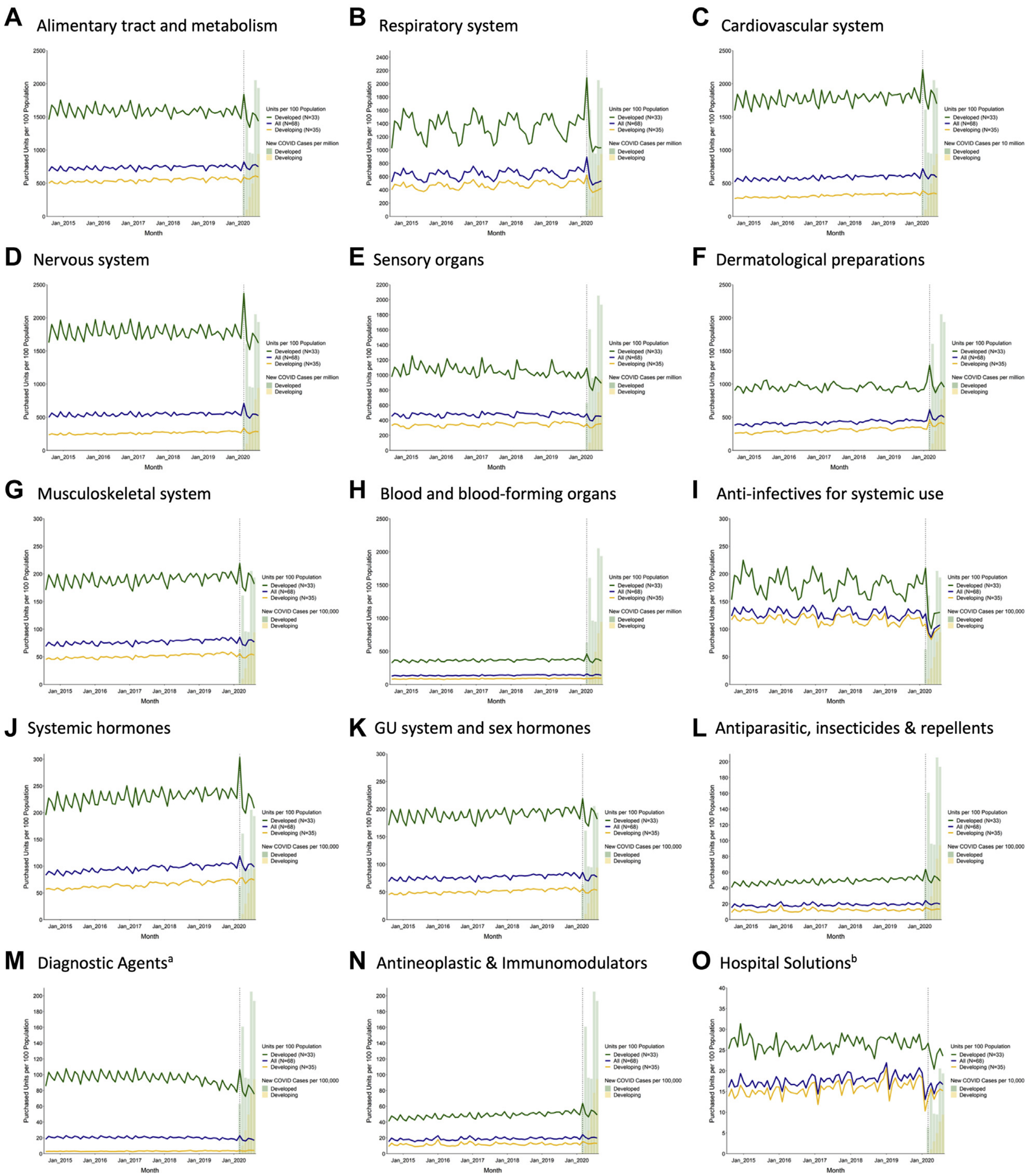

Figure 2. Global purchasing trends per 100 population, by WHO ATC1 class, August 2014 to August 2020. Source: authors' analysis of MIDAS monthly sales data, August 2014 to August 2020. Notes: (A) There were no available data for diagnostic agents in Luxembourg for 92% of the study period. Peru has missing data for this class in 7 months. (B) There were no available data for hospital solutions in Switzerland across the study period. Algeria has missing data for this class in 21 months. Abbreviations used: ATC1, level-1 Anatomical Therapeutic Chemical; WHO, World Health Organization.

