RESEARCH LETTER

Prescription Fill Patterns for Commonly Used Drugs During the COVID-19 Pandemic in the United States

Conflicting information regarding the benefits of hydroxychloroquine/chloroquine and azithromycin in coronavirus disease 2019 (COVID-19) treatment and hypothetical concerns for drugs, such as angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs), have challenged care during the pandemic.[1] However, limited data are available about how prescription of these therapies has changed. The objective of this exploratory analysis was to evaluate prescription patterns of these therapies, along with other commonly used drugs for reference, in the United States during the COVID-19 pandemic. We hypothesized that the prescription of hydroxychloroquine/chloroquine and azithromycin would exceed historical estimates while ACE inhibitor/ARB use would be reduced.

Methods | Trends in mean weekly prescriptions dispensed between February 16 and April 25, 2020, of hydroxychloroquine/chloroquine, azithromycin, and the top 10 drugs based on total claims in 2019, which included the most common ACE inhibitor (lisinopril) and ARB (losartan), were compared with mean weekly prescriptions dispensed from February 17 to April 27, 2019 (**Table**). We used all-payer US pharmacy data from 58 332 chain, independent, and mail-order pharmacies across 14 421 zip codes in 50 states, reflecting approximately 17 million deidentified claims.[2] Prescriptions of hydroxychloroquine/chloroquine were also examined based on fill quantity (<28 tablets, 28-60 tablets, or >60 tablets). Pharmacy claims were assigned weights to match prescription data from the Medical

Table. Estimates of Total Weekly Fills and Relative Percentage Change From 2019 Estimates of Commonly Prescribed Drugs, Azithromycin, and Hydroxychloroquine/Chloroquine[a]

