

Persistence of Misinformation Among Experts: Evidence from Healthcare

Abstract

Efforts to debunk misinformation are at the forefront of combating misinformation amongst the lay public and experts alike. This study investigates the persistence of misinformation among healthcare experts (physicians), after institutional debunking efforts or countermeasures. We analyze physician prescription behaviors for Hydroxychloroquine (HCQ). Using drug-level physician prescription claims data from GoodRx and employing synthetic control, we estimate the effect of misinformation, after countermeasures, on HCQ prescription claims. Implementation of various countermeasures reduced prescription claims from the initial increase of 482.44% to 137.59%. HCQ claims remained elevated and registered an increase of 57.73% on average over eighteen months after the availability of definitive evidence against HCQ use and of the Covid-19 vaccine. Notably, the effectiveness of countermeasures was weaker in states where Trump won, suggesting that persuasive aspects of misinformation are important. Furthermore, a causal analysis of Ivermectin (IVM) misinformation also reveals similar findings. In particular, IVM averages an astounding 1617.64 % increase in prescriptions after Covid-19 vaccines become widely available. These findings highlight the challenges in combating misinformation and its enduring effects on experts, even in the presence of definitive contrary evidence and medical advancements.

Keywords: misinformation, quasi-experiment, healthcare, hydroxychloroquine

Introduction

“The greatest enemy of knowledge is not ignorance, it is the illusion of knowledge.”

— Daniel J. Boorstin

Misinformation presents a significant threat, leading to a false sense of understanding that can have serious consequences for individuals and society as a whole. The advent of technology has amplified these concerns, spreading misinformation across various fields, including politics, science, and consumer decision-making. In the realm of healthcare, misinformation becomes especially perilous, as it jeopardizes both individual well-being and community health (Rubin 2022). Recognizing the gravity of this issue, the United States Surgeon General and the World Health Organization have prioritized combating healthcare misinformation and have actively promoted various misinformation debunking efforts or countermeasures.¹

One might expect healthcare experts such as physicians to respond to debunking efforts or countermeasures that provide corrective information by eliminating any healthcare practices that have been influenced by misinformation. Physicians are trained to practice evidence-based care, which entails promptly responding to new scientific evidence and abandoning treatments that have been discredited. Further, well established evidentiary standards help identify factually inaccurate claims (Chou, Oh, and Klein 2018). Regulatory bodies, including the U.S. Food and Drug Administration (FDA), utilize these standards to assess health claims concerning drugs and therapies (U.S. Department of Health and Human Services et al., 2009). However, physicians may also disregard new scientific evidence. For

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<https://www.cnn.com/2021/08/24/who-says-covid-misinformation-is-a-major-factor-driving-pandemic-around-the-world.html>

example, physicians could be subject to personal biases, or may disbelieve new evidence, or may capitulate to patient pressure. Indeed, (Rubin 2022) documents anecdotal evidence that physicians spread misinformation about Covid-19. Furthermore, physicians enjoy significant protection from liability when prescribing drugs for unapproved purposes ; a practice termed off-label drug use (OLDU) (Wittich, Burkle, and Lanier, 2012). In other words, how physicians respond to countermeasures is an empirical question. Consequently, our *first research question* is: Can misinformation continue to influence the decisions of healthcare professionals/experts despite countermeasures?

In addition, the response to misinformation can be heterogeneous across individuals. How strongly individuals respond to misinformation (or the degree of susceptibility to misinformation) can moderate the effects of misinformation (Van Der Linden 2022). This is because misinformation often combines flawed information with persuasive elements. For instance, individuals may be more susceptible to misinformation from people who they perceive to be similar to themselves or part of their social group (Esposito, Hornsey, and Spoor 2013; Mackie, Worth, and Asuncion 1990). However, there is limited research on the heterogeneity of experts' susceptibility to misinformation. One exception is a survey-based study that offers evidence of the moderating effect of susceptibility on misinformation amongst physicians (Levin et al. 2023). The study reports that political orientation strongly correlates with self-reported willingness to prescribe drugs for unapproved purposes or off-label drug use (OLDU). Further, the study reports that conservative leaning physicians were more skeptical of new evidence discrediting a drug's purported efficacy, suggesting there could also be heterogeneity in response to misinformation and countermeasures among

experts. As a result, our *second research question* is: Is the net effect of misinformation and countermeasures moderated by the degree of susceptibility to misinformation?

