

## **Bing and hydroxychloroquine is a bad mix**

Roger Bate

### **Summary**

When President Trump promoted the malaria drug hydroxychloroquine as a possible preventative treatment for COVID-19 in the spring, demand for the product jumped. Analysis of hydroxychloroquine procured from the web in US and UK between April and July 2020 found that an alarmingly high number of the samples (13%) were fake or substandard, with all failures coming from uncredentialed sites. There is debate as to whether the real drug has any benefit for COVID-19 patients, but taking inferior versions of this medicine might prove fatal. Demand is likely to spike for any real treatments or vaccines that are developed against the coronavirus. Shortages are likely and web buyers should be aware of the dangers of buying from non-credentialed web sellers. Unfortunately, the search engine Bing's overt policy, aligned with US pharma industry interests, is driving users to the very worst sites, those most likely to sell bogus treatments (in this sampling roughly 20% sold inferior medicines).

### **Introduction**

In the spring President Trump told the world he was using hydroxychloroquine to ward off COVID-19 and internet searches went up 14-fold as a result, according to one study<sup>1</sup>. Hospitals also briefly faced shortages until concerns about adverse effects reduced the spike in demand<sup>2</sup>. The drug is primarily used to treat malaria but also for combatting lupus and other auto-immune conditions. It has never successfully treated any virus, however, early results showed an *in vitro* action against COVID-19, a reduction in viral load, and in recovery time in patients.<sup>3</sup>

Because of its myriad uses every major US pharmacy and web pharmacy either stocks it or can order and sell the drug. It was widely, although not universally, available from searches of web pharmacies for buyers in UK and US.

### **The Bing Paradox**

To warn US consumers of the dangers of importing medicine, the search engine Bing has placed pop-up warnings against foreign websites selling medicines.<sup>4</sup> Bing's list of sites are those flagged by the National Association of Boards of Pharmacy (NABP) as appearing "to be out of compliance with state or federal laws or NABP patient safety and pharmacy practice standards."<sup>5</sup> Simply dispensing foreign medicines is sufficient to make the list.

Bing is trying to alert those seeking drugs from overseas of the potential dangers of such practices. There are numerous risks of buying pharmaceuticals online, ranging from bogus medicines to identity theft. However, as I have attested in the peer-review literature, buying from credentialed overseas sites can be done safely, at least in the general understanding of that word.<sup>6</sup> Bing's policy is also not consistent across the world, as we found that UK users of Bing are not warned about the same sites. In short, the sites targeted by Bing are credentialed foreign pharmacies, while potentially rogue sites are, in effect, given a clean bill of health by having no pop-up warnings.

Sites credentialed by monitoring groups pharmacychecker.com and CIPA (Canadian Internet Pharmacy Association) such as

- [buylowdrugs.com](http://buylowdrugs.com) (Buylowdrugs.com)

- and [ycdscc.com](http://ycdscc.com) (YourCanadaDrugstore.com)

have pop-up warnings in US (although not in UK), but sell good quality medications (in previous work we procured good quality Viagra, Celebrex, Nexium and Lipitor from these sites).<sup>7</sup>

### **Procuring Hydroxychloroquine**

Following protocols established in prior peer review research, we sampled hydroxychloroquine from 28 sites that were credentialed and also sampled from 53 non-credentialed sites. In all, 28 of the credentialed sites a pop-up warning was provided by Bing when a search was done in US and yet when a Bing search was done in UK none of these sites had pop-up warnings. From every site a sample of hydroxychloroquine was ordered from US. Due to budget constraints only 22 of the credentialed sites were procured from in UK, but all 53 non-credentialed sites were procured from in UK (given the expectation based on previous research that these sites would be the ones more likely selling inferior medicines).

This study only analyzes sites that actually sold the drug. Fourteen sites (six credentialed and eight non-credentialed) were out of stock or otherwise unable to sell and are not included in this study). Additionally, three uncredentialed sites took payment, but have so far failed to deliver any product. Of the remainder analyzed, delivery times ranged from ten days to six weeks.