Drug	February 16-22	February 23-29	March 1-7	March 8-14	March 15-21	March 22-28	March 29-Apr 4	April 5-11	April 12-18	April 19-25
Amlodipine										
Change from 2019, % (95% CI)	3.9 (2.4 to 5.4)	9.1 (7.0 to 11.5)	13.2 (10.9 to 15.9)	19.4 (15.0 to 25.2)	32.3 (23.7 to 43.7)	4.3 (−2.3 to 13.3)	−3.7 (−9.3 to 3.6)	−7.4 (−13.4 to 0.1)	−8.0 (−14.2 to 0.2)	−9.2 (−15.5 to −1.3)
Weekly fill volume[b]	1 795 987	1 885 745	1 956 234	2 064 406	2 286 352	1 802 359	1 664 743	1 599 726	1 590 300	1 568 986
Amoxicillin										
Change from 2019, % (95% CI)	0.2 (−1.6 to 2.1)	−0.5 (−2.3 to 1.3)	−2.8 (−4.4 to −1.1)	−5.0 (−6.8 to −3.2)	−20.2 (−22.6 to −17.6)	−44.5 (−46.6 to −42.0)	−54.7 (−56.6 to −52.3)	−61.9 (−63.4 to −60.0)	−63.3 (−64.7 to −61.7)	−64.4 (−65.8 to −63.0)
Weekly fill volume[b]	750 589	745 429	728 587	711 556	597 551	415 937	339 287	285 352	275 002	266 455
Atorvastatin										
Change from 2019, % (95% CI)	1.4 (0.0 to 3.0)	7.0 (4.6 to 9.5)	11.2 (8.7 to 14.1)	17.0 (12.4 to 22.4)	30.9 (19.4 to 46.0)	4.7 (−5.2 to 18.1)	−5.3 (−11.9 to 2.2)	−8.1 (−14.8 to −0.2)	−8.0 (−15.0 to 0.2)	−9.1 (−16.0 to −0.9)
Weekly fill volume[b]	2 450 791	2 583 872	2 686 683	2 826 689	3 161 659	2 529 696	2 286 659	2 219 255	2 223 731	2 195 951
Azithromycin										
Change from 2019, % (95% CI)	1.3 (−0.7 to 3.6)	3.3 (1.4 to 5.6)	3.0 (0.9 to 5.0)	5.1 (3.2 to 7.3)	8.7 (5.7 to 12.3)	−12.0 (−14.6 to −8.7)	−31.5 (−34.0 to −28.2)	−47.9 (−49.8 to −45.5)	−57.6 (−59.0 to −56.0)	−62.7 (−63.8 to −61.3)
Weekly fill volume[b]	373 638	380 949	379 756	387 598	400 781	324 522	252 534	192 014	156 166	137 642
Gabapentin										
Change from 2019, % (95% CI)	−0.9 (−2.5 to 0.9)	3.6 (1.6 to 6.0)	6.5 (4.6 to 8.7)	7.8 (4.6 to 12.0)	15.0 (9.2 to 23.3)	−0.6 (−6.2 to 7.1)	−5.8 (−10.4 to 0.2)	−7.3 (−12.5 to −0.5)	−5.9 (−10.8 to 0.6)	−7.9 (−12.5 to −1.7)
Weekly fill volume[b]	1 189 617	1 242 901	1 278 137	1 293 476	1 379 772	1 192 865	1 130 251	1 111 808	1 129 336	1 105 475
Hydrocodone-acetaminophen										
Change from 2019, % (95% CI)	−0.3 (−2.2 to 1.6)	0.1 (−2.0 to 2.4)	4.0 (1.8 to 6.1)	1.5 (−0.5 to 3.5)	−5.0 (−7.1 to −2.9)	−20.0 (−22.4 to −17.8)	−23.1 (−25.5 to −20.6)	−23.4 (−25.9 to −20.9)	−22.0 (−24.6 to −19.4)	−21.8 (−24.6 to −19.1)
Weekly fill volume[b]	668 493	671 374	697 461	680 318	637 300	536 497	515 708	513 472	523 161	524 289
Hydroxychloroquine/chloroquine										
Change from 2019, % (95% CI)	4.2 (0.8 to 7.8)	8.7 (5.2 to 11.9)	14.6 (11.1 to 18.0)	30.9 (26.0 to 36.0)	214.1 (205.0 to 224.5)	70.3 (53.0 to 84.1)	16.1 (3.8 to 25.9)	15.9 (4.2 to 26.0)	14.6 (2.9 to 24.4)	23.9 (15.7 to 32.2)
Weekly fill volume[b]	121 865	127 059	134 008	153 119	367 297	199 157	135 746	135 528	133 972	144 921

(continued)

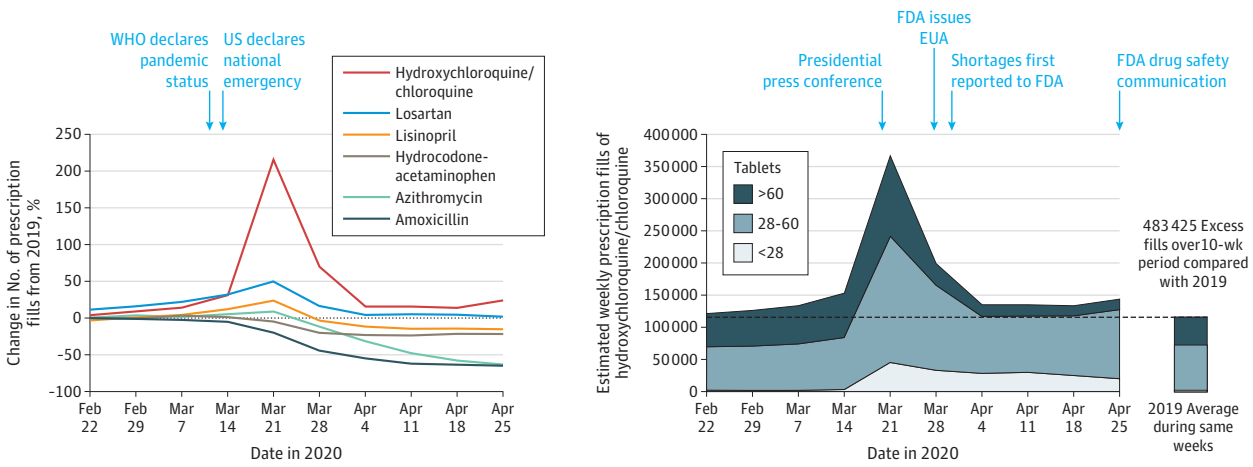
Table. Estimates of Total Weekly Fills and Relative Percentage Change From 2019 Estimates of Commonly Prescribed Drugs, Azithromycin, and Hydroxychloroquine/Chloroquine[a] (continued)