Strengths and weaknesses in relation to other studies

There are limited data on the global distribution of medications. Wealthier countries have higher rates of medicine use.[1] Although developing and emerging markets account for most of medication growth in recent years, per-capita use still lags behind wealthier countries.[1] International assessments of antibiotic purchases before the

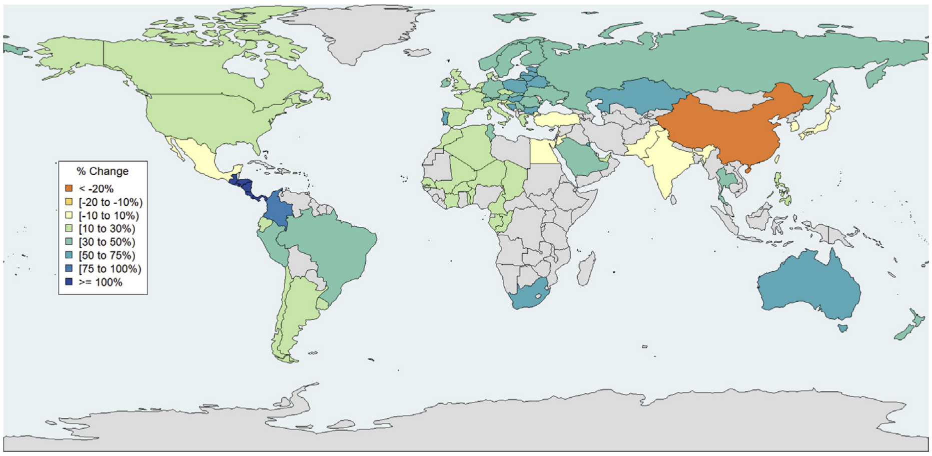

Figure 3. Changes in purchased units, all drugs, by jurisdiction, March 2020 vs. March 2019. Source: authors' analysis of MIDAS monthly sales data, August 2014 to August 2020. Notes: Individual country-level data were not available for Central America (Costa Rica, El Salvador, Honduras, Guatemala, Nicaragua, and Panama) and French West Africa (Benin, Burkina Faso, Cameroon, Chad, Congo, Gabon, Guinea, Cote d'Ivoire, Mali, Niger, Senegal, and Togo); these countries were therefore analyzed in aggregate.

COVID-19 pandemic found that low- and middle-income countries (LMICs) had a large increase in antibiotics with slight decreases by high-income countries.[23]A subsequent study suggests that LMICs have less access to newer antibiotics with effectiveness against multidrug-resistant pathogens even though multidrug resistance was more prevalent in LMICs.[24] To the best of our knowledge, our analysis is the first international comparison of drug supply in aggregate and for all therapeutic categories. Importantly, we provide the first evidence of the impact of a global pandemic on drug purchases and supply.

Meaning of the study

We believe our results provide important insights on the global distribution of drugs. Our results reflect drug purchases during a global pandemic and may be relevant to future unanticipated events affecting the global drug supply chain. Worldwide increases for most drugs likely caused substantial pressure on the drug supply chain. There was variation by country and economic status, which suggests an uncoordinated approach to supply chain drug distribution. Medications are essential for health in all countries and are a global resource. As observed with COVID-19, border closings and countries prohibiting drug export potentially threatened global access to essential medicines.[13–16] Important lessons from this pandemic highlight the need for global action. International treaties must ensure access and equitable distribution of medications similar to other resources essential to health.

Unanswered questions and future research

Future research is needed on the extent to which inequitable drug distribution affects patient outcomes and access to first-line medications. The impact of international laws (e.g., patent laws) and country-specific policies on drug supply and shortages is unknown. In addition, identifying solutions to improve resiliency of the drug supply chain is urgently needed, especially during unanticipated events.