Countering misinformation also requires trust in the scientific evidence. Chou, Oh, and Klein (2018) define *health* misinformation as a health-related claim of fact that is currently false due to a lack of scientific evidence. However, in desperate circumstances, experts may pursue treatments with limited evidence. However, once the scientific evidence is definitive and unambiguous and shows that a course of treatment does not work, experts should pursue evidence-based treatments. This leads us to our *third research question*: How do experts respond to definitive evidence contradicting misinformation? A related *fourth research question* we address in this paper is : Are some countermeasures more effective than others, in combating misinformation in patient-physician decisions?

To answer these questions, we examine misinformation concerning two prescription drugs, Hydroxychloroquine (HCQ) and Ivermectin (IVM). These drugs have been at the center of misinformation during Covid-19, and efforts to debunk false claims have been undertaken at both federal and state levels. The stakes were exceptionally high in this context, as a physician's belief in misinformation could lead to severe risks for both the patient and the wider community, potentially resulting in fatal outcomes.

In this high stakes life or death context, these two drugs also serve as good case studies to answer our research questions for at least four reasons. First, following Chou, Oh, and Klein (2018), touting HCQ and IVM as Covid-19 treatments in the absence of evidence can be classified as an act of misinformation. Second, short term studies such as (Barnett et al. 2022; Vaduganathan et al. 2020) as well as media reports² suggest that prescription claims for HCQ and IVM increased above prior year levels after particular misinformation

² <https://www.nytimes.com/2021/08/30/health/covid-ivermectin-prescriptions.html>

events. So, we expect misinformation to have affected prescription behavior for these drugs. Consequently, we can observe the response of experts to countermeasures. Third, we have clear time points when misinformation started and dates when definitive scientific evidence emerged that HCQ was ineffective against Covid-19. In the case of IVM, we have a specific start date and the date when the studies that first brought attention to IVM were discredited and withdrawn altogether. We can therefore rule out explanations that argue that HCQ and IVM may well have been prescribed in desperation, and the evolving evidence was unclear. Fourth, for HCQ some countermeasures were implemented at the federal and state level in response to misinformation about these drugs. These countermeasures can further be classified into two types. Informative countermeasures (Borges Do Nascimento et al. 2022) aim to provide accurate information, promote the current scientific consensus, and debunk false claims. Another type of countermeasure is restrictive countermeasures. Restrictive countermeasures focus on limiting the dissemination and impact of misinformation, as well as mitigating the actions resulting from misinformation (Courchesne, Ilhardt, and Shapiro 2021). While, federal, and some state, countermeasures were informative in nature, several states implemented restrictive countermeasures. This allows us to conduct analyses to contrast these different types of countermeasures. For IVM all countermeasures were informative. Consequently, HCQ and IVM serve as useful case studies to study misinformation, moderating the effect of degree of susceptibility to misinformation, and the effect of different types of countermeasures.

Our analysis approach across both drugs is very similar. For exposition purposes we will use HCQ as our focal example. Where relevant, we will call out meaningful differences for IVM.

To assess the causal impact of misinformation on HCQ consumption, we adopt a quasi-experimental approach by analyzing prescription claims (Abadie 2021). Prescription claims serve as a reliable indicator of actual consumption and have been widely employed in previous studies (Vaduganathan et al. 2020). To establish a baseline for HCQ prescription claims, we compare them to prescription claims for other drugs. In other words, other drugs serve as control groups. This approach enables us to account for various confounding factors, including seasonality, trends, and Covid-related measures such as shelter-in-place orders, indoor mask mandates, and travel restrictions. To causally estimate the incremental change in prescription claims for HCQ, we employ Bayesian synthetic control methodology (Kim, Lee, and Gupta 2020). Note that this incremental change reflects a “net effect”, i.e., the incremental change in HCQ claims is the result of misinformation regarding HCQ *and* the resultant countermeasures at the state and federal level, wherever countermeasures were implemented.