Drug	February 16-22	February 23-29	March 1-7	March 8-14	March 15-21	March 22-28	March 29-Apr 4	April 5-11	April 12-18	April 19-25
Levothyroxine										
Change from 2019, % (95% CI)	−3.6 (−6.0 to −1.2)	1.7 (−1.8 to 6.2)	4.9 (1.2 to 9.3)	13.9 (7.5 to 22.0)	26.5 (15.4 to 40.5)	−4.2 (−12.5 to 5.7)	−13.4 (−20.1 to −5.9)	−17.2 (−23.9 to −9.7)	−18.4 (−25.6 to −10.0)	−20.0 (−26.8 to −11.8)
Weekly fill volume[b]	2 152 395	2 270 747	2 343 272	2 543 319	2 824 392	2 138 545	1 933 865	1 849 352	1 821 221	1 785 567
Lisinopril										
Change from 2019, % (95% CI)	−2.8 (−4.5 to −1.0)	1.3 (−0.9 to 4.0)	5.0 (2.6 to 7.7)	12.1 (8.0 to 17.4)	23.2 (15.1 to 33.8)	−3.1 (−9.5 to 4.9)	−11.4 (−17.0 to −4.6)	−14.6 (−20.3 to −7.7)	−14.2 (−19.8 to −7.4)	−15.3 (−21.4 to −7.7)
Weekly fill volume[b]	2 159 871	2 252 153	2 333 755	2 491 220	2 739 128	2 152 981	1 968 396	1 897 783	1 906 602	1 883 315
Losartan										
Change from 2019, % (95% CI)	10.9 (9.3 to 12.5)	16.5 (14.5 to 18.6)	22.4 (20.1 to 24.8)	32.1 (28.6 to 36.7)	48.8 (39.2 to 60.9)	16.4 (7.6 to 27.3)	4.8 (−0.4 to 11.5)	5.1 (−2.0 to 13.9)	4.4 (−0.6 to 10.5)	1.7 (−3.8 to 8.7)
Weekly fill volume[b]	1 352 577	1 419 968	1 492 463	1 610 414	1 813 521	1 419 037	1 278 113	1 281 056	1 273 222	1 240 067
Omeprazole										
Change from 2019, % (95% CI)	2.0 (−0.2 to 4.2)	5.4 (3.3 to 7.5)	8.8 (6.6 to 11.0)	11.9 (8.4 to 15.8)	18.8 (12.7 to 27.3)	−0.8 (−6.0 to 6.2)	−5.7 (−10.6 to 0.2)	−7.8 (−12.9 to −1.2)	−5.8 (−11.1 to 1.0)	−8.2 (−12.9 to −2.2)
Weekly fill volume[b]	1 215 299	1 256 402	1 296 361	1 333 007	1 416 179	1 182 500	1 123 370	1 099 150	1 122 857	1 093 923
Sertraline										
Change from 2019, % (95% CI)	2.8 (0.9 to 5.0)	5.8 (3.1 to 9.0)	8.9 (6.2 to 11.8)	16.2 (11.2 to 23.0)	26.2 (16.8 to 38.6)	2.2 (−5.3 to 12.2)	−5.0 (−12.0 to 3.7)	−4.5 (−11.2 to 4.0)	−6.1 (−12.4 to 2.2)	−8.4 (−14.9 to 0.2)
Weekly fill volume[b]	920 698	947 224	974 883	1 040 632	1 130 214	915 002	850 676	855 155	840 862	820 444

[a] Volume of prescriptions during study period (February 16 to April 25, 2020) were compared with February 17 to April 27, 2019.