In the UK, stock issues gave new impetus to the discussion of fragility of supply, with an appeal for government support to repatriate manufacture of critical medicines. One UK generic producer has undertaken to produce 70% of current national demand of hydroxychloroquine in the north of England by October this year.<sup>8</sup>

### **Analysis**

All of the packaging was inspected and several samples (all from non-credentialed sites, two from US procurement and two from UK procurement) looked suspect and possibly counterfeit.

Following the methodology of previously published peer-review studies,<sup>9</sup> and using a handheld Raman spectrometer, I tested for authenticity. Raman spectrometers are frequently used as a quick, reliable, and cost-effective way to differentiate between genuine and counterfeit drugs.<sup>10</sup> The device compares an unknown sample—in this case a pill—to a reference standard by comparing the frequencies of certain kinds of light that are scattered after the two substances have been illuminated with a monochromatic laser.<sup>11</sup> The device compares the resulting “spectra” from the scans, which generates a p-value denoting the probability that the difference between the reference standard and the sample is due to measurement uncertainty rather than the difference in molecular structure. Therefore, a p-value of greater than or equal to 0.05 would represent a pass result (i.e., any difference is due to measurement uncertainty), while a p-value of less than 0.05 would represent a failed result.<sup>12</sup>

### **Results**

A total of 156 samples of hydroxychloroquine were procured. Of these, 21 failed spectrometry testing (13.5%). This is far higher than any previous testing undertaken using this methodology, including procuring Viagra from uncredentialed sites – Viagra is widely thought of as one of the most

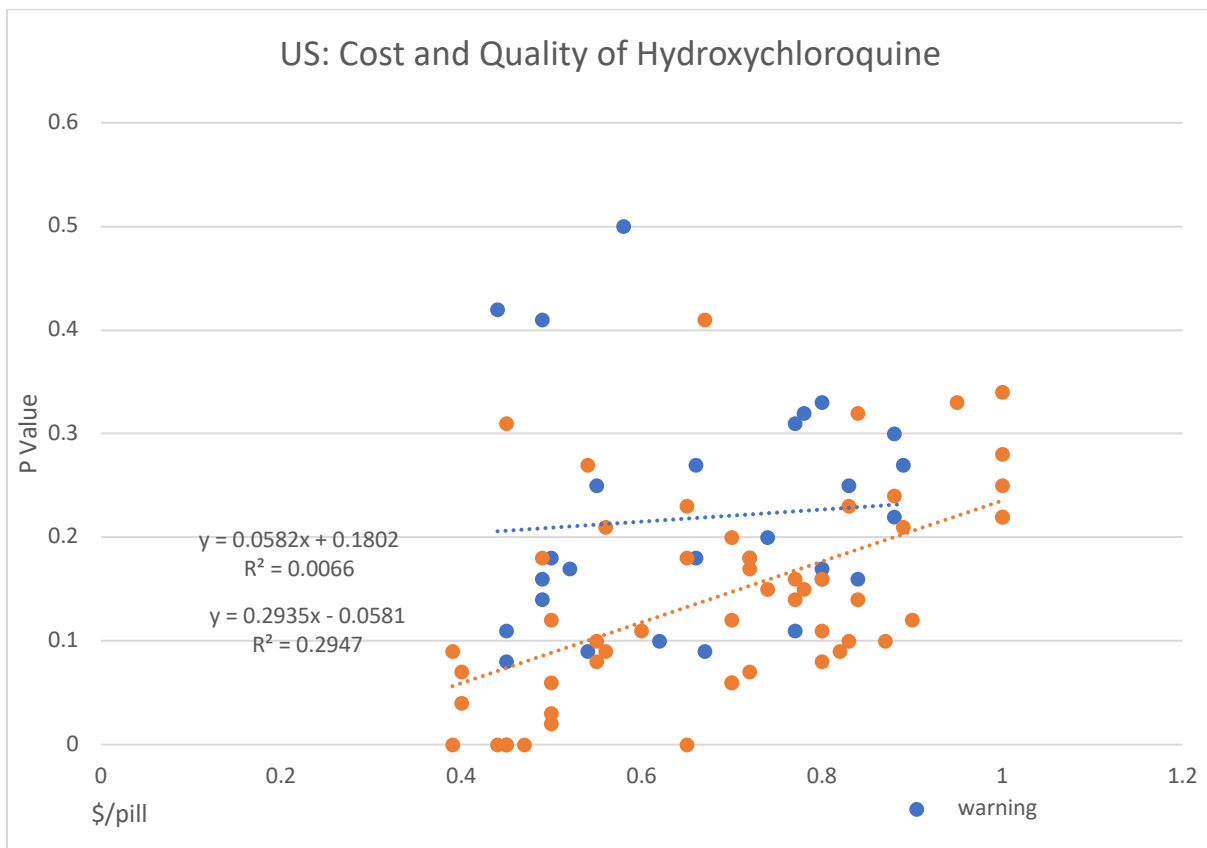
counterfeited medicines because of its high demand and the fact that buyers will often want discretion in procurement and may not complain if they receive and use an inferior product.