We obtained our prescription claims data from GoodRx, a company that offers a telemedicine platform, as well as a website and mobile app that provide free drug coupons for discounted medications in the United States. The dataset comprises detailed claims information at the drug name level for the years 2019 to 2021 (inclusive), covering all 50 states in the US. It is important to note that our data specifically focuses on prescription claims in non-hospital settings. In other words, we measure HCQ and IVM claims in settings where HCQ and IVM use was never approved by the FDA. Further, as we observe prescriptions till the end of 2021, we have a period where Covid vaccines were available to the general population.

To examine the role of the degree of susceptibility on the net effect of misinformation and countermeasures, we need a measure of degree of susceptibility. As an indicator of degree of susceptibility or persuadability regarding HCQ and IVM misinformation, we use state-level results for President Trump in the 2016 presidential elections. This choice is motivated as follows. The persuasive effects of messages delivered by in-group members can be stronger compared to messages from out-group members (Mackie, Worth, and Asuncion 1990). In the case of HCQ, President Trump personally promoted HCQ use for Covid treatment. In contrast, there is no evidence that President Trump publicly promoted IVM. However, IVM gained substantial attention as a potential treatment for Covid-19 primarily in the conservative media.^{3,4,5} Viewership of conservative media is strongly correlated with support for President Trump⁶. Consequently, a measure of support for President Trump is a plausible measure of the degree of susceptibility to off-label drug use (OLDU) by physicians for both HCQ and IVM. Note that OLDU can be helpful in certain scenarios (Wittich, Burkle, and Lanier, 2012), but it can also be misused. We use a regression framework to examine the relationship between the heterogeneity in ATT across states and weeks, and the degree of susceptibility.

We also study the short-term effect of definitive evidence against HCQ. To ensure that our results are not driven by heterogeneity in countermeasures, we collect detailed

³ It is important to note that this measure is not intended to assess susceptibility in a broader sense. It is plausible that individuals from various political backgrounds may exhibit equal susceptibility to persuasion depending on the specific context.

⁴ <https://www.cnn.com/2021/08/23/media/right-wing-media-ivermectin/index.html>

⁵ Whether the conservative media influenced its audience, or whether the conservative audience dictated the news that conservative media aired is not relevant here, as we are only interested in a measure of susceptibility. <https://www.annenbergpublicpolicycenter.org/heavy-users-of-conservative-media-more-willing-to-take-ivermectin-for-covid-19/>

⁶

<https://www.pewresearch.org/journalism/2017/01/18/trump-clinton-voters-divided-in-their-main-source-for-election-news/>

policy data on the federal and state-level countermeasures and control for state level differences in countermeasures in a regression model. Finally, we also formally compare HCQ countermeasures in a regression framework.

Our national-level quasi-experimental analysis reveals a notable 482.44% increase in HCQ prescription claims over baseline immediately following President Trump's endorsement. However, within four weeks HCQ prescription claims declined but remained at a substantial 137.59% increase with respect to the baseline. Prescription claims remained persistently higher than the baseline (57.73%) over 18 months after definitive evidence and statements against the efficacy of HCQ emerged on June 21, 2020. This finding is concerning because it shows that some healthcare professionals, either due to patient pressure or their own convictions, disregarded new scientific evidence and persisted in prescribing HCQ under off-label drug use (OLDU). We observe sustained effects even after 67% of the US population received its first dose of the Covid vaccine.⁷

Further, we find that persistence was moderated by the degree of susceptibility or persuadability across states. Specifically, in states that President Trump won in 2016, the available evidence and state level restrictions were less effective than in other states. This finding suggests that the degree of susceptibility, measured by Trump support, may have contributed to the persistence of the effects of misinformation. Notably, the initial peak in HCQ prescription claims did not vary with political leaning suggesting that factors in addition to susceptibility were active initially. Importantly, we observe that the introduction of definitive evidence against the use of HCQ had, at best, a short-lived effect in reducing HCQ prescription behavior in either Trump supporting or Trump opposing states. Further, from state-level synthetic controls and treatment effect heterogeneity analysis we find that

⁷ <https://www.cbsnews.com/news/biden-covid-19-vaccine-goal-missed/>

state level restrictive measures were more effective than state level informative measures. Similar patterns are observed for IVM. These results for HCQ and IVM are robust to a placebo test, and we rule out alternative accounts such as stockpiling drug shortages, and differences in media coverage of countermeasures across states in the robustness section.