[b] Estimated absolute volume of national weekly fills in 2020.

Figure. Prescription Fill Patterns for Commonly Used Drugs During the Coronavirus Disease 2019 Pandemic in the United States



Weekly prescriptions from February 16 to April 25, 2020, were compared with those from February 17 to April 27, 2019. Each date on the x-axis refers to the last day of the week. EUA indicates Emergency Use Authorization; FDA, Food and Drug Administration; and WHO, World Health Organization.

Expenditures Panel Survey 2015-2017 to generate national estimates.[2] Estimates were scaled to total retail prescription drug fills in the United States in 2019 to obtain weekly fill estimates at the drug level. Confidence intervals were obtained using bootstrapping methods, resampling pharmacies with replacement, with 1000 replications. Analyses were performed using R software version 3.6.1 (R Foundation).

Results | Fills for all drugs, except amoxicillin and hydrocodone-acetaminophen, peaked during the week of March 15 to March

21, 2020, followed by subsequent declines (**Figure**, A). During this week, hydroxychloroquine/chloroquine fills increased from 2208 in 2019 to 45 858 prescriptions for fewer than 28 tablet fills (+1977.0% increase), 70 472 to 196 606 prescriptions for 28 to 60 tablet fills (+179.0%), and 44 245 to 124 833 prescriptions for more than 60 tablet fills (+182.1%) (Figure, B). At study end, these increases remained sustained for fewer than 28 tablet fills (+848.4%) and 28 to 60 tablet fills (+53.3%), while more than 60 tablet fills of hydroxychloroquine/chloroquine were below 2019 estimates (−64.0% decrease). Overall, there were 483 425 excess fills of hydroxychloroquine/chloroquine during the 10-week period in 2020 compared with 2019. The sharpest declines at study end were noted for amoxicillin (−64.4%), azithromycin (−62.7%), and hydrocodone-acetaminophen (−21.8%); however, cardiometabolic therapies remained stable or declined slightly (amlodipine [−9.2%], atorvastatin [−9.1%], lisinopril [−15.3%], and losartan [+1.7%]) compared with 2019 estimates.

Discussion | These data demonstrated a surge in hydroxychloroquine/chloroquine prescription fills, likely due to off-label prescriptions for COVID-19. The growth observed in the week of March 15 to March 21 followed the World Health Organization declaring a global pandemic on March 11, the United States declaring a national emergency on March 13, a single-group nonrandomized study[3] published on March 17, and President Trump's support of the drug on March 19. This surge in prescriptions corresponds to a previously reported spike in internet searches for purchasing hydroxychloroquine/chloroquine.[4] There was subsequent reduction in longer-term prescription fills, which could indicate decreased availability for patients with systemic lupus erythematosus and rheumatoid arthritis. These observed patterns appear to be in keeping with drug shortages of hydroxychloroquine reported to the US Food and Drug Administration starting March 31.[5]

Theoretical concerns have been raised that ACE inhibitors/ARBs may increase susceptibility to COVID-19 illness. However, in this analysis, prescriptions of the most frequently used ACE inhibitor (lisinopril) and ARB (losartan) did not appear to substantially decline compared with other commonly prescribed medications for chronic conditions.[1] The modest decline for most common long-term therapies after peak could represent reduced contact with prescribing clinicians, restricted access to pharmacies, pharmacist rationing, loss of insurance from unemployment, or replete supplies from early stockpiling. Steep declines for amoxicillin and azithromycin appeared out of proportion to expected seasonal declines and could represent fewer outpatient prescriptions for upper respiratory tract infection symptoms.

The limitations of the study included that prescription indications, patient or prescriber information, new or refill prescription status, or barriers to access could not be accounted for. Mechanisms to safeguard patients against both overprescription and drug shortages during public health crises should be explored.

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