The profile between US and UK procurement was similar. Of the 50 samples (28 US and 22 UK) procured from credentialed sites (those with warning from Bing in US), none failed spectrometry testing. Whereas of the 106 (53 in UK and 53 in US) samples from uncredentialed sites both had significant numbers of failures UK 12 failures (22%) and US 9 failures (17%).

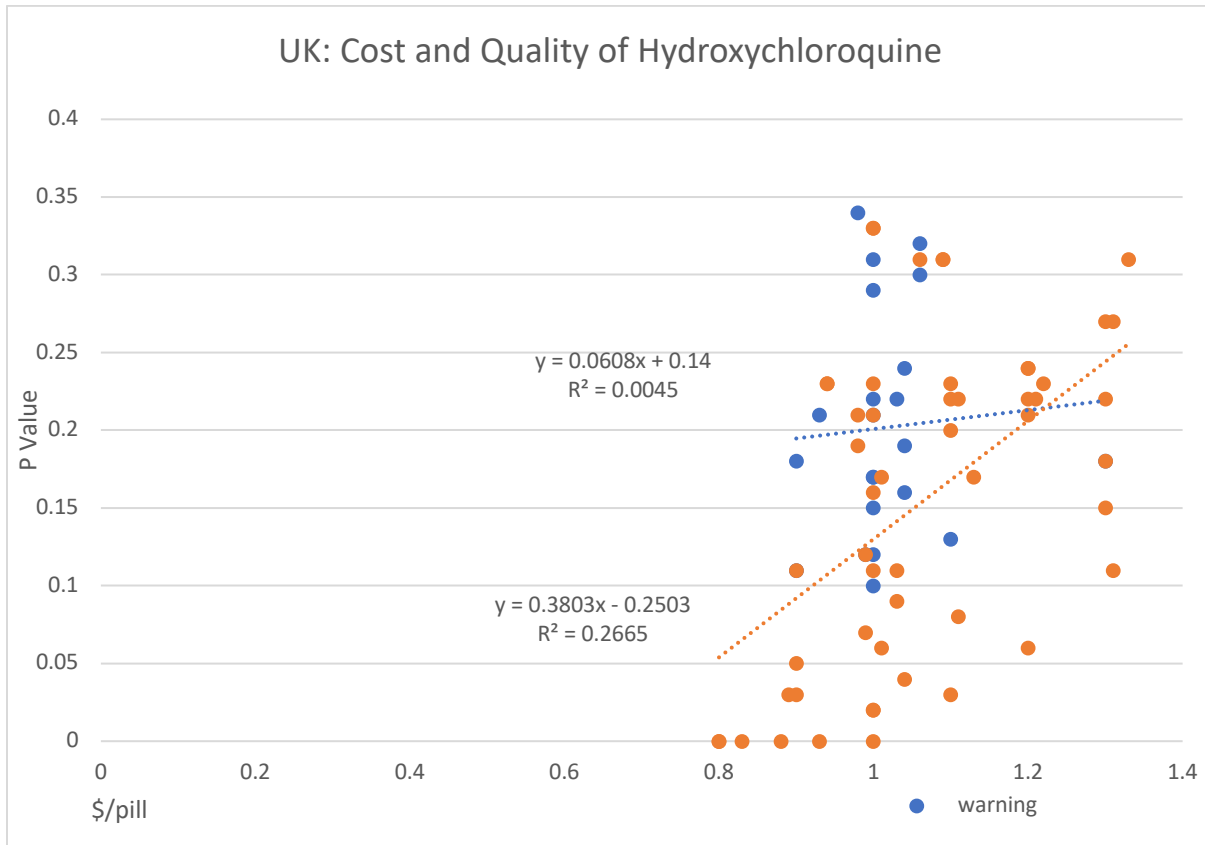
Based on assessments of packaging and spectrometry results six of each nation's procurement were fakes with US procurement having three substandard medicines and UK procurement six substandards.

