

# Hydroxychloroquine Use in the United States and the Potential Impact of Critical Shortages from SARS-CoV-2

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## **Abstract**

Hydroxychloroquine (HCQ) is in critical shortage in the U.S. because of its use off-label for treatment of viral pneumonia secondary to the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). A repeated cross-sectional study of the Medical Expenditure Panel Survey was used to describe trends in HCQ medication use over time to estimate the impact of HCQ shortage. As of 2017, approximately 81% of over 1 million individuals prescribed HCQ use this medication longitudinally. Critical drug shortages related to off-label use for SARS-COV-2 infection could impact hundreds of thousands of individuals who use the medication for rheumatological diseases.

**Keywords:** covid-19; sars-cov-2; novel coronavirus; hydroxychloroquine; drug shortages; rheumatology

## **Introduction**

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) outbreak was declared a pandemic on March 11, 2020.<sup>1</sup> To-date, no randomized trial has robustly demonstrated treatment efficacy for viral pneumonia secondary to SARS-CoV-2. Nevertheless, the antimalarial hydroxychloroquine (HCQ) is currently being used ubiquitously in the U.S. despite inconclusive evidence from a few small, poorly controlled or non-randomized trials.<sup>2</sup> Shortly after uptake of HCQ in the pandemic, the Food and Drug Administration (FDA) announced critical shortages of this medication.<sup>3</sup> Given the important use of HCQ for rheumatologic disorders, such as systemic lupus erythematosus and rheumatoid arthritis,<sup>4</sup> we sought to investigate the use of HCQ in the U.S. to determine the potential impact of critical shortages of HCQ will have on the non-pandemic population.

## **Methods**

A repeated cross-sectional study of the Medical Expenditure Panel Survey (MEPS) was used to describe trends in HCQ medication use over time. Sponsored by the Agency of Healthcare Research and Quality (AHRQ), MEPS is representative of the noninstitutionalized population of the United States. Each year of the survey comprises two overlapping cohorts, which are interviewed five times over the 2 years. The survey includes information regarding demographics and prescription medication utilization. All adult individuals included in the survey between 2002-2017 were included in the analysis. Survey years were grouped into two year groups. HCQ was identified through the prescription medication name. The survey uses numerous methods to achieve accurate reporting of prescription medications including contacting pharmacies.<sup>5</sup> Previous studies have validated the accuracy of chronic medication

reporting in MEPS.<sup>6</sup> An individual was identified as a medication user if he or she had any use of the medication during a given year.

Complex survey weights were used in all analyses to make these analyses representative of the non-institutionalized population of the United States. 95% confidence intervals are reported in the figures. The OhioHealth Institutional Review Board ruled the study exempt. All analyses used STATA 15 (College Station, Tx).

## **Result**

Between 2002-2003 to 2016-2017, the use of HCQ increased 363.6% from 226,242 individuals per year (95% CI, 159,425-293,060) to 1,048,901 individuals per year (95% CI, 853,550-1,244,251), respectively. Figure 1 provides a graphical depiction of HCQ prescription fills over time. Notably, the proportion of patients with greater than 1 prescription fill ranged from a low of 81.6% (95%CI: 72.7-88.2) in 2016-2017 to a high of 92.1% (95%CI: 85.8-95.7) in 2012-2013.

## **Discussion**

Between 2002 to 2016 the use of HCQ in the U.S. population increased substantially. Importantly, over 80 percent of patients prescribed HCQ use this prescription more than once in any given two-year period. These data suggest that the vast majority of HCQ use in the U.S. are by patients who use this drug longitudinally.

This study was limited by self-reported medication use, possible under-reporting of medications use, and an inability to determine the precise reason for HCQ prescription fills.

According to the FDA's list of drug shortages, nine pharmaceutical manufacturers have provided updates regarding HCQ shortages.<sup>6</sup> Most reasons are secondary to limited supply in the setting of significantly increased demand for this medication. Companies like Amneal Pharmaceuticals and Novartis have announced plans to increase production of HCQ to meet national demand during the pandemic.<sup>6</sup> Regardless, critical drug shortages for the foreseeable future related to off-label use for SARS-COV-2 infection could impact hundreds of thousands of individuals who use the medication for rheumatological diseases, such as rheumatoid arthritis and systemic lupus erythematosus.

