Association of Stay-at-Home Orders With COVID-19 Hospitalizations in 4 States

In analyses of the effectiveness of response measures to the outbreak of coronavirus disease 2019 (COVID-19), most studies have used the number of confirmed cases or deaths. However, case count is a conservative estimate of the actual number of infected individuals in the absence of community-wide serologic testing. Death count is a lagging metric and insufficient for proactive hospital capacity planning. A more valuable metric for assessing the effects of public health interventions on the health care infrastructure is hospitalizations. As of April 18, 2020, governors in 42 states had issued statewide executive “stay-at-home” orders to help mitigate the risk that COVID-19 hospitalizations would overwhelm their state’s health care infrastructure. This study assessed the association between these orders and hospitalization trends.

Methods | In March 2020, we began collecting data on cumulative confirmed COVID-19 hospitalizations from each state’s department of health website on a daily basis. Among states issuing a statewide stay-at-home order, we identified states with at least 7 consecutive days of cumulative hospitalization data for COVID-19 (including patients currently hospitalized and those discharged) before the stay-at-home order date and at least 17 days following the order date. Because the median incubation period of COVID-19 was reported to be 4 to 5.1 days, and the median time from first symptom to hospitalization was found to be 7 days, we hypothesized that any association between stay-at-home orders and hospitalization rates would become evident after 12 days (median effective date). States included in this sample were Colorado, Minnesota, Ohio, and Virginia. Among the 4 states meeting the inclusion criteria, the earliest date with data on hospitalizations was March 10. All states were observed through April 28. We fit the best exponential growth function to cumulative hospitalization data in each state for dates up to and including the median effective date of that state’s stay-at-home order. We computed 95% prediction bands on the exponential fit line to determine if the observed number of hospitalizations fell within the interval. We then examined whether the observed cumulative hospitalizations for dates after the median effective date deviated from the projected exponential growth in cumulative hospitalizations. In an additional analysis, a linear growth function was fit to cumulative hospitalization data for dates up to and including the median effective date, and goodness of fit was assessed with an $R^2$ comparison. All analyses were performed using Microsoft Excel version 14.1.

Results | In all 4 states, cumulative hospitalizations up to and including the median effective date of a stay-at-home order closely fit and favored an exponential function over a linear fit ($R^2 = 0.973$ vs 0.695 in Colorado; $0.965$ vs 0.865 in Minnesota; $0.98$ vs 0.803 in Ohio; $0.994$ vs 0.775 in Virginia) (Table). However, after the median effective date, observed hospitalization growth rates deviated from projected exponential growth rates with slower growth in all 4 states. Observed hospitalizations consistently fell outside of the 95% prediction bands of the projected exponential growth curve (Figure).

For example, Minnesota’s residents were mandated to stay at home starting March 28. On April 13, 5 days after the median effective date, the cumulative projected hospitalizations were 988 and the actual hospitalizations were 361. In Virginia, projected hospitalizations 5 days after the median effective date were 2335 and actual hospitalizations were 1048.

Discussion | In 4 states with stay-at-home orders, cumulative hospitalizations for COVID-19 deviated from projected best-fit exponential growth rates after these orders became effective. The deviation started 2 to 4 days sooner than the median effective date of each state’s order and may reflect the use of a median incubation period for symptom onset and time to hospitalization to establish this date. Other factors that potentially decreased the rate of virus spread and subsequent hospitalizations include school closures, social distancing guidelines, and

Table. Cumulative Hospitalizations Due to COVID-19 in Colorado, Minnesota, Ohio, and Virginia, March 10 Through April 28, 2020

<table>
<thead>
<tr>
<th>State</th>
<th>Fitting perioda</th>
<th>Stay-at-home issue date</th>
<th>Median effective date</th>
<th>Cumulative hospitalizations</th>
<th>Best exponential fit: $\ln(y) = \ln(a) + bt$</th>
<th>Linear fit: $y = ct$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorado</td>
<td>March 10-April 6</td>
<td>March 26</td>
<td>April 6</td>
<td>2</td>
<td>2671.00 ($1.02-1.54$) $0.24$ ($0.22-0.25$) $0.973$</td>
<td>30.89 ($25.28-36.5$) $0.695$</td>
</tr>
<tr>
<td>Minnesota</td>
<td>March 19-April 8</td>
<td>March 28</td>
<td>April 8</td>
<td>7</td>
<td>912.00 ($1.8-2.24$) $0.19$ ($0.17-0.21$) $0.965$</td>
<td>9.993 ($8.66-11.12$) $0.865$</td>
</tr>
<tr>
<td>Ohio</td>
<td>March 17-April 4</td>
<td>March 24</td>
<td>April 4</td>
<td>17</td>
<td>3340.00 ($2.75-3.13$) $0.23$ ($0.21-0.24$) $0.98$</td>
<td>38.23 ($32.78-43.67$) $0.803$</td>
</tr>
<tr>
<td>Virginia</td>
<td>March 19-April 10</td>
<td>March 30</td>
<td>April 10</td>
<td>19</td>
<td>2165.00 ($2.69-2.85$) $0.178$ ($0.172-0.184$) $0.994$</td>
<td>23.31 ($19.74-26.9$) $0.775$</td>
</tr>
</tbody>
</table>


aData fitting period consists of observed data from the first day of reporting up to and including the median effective date of the state’s stay-at-home order.
general pandemic awareness. In addition, economic insecurity and loss of health insurance during the pandemic may have also decreased hospital utilization. Limitations of the study include that these other factors could not be modeled in the analysis and that data on only 4 states were available.

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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 de-identified 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 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 study3 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