The charts below show the price of medicine (more expensive in UK largely due to transportation costs from Canadian-based pharmacies) versus the p-values. There is no relationship between price and quality with the credentialed sites (in blue), but there is a reasonably strong one for the non-credentialed sites (r-squared of over a quarter) in orange. The implication of this is that at least some of the sellers know that they are selling cheaper products and probably know they are selling fake or substandard medicine and take market share by selling at a lower price.

**Figure 1: US sampling**



**Figure 2: UK Sampling**



Furthering the notion that some sellers know the inferiority of their products, the more obvious fakes (with zero p-value) are usually the cheapest products across samplings.

### Conclusions

The sample size for this study is not large but it is significant enough to show several things. First, credentialed sites sell good quality medicines, even those in high demand. Some of them did not deliver quickly, or were unable to deliver at all, but all delivered good quality. Second, there is a large amount of inferior hydroxychloroquine available via the web for the unwary. Roughly 20% of the products bought from uncredentialed sites failed testing – this is far higher than any prior study we have undertaken. In and of itself this is worrying for those needing the medicine. But the third, and probably most important, conclusion is that once a cure or vaccine becomes available for COVID-19 demand will be higher than

even for hydroxychloroquine. Those with the ability to pass off inferior products as legitimate will attempt to find buyers and the likelihood is they will find many takers. COVID-19 may not kill you but any touted cure just might.

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<sup>5</sup> National Association of Boards of Pharmacy, “Not Recommended Sites,” January 2, 2019, <https://safe.pharmacy/not-recommended-sites/>.

<sup>6</sup> Roger Bate and Kimberly Hess, “Assessing Website Pharmacy Drug Quality: Safer Than You Think?,” *PloS One* 5, no. 8 (August 13, 2010), <https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0012199>; and Roger Bate, Ginger Zhe Jin, and Aparna Mathur, “In Whom We Trust: The Role of Certification Agencies in Online Drug Markets,” *B. E. Journal of Economic Analysis & Policy* 14, no. 1 (2013): 111–50.

<sup>7</sup>Roger Bate, Aparna Mathur, and Ginger Zhe Jin, “Unveiling the mystery of online pharmacies: An audit study,” The American Enterprise Institute, March 29, 2012, <https://www.aei.org/research-products/working-paper/unveiling-the-mystery-of-online-pharmacies-an-audit-study/>

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<sup>9</sup> See Bate and Hess, "Assessing Website Pharmacy Drug Quality."

<sup>10</sup> Bate and Hess, "Assessing Website Pharmacy Drug Quality."

<sup>11</sup> Mark R. Witkowski, "The Use of Raman Spectroscopy in the Detection of Counterfeit and Adulterated Pharmaceutical Products," *American Pharmaceutical Review* (January/February 2005), <http://www.horiba.com/fileadmin/uploads/Scientific/Documents/Raman/aprraman.pdf>.

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