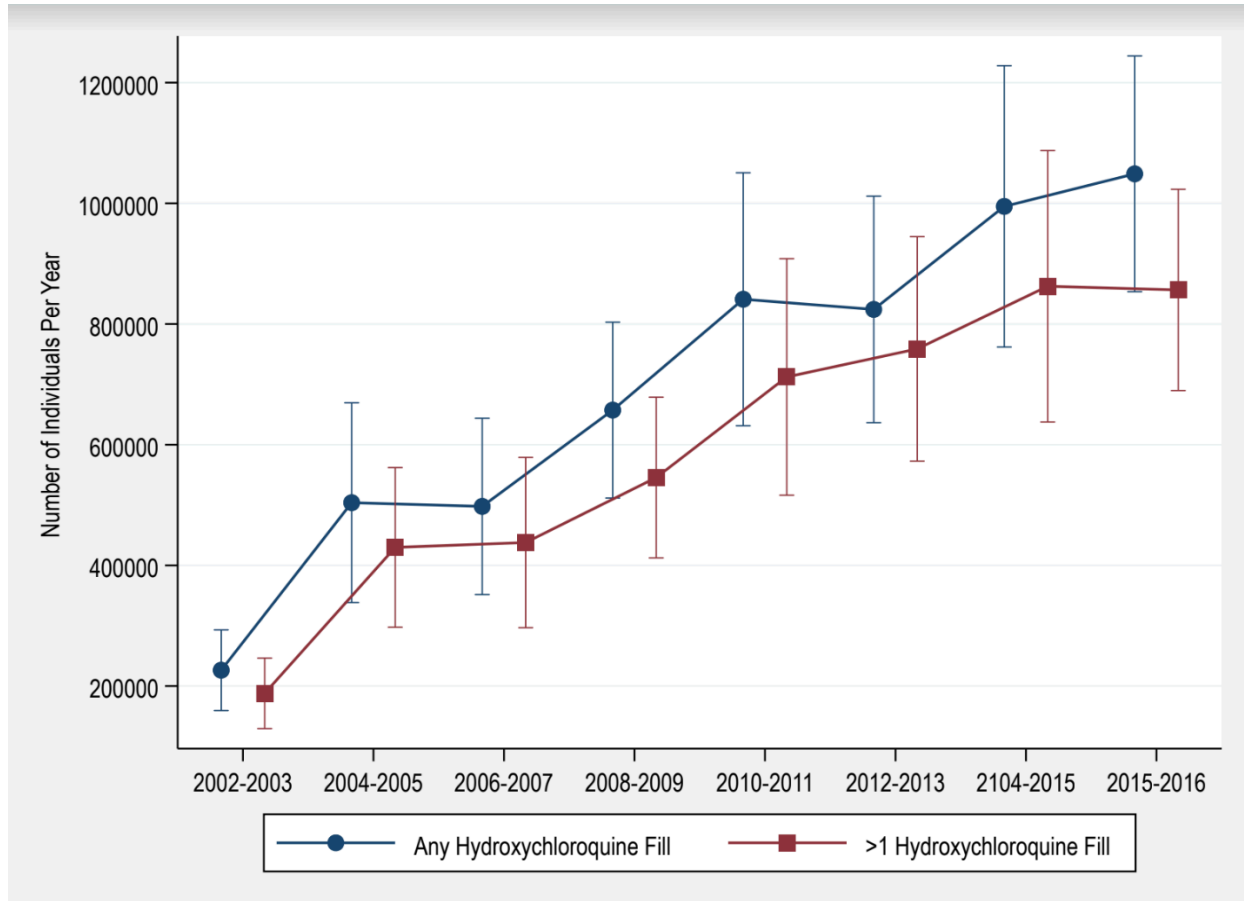
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**Conflict of Interest Statement:** None declared

## References

1. WHO Director-General's opening remarks at the media briefing on COVID-19: 11 March 2020. Published March 11, 2020. Accessed April 7, 2020.  
<https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020>.
2. Yazdany J, Kim AHJ. Use of Hydroxychloroquine and Chloroquine During the COVID-19 Pandemic: What Every Clinician Should Know [published online ahead of print, 2020 Mar 31]. *Ann Intern Med.* 2020;10.7326/M20-1334. doi:10.7326/M20-1334.
3. FDA Drug Shortages: Current and Resolved Drug Shortages and Discontinuations Reported to FDA. Published March 31, 2020. Accessed April 7, 2020.  
[https://www.accessdata.fda.gov/scripts/drugshortages/dsp\\_ActiveIngredientDetails.cfm?AI=Hydroxychloroquine%20Sulfate%20Tablets&st=c](https://www.accessdata.fda.gov/scripts/drugshortages/dsp_ActiveIngredientDetails.cfm?AI=Hydroxychloroquine%20Sulfate%20Tablets&st=c).
4. Schrezenmeier E, Dörner T. Mechanisms of action of hydroxychloroquine and chloroquine: implications for rheumatology. *Nat Rev Rheumatol.* 2020;16(3):155–166.
5. Cohen JW, Cohen SB, Banthin JS. The medical expenditure panel survey: a national information resource to support healthcare cost research and inform policy and practice. *Med Care.* 2009;47(7 Suppl 1):S44-50. doi:10.1097/MLR.0b013e3181a23e3a.
6. Hill SC, Zuvekas SH, Zodet MW. Implications of the accuracy of MEPS prescription drug data for health services research. *Inq J Med Care Organ Provis Financ.* 2011;48(3):242-259. doi:10.5034/inquiryjrnl\_48.03.04

**Figure 1. Hydroxychloroquine Use in the United States, 2002-2016**



Rate of hydroxychloroquine use with any fill and > 1 fill in both years across the United States population.