Conclusion

A significant increase in drug purchases occurred in March 2020 when the WHO declared COVID-19 a pandemic. However, a large variation was observed across countries, with developed countries increasing their purchases of drugs to a higher extent than developing countries. The equitable distribution of medicines through a resilient drug supply chain is essential for reducing the global burden of disease, improving the health and productivity of communities. Therefore, global action should be taken to ensure equitable distribution of drugs.

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Appendix

Appendix 1
List of MIDAS Regions summarizes the population coverage of the MIDAS SMART dataset in 2020

Geographic Group	Included Regions[a]	2020 Mid-Year Population (millions)	% of 2020 Global Population
North America – Developed	Canada, USA	357.4	4.6%
North America – Developing	Puerto Rico	3.7	0.05%
Europe - Developed	Austria, Belgium, Bulgaria, Croatia, Czech Rep., Denmark, Estonia*, Finland, France, Germany, Greece*, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg*, Netherlands, Norway, Poland, Portugal, Romania, Slovak Rep., Slovenia, Spain, Sweden, Switzerland, UK	523.4	6.7%
Europe - Developing	Belarus, Bosnia, Kazakhstan, Russian Fed., Serbia, Turkey, Ukraine	311.6	4.0%
Latin America - Developing	Argentina*, Brazil, Central America*,[b], Chile*, Colombia*, Ecuador*, Mexico, Peru*, Uruguay*	565.9	7.3%
Middle East and Africa - Developing	Algeria*, Egypt*, French West Africa*,[c], Jordan*, Kuwait*, Lebanon*, Morocco*, Saudi Arabia, South Africa, Tunisia, UAE*	523.6	6.7%
Asia Pacific - Developed	Australia, Japan, New Zealand	156.7	2.0%
Asia Pacific – Developing	China, India, Korea, Pakistan*, Philippines, Taiwan, Thailand	3270.5	42.0%

Source: MIDAS, UN 2018 Population Prospectus
[a] Asterisk denotes a region for which only retail pharmacy sales were available.
[b] Central America included Costa Rica, El Salvador, Honduras, Guatemala, Nicaragua & Panama.
[c] French West Africa included Benin, Burkina Faso, Cameroon, Chad, Congo, Gabon, Guinea, Cote d'Ivoire, Mali, Niger, Senegal, Togo.

Appendix 2
Example subclasses included in each ATC1 class defined by the WHO describes subclasses within the WHO ATC1 drug classes

WHO ATC1 Class	Example drug classes
Alimentary tract and metabolism	Drugs for peptic ulcer and gastro-esophageal reflux disease, antiemetics, laxatives, antiobesity, antidiabetics, anabolic agents
Respiratory system	Respiratory inhalers, systemic adrenergics, cough and cold products
Cardiovascular system	Cardiac glycosides, antiarrhythmics, antihypertensives, diuretics, peripheral vasodilators, lipid modifying agents
Nervous system	Anesthetics (general and local), opioids, salicylate analgesics, antimigraine, antiepileptics, anti-parkinson drugs, psycholeptics, psychoanaleptics
Sensory organs	Opthamological and ontological agents
Dermatological preparations	Predominately topical agents including antimicrobials, antipruritics, acne products, wound preparations
Various	Allergens, antidotes, contrast media, radiopharmaceuticals
Musculoskeletal system	Antiinflammatory and antirheumatic products (systemic and topical), muscle relaxants, antigout products, bone disease agents
Blood and blood-forming organs	Antithrombotics, antihemorrhagics, antianemics, and blood substitutes
Anti-infectives for systemic use	Antibacterials, antimycotics, antivirals, vaccines
Systemic hormones[a]	Corticosteroids, thyroid products, pituitary and hypothalamic agents
GU system and sex hormones	Gynecological products, contraceptives, urologicals (includes drugs for benign prostatic hypertrophy)
Antiparasitic, insecticides & repellents	Antiprotozoals, antihelmintics, ectoparasiticides
Diagnostic Agents	Urine tests, diagnostics agents for diabetes and other diseases
Antineoplastic and immunomodulators	Antineoplastics, endocrine therapy, immunostimulants, immunosuppresants
Hospital Solutions	Normal saline, dextrose in water

Appendix 3
Final Fitted ARIMA Models provides the model specifications for the main ARIMA analyses presented in Table 1

WHO ATC1 Class	All Regions (N=68)	Developed Regions (N=33)	Developing Regions (N=35)
All Drugs	MA model w/autocorrelation at lags 1 & 12. [AR (p=0, d=12, q=1,12)]. Specified w/o intercept.		
Alimentary tract & metabolism	AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].	Differenced model at lag 12. [AR (p=0, d=12, q=0)].	AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].
Blood and blood-forming organs	Differenced model at lag 12. [AR (p=0, d=12, q=0)].	MA model w/autocorrelation at lags 1 & 12. [AR (p=0, d=12, q=1,12)]. Specified w/o intercept.	Differenced model at lag 12. [AR (p=0, d=12, q=0)].
Cardiovascular system	AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].	Differenced model at lag 12. [AR (p=0, d=12, q=0)].	AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].
Dermatological preparations	Moving average model accounting for autoregression at lags 1 & 12. [AR (p=0, d=12, q=1,12)]. Specified w/o intercept.	Differenced model at lag 12. [AR (p=0, d=12, q=0)].	Moving average model accounting for autoregression at lags 1 & 12. [AR (p=0, d=12, q=1,12)]. Specified w/o intercept.
GU system and sex hormones	AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].	Differenced model at lag 12. [AR (p=0, d=12, q=0)].	AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].
Systemic hormones[a]	AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].	MA model w/autocorrelation at lags 1 & 12. [AR (p=0, d=12, q=1,12)]. Specified w/o intercept.	AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].
Anti-infectives for systemic use	MA model w/autocorrelation at lags 1 & 12. [AR (p=0, d=12, q=1,12)]. Specified w/o intercept.		
Hospital Solutions	AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].		
Antineoplastic and immunomodulators	AR model w/autocorrelation at lag 11. [AR (p=11, d=12, q=0)].		
Musculoskeletal system	MA model w/autocorrelation at lags 1 & 12. [AR (p=0, d=12, q=1,12)]. Specified w/o intercept.		AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].
Nervous system	AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].	MA model w/autocorrelation at lags 1 & 12. [AR (p=0, d=12, q=1,12)]. Specified w/o intercept.	AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].
Antiparasitic, insecticides & repellents	AR model w/autocorrelation at lag 11. [AR (p=11, d=12, q=0)].		
Respiratory system	MA model w/autocorrelation at lags 1 & 12. [AR (p=0, d=12, q=1,12)]. Specified w/o intercept.		
Sensory organs	MA model w/autocorrelation at lags 1 & 12. [AR (p=0, d=12, q=1,12)]. Specified w/o intercept.		
Diagnostic Agents	MA model w/autocorrelation at lags 1 & 12. [AR (p=0, d=12, q=1,12)]. Specified w/o intercept.	AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].	
Various	AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].	Differenced model at lag 12. [AR (p=0, d=12, q=0)].	AR model w/autocorrelation at lag 3. [AR (p=3, d=12, q=0)].

Source: Authors' analysis of MIDAS Monthly Sales Data, August 2014-August 2020.**Source:** Authors' analysis of MIDAS Monthly Sales Data, August 2014-August 2020.
Abbreviations: ATC, Anatomical Therapeutic Chemical; AR, autoregressive; MA, moving average; p, number of autoregressive terms; d, number of nonseasonal differences needed for stationarity; q, number of lagged forecast errors in the prediction equation.
[a] Excludes sex hormones and insulins.

Appendix 4

Changes in Purchased Units per 100 Population, March 2020 vs. March 2019, by Jurisdiction shows country-level changes in units purchased per 100 population in March 2020, relative to March 2019

A. Developed Regions (N=33) B. Developing Regions (N=35)

Source: Authors' analysis of MIDAS Monthly Sale**s** Data, August 2014-August 2020.**Source:** Authors' analysis of MIDAS Monthly Sales Data, August 2014-August 2020.

Abbreviations: ATC, Anatomical Therapeutic Chemical; AR, autoregressive; MA, moving average; p, number of autoregressive terms; d, number of nonseasonal differences needed for stationarity; q, number of lagged forecast errors in the prediction equation.

Appendix 5

Changes in Purchased Units per 100 Population, by ATC1 Class, March 2020 vs. March 2019, Excluding Regions without Available Hospital Data presents a sensitivity analysis, excluding regions without hospital data

WHO ATC1 Class	All Regions (N=49)				Developed Regions (N=30)				Developing Regions (N=19)			
	Units per 100 Pop.		% Change	p-val.[a]	Units per 100 Pop.		% Change	p-val.[a]	Units per 100 Pop.		% Change	p-val.[a]
	Mar. 2019	Mar. 2020			Mar. 2019	Mar. 2020			Mar. 2019	Mar. 2020		
All Drugs	4840.8	5521.4	14.1	**<0.001**	11118.2	13147.8	18.3	**<0.001**	3030.5	3331.1	9.9	**<0.001**
Alimentary tract and metabolism	774.1	841.4	8.7	**0.008**	1631.9	1846.1	13.1	**<0.001**	526.8	552.9	5.0	0.452
Respiratory system	708.6	917.4	29.5	**<0.001**	1547.6	2085.7	34.8	**<0.001**	466.7	581.8	24.7	**<0.001**
Cardiovascular system	685.7	794.0	15.8	**<0.001**	1875.3	2222.8	18.5	**<0.001**	342.7	383.7	12.0	**<0.001**
Nervous system	616.5	753.6	22.2	**<0.001**	1904.2	2373.3	24.6	**<0.001**	245.1	288.4	17.7	**<0.001**
Sensory organs	525.5	484.9	-7.7	0.864	1219.8	1103.5	-9.5	0.448	325.3	307.3	-5.5	0.381
Dermatological preparations	436.8	587.4	34.5	**<0.001**	964.1	1280.6	32.8	**<0.001**	284.7	388.3	36.4	**<0.001**
Various	322.7	319.8	-0.9	0.536	239.4	279.7	16.8	**<0.001**	346.7	331.3	-4.5	0.856
Musculoskeletal system	213.1	218.2	2.4	**0.046**	516.2	543.3	5.3	**0.003**	125.7	124.8	-0.8	0.593
Blood and blood-forming organs	150.9	168.2	11.5	**0.003**	380.7	456.1	19.8	**<0.001**	84.6	85.5	1.1	0.801
Anti-infectives for systemic use	126.6	127.5	0.7	**0.006**	189.8	211.8	11.6	**<0.001**	108.4	103.3	-4.7	0.435
Systemic hormones[b]	110.3	129.5	17.4	**<0.001**	247.8	302.3	22.0	**<0.001**	70.6	79.8	13.1	**0.005**
GU system and sex hormones	84.0	88.7	5.6	0.089	200.6	219.3	9.3	**0.008**	50.4	51.2	1.6	0.552
Antiparasitic, insecticides & repellents	17.9	18.7	4.4	0.198	23.1	25.4	9.9	**0.005**	16.3	16.7	2.2	**<0.001**
Diagnostic Agents[c]	23.7	25.9	9.2	**<0.001**	98.2	107.6	9.6	**<0.001**	2.2	2.4	9.6	0.983
Antineoplastic and immunomodulators	22.8	28.2	23.9	**<0.001**	53.1	63.9	20.2	**<0.001**	14.0	18.0	28.3	**<0.001**
Hospital Solutions[d]	21.8	18.2	-16.6	0.087	26.8	26.6	-0.4	0.277	20.4	15.8	-22.6	**0.034**

Source: Authors' analysis of MIDAS Monthly Sales Data, August 2014-August 2020.

Abbreviations: ATC, Anatomical Therapeutic Chemical; Pop., population; p-val., p-value; GU, genito-urinary.

[a] Reported p-values are for an ARIMA pulse intervention in March 2020. Bold denotes p-value < 0.05.

[b] Excludes sex hormones and insulins.

[c] There was no available data for diagnostic agents in Luxembourg for 92% of the study period. Peru was missing data for this class in 7 months.

[d] There was no available data for hospital solutions in Switzerland across the study period. Algeria was missing data for this class in 21 months.

Appendix 6

Changes in Purchased Units per 100 Population, by ATC1 Class, March 2020 vs. March 2019, Restricting to Retail Purchases presents a sensitivity analysis, limiting data to the retail sector

WHO ATC1 Class	All Regions (N=68)				Developed Regions (N=33)				Developing Regions (N=35)			
	Units per 100 Pop.		% Change	p-val.[a]	Units per 100 Pop.		% Change	p-val.[a]	Units per 100 Pop.		% Change	p-val.[a]
	Mar. 2019	Mar. 2020			Mar. 2019	Mar. 2020			Mar. 2019	Mar. 2020		
All Drugs	3932.2	4666.7	18.7	**<0.001**	9841.0	11782.4	19.7	**<0.001**	2571.3	3038.0	18.1	**<0.001**
Alimentary tract and metabolism	649.8	726.9	11.9	**<0.001**	1458.4	1670.2	14.5	**<0.001**	463.6	511.0	10.2	**0.001**
Respiratory system	650.0	852.1	31.1	**<0.001**	1449.6	1950.4	34.5	**<0.001**	465.9	600.7	28.9	**<0.001**
Cardiovascular system	534.0	630.2	18.0	**<0.001**	1713.3	2048.1	19.5	**<0.001**	262.4	305.7	16.5	**<0.001**
Nervous system	497.6	631.4	26.9	**<0.001**	1686.0	2135.4	26.7	**<0.001**	223.9	287.2	28.3	**<0.001**
Sensory organs	463.7	441.8	-4.7	0.546	1089.4	995.1	-8.7	0.50	319.6	315.2	-1.4	0.06
Dermatological preparations	357.2	514.2	43.9	**<0.001**	715.6	1011.7	41.4	**<0.001**	274.6	400.3	45.8	**<0.001**
Various	139.3	173.0	24.2	**<0.001**	194.0	232.1	19.7	**<0.001**	126.7	159.5	25.9	**<0.001**
Musculoskeletal system	204.6	209.4	2.4	**0.008**	478.1	504.2	5.5	**0.004**	141.6	141.9	0.2	**0.007**
Blood and blood-forming organs	121.1	135.9	12.2	**<0.001**	339.7	411.4	21.1	**<0.001**	70.8	72.9	2.9	0.895
Anti-infectives for systemic use	97.6	103.5	6.1	**<0.001**	152.2	168.0	10.3	**<0.001**	85.0	88.7	4.4	**0.001**
Systemic hormones[b]	89.5	107.9	20.5	**<0.001**	227.2	279.9	23.2	**<0.001**	57.8	68.5	18.4	**<0.001**
GU system and sex hormones	72.9	77.9	6.8	**0.003**	186.2	204.5	9.9	**0.006**	46.8	48.9	4.5	**0.002**
Antiparasitic, insecticides & repellents	21.4	22.2	3.4	**<0.001**	21.9	22.6	3.2	**0.03**	21.3	22.1	3.4	**<0.001**
Diagnostic Agents[c]	18.9	20.5	8.7	**<0.001**	85.9	96.3	12.1	**<0.001**	3.5	3.2	-7.9	0.265
Antineoplastic and immunomodulators	12.4	17.4	39.6	**<0.001**	40.3	48.9	21.5	**<0.001**	6.0	10.2	68.2	**<0.001**
Hospital Solutions[d]	2.0	2.3	15.0	**<0.001**	3.4	3.8	13.1	**0.008**	1.7	2.0	16.0	**<0.001**

Source: Authors' analysis of MIDAS Monthly Sales Data, August 2014-August 2020.

Abbreviations: ATC, Anatomical Therapeutic Chemical; Pop., population; p-val., p-value; GU, genito-urinary.

[a] Reported p-values are for an ARIMA pulse intervention in March 2020. Bold denotes p-value < 0.05.

[b] Excludes sex hormones and insulins.

[c] There was no available data for diagnostic agents in Luxembourg for 92% of the study period. Peru was missing data for this class in 7 months.

[d] There was no available data for hospital solutions in Switzerland across the study period. Algeria was missing data for this class in 21 months.

Appendix 7

Changes in Purchased Units per 100 Population, by ATC1 Class, March 2020 vs. March 2019, Excluding China presents a sensitivity analysis, excluding China

WHO ATC1 Class	All Regions (N=67)				Developed Regions (N=33)				Developing Regions (N=34)			
	Units per 100 Pop.		% Change	p-val.[a]	Units per 100 Pop.		% Change	p-val.[a]	Units per 100 Pop.		% Change	p-val.[a]
	Mar. 2019	Mar. 2020			Mar. 2019	Mar. 2020			Mar. 2019	Mar. 2020		
All Drugs	5529.4	6602.0	19.4	**<0.001**	11081.0	13127.4	18.5	**<0.001**	3716.8	4489.4	20.8	**<0.001**
Alimentary tract and metabolism	918.5	1025.2	11.6	**<0.001**	1626.0	1840.5	13.2	**<0.001**	687.4	761.2	10.7	**0.001**
Respiratory system	896.3	1175.1	31.1	**<0.001**	1553.4	2092.0	34.7	**<0.001**	681.7	878.2	28.8	**<0.001**
Cardiovascular system	753.9	888.1	17.8	**<0.001**	1869.2	2214.2	18.5	**<0.001**	389.8	458.8	17.7	**<0.001**
Nervous system	735.4	919.8	25.1	**<0.001**	1898.3	2370.0	24.8	**<0.001**	355.7	450.3	26.6	**<0.001**
Sensory organs	644.1	618.8	-3.9	0.433	1206.5	1093.1	-9.4	0.47	460.5	465.3	1.0	**0.034**
Dermatological preparations	556.8	802.6	44.1	**<0.001**	956.4	1286.7	34.5	**<0.001**	426.4	645.9	51.5	**<0.001**
Various	123.0	181.7	47.7	**<0.001**	234.1	273.9	17.0	**<0.001**	86.7	151.9	75.1	**<0.001**
Musculoskeletal system	284.6	291.6	2.5	**0.03**	516.6	544.1	5.3	**0.003**	208.8	209.8	0.50	**0.008**
Blood and blood-forming organs	172.0	194.4	13.0	**<0.001**	383.5	458.9	19.7	**<0.001**	102.9	108.8	5.7	0.884
Anti-infectives for systemic use	129.5	146.6	13.2	**<0.001**	189.0	210.4	11.3	**<0.001**	110.0	125.9	14.4	**0.002**
Systemic hormones[b]	125.1	149.7	19.6	**<0.001**	248.1	303.3	22.3	**<0.001**	85.0	99.9	17.6	**<0.001**
GU system and sex hormones	101.3	108.5	7.1	**0.008**	200.5	218.9	9.2	0.009	69.0	72.8	5.5	**0.012**
Antiparasitic, insecticides & repellents	28.9	30.4	5.0	**<0.001**	22.8	25.0	9.8	0.005	31.0	32.1	3.8	**<0.001**
Diagnostic Agents[c]	28.2	30.2	7.2	**<0.001**	97.0	106.2	9.5	**<0.001**	5.7	5.6	-2.0	0.783
Antineoplastic and immunomodulators	20.2	27.3	35.1	**<0.001**	53.0	63.8	20.3	**<0.001**	9.5	15.5	62.9	**<0.001**
Hospital Solutions[d]	11.4	12.1	6.0	**0.018**	26.7	26.7	-0.2	0.281	6.5	7.4	14.8	**0.012**

Source: Authors' analysis of MIDAS Monthly Sales Data, August 2014-August 2020.

Abbreviations: ATC, Anatomical Therapeutic Chemical; Pop., population; p-val., p-value; GU, genito-urinary.

[a] Reported p-values are for an ARIMA pulse intervention in March 2020. Bold denotes p-value < 0.05.

[b] Excludes sex hormones and insulins.

[c] There was no available data for diagnostic agents in Luxembourg for 92% of the study period. Peru was missing data for this class in 7 months.

[d] There was no available data for hospital solutions in Switzerland across the study period. Algeria was missing data for this class in 21 months.