Existing research on countermeasures against misinformation primarily focuses on consumer products and over-the-counter medications (Fong, Guo, and Rao 2022; Rao 2022; Rao and Wang 2017). Our research covers new ground by examining decisions by experts (physicians). We examine the role of susceptibility in moderating the effects of misinformation. We also examine the causal effect of misinformation on physician prescription behaviors for two drugs for a sustained duration after definitive evidence countering the misinformation was available; 18 months for HCQ and 12 months for IVM. Finally, we contrast the effectiveness of informative and restrictive countermeasures.

The remainder of this paper is organized as follows: Up next is the literature review followed by a description of the data. We then provide an overview of institutional factors surrounding HCQ and IVM misinformation along with model-free evidence. This is followed by details on identification strategy, synthetic control estimation, and treatment effect heterogeneity analysis. We then present our findings for HCQ and IVM, followed by robustness tests. Finally, we conclude by discussing the implications of our findings and suggesting potential avenues for future research.

Related Literature

Misinformation is an actively studied research area (see Courchesne, Ilhardt, and Shapiro (2021) for an extensive summary). There are three streams of literature that are directly relevant to this study: how physicians can be influenced, persistence of

misinformation after countermeasures, and factors governing the degree of susceptibility to misinformation. We discuss each in turn.

There is extensive literature in marketing that suggests that physician decisions can be influenced, a potential entry point for misinformation. Pharmaceutical firms engage in detailing activities to influence physicians (Liu, Liu, and Chintagunta 2017; Liu et al. 2016; Mizik and Jacobson 2004). Further, Ching and Ishihara (2012) find that detailing can include informative and persuasive elements, though the effect of persuasive elements is minor. Unlike our context, it is important to note that these papers on detailing are not in the context of misinformation. At most, detailing efforts can be thought of as embellishments of drug performance data. Patients also serve as a point of influence on physician decisions (Bala and Bhardwaj 2010; Bala, Bhardwaj, and Chen 2013; Fischer and Albers 2010; Yoon and Kim 2022). In addition, short term studies such as (Barnett et al. 2022; Vaduganathan et al. 2020) report an increase in prescription claims for HCQ and IVM during the pandemic. Collectively, prior research suggests that misinformation could potentially influence physicians as well in the short term. In contrast, this paper causally examines the persistence of misinformation effects on prescription behavior over the medium term, after explicitly accounting for countermeasures.

Central to our investigation is whether misinformation persists after countermeasures are deployed in the healthcare setting. The extant research is primarily in non-healthcare settings, and the evidence is mixed. For example, Fong, Guo, and Rao (2022) demonstrates, using experiments, that informative countermeasures, especially from regulators, can mitigate misinformation. An important finding is that the source of countermeasures can moderate the effectiveness of countermeasures. (Rao and Wang 2017)

is a study on misinformation in the healthcare domain, that finds that restrictive measures are effective for over-the-counter drugs that do not require physician approval. In contrast, there is evidence that misinformation can persist after informative countermeasures (Ecker et al. 2022; Ecker, Lewandowsky, and Tang 2010; Lewandowsky et al. 2012). In fact in some domains such as politics, misinformation can persist or even increase (“backfire”) after informative countermeasures are in place (Nyhan 2021; Nyhan and Reifler 2010). Further, there is some experimental evidence that experts/physicians may be slow to update their beliefs given new evidence (Kostopoulou et al. 2012). As a result, it remains an empirical question whether countermeasures can be effective in situations where experts are involved in the healthcare setting; a question that this paper addresses.

It is also possible that the effects of misinformation can vary by the degree of susceptibility of the individuals or groups. This is especially relevant for policymakers who may wish to better target their countermeasures. In a survey of physicians, Levin et al. (2023) find that self-reported willingness to prescribe HCQ and ignore new scientific evidence is correlated with their political orientation. Susceptibility to misinformation may arise in many other forms as well ; Ecker et al. (2022) provides an excellent review.

We examine the degree of susceptibility to misinformation from a different perspective, that offers some advantages. First, our perspective on susceptibility is that individuals are more susceptible to influence from those they perceive as similar or belonging to their social group (Mackie, Worth, and Asuncion 1990). In-group (out-group) messages are more (less) likely to resonate with the shared experiences and interests of the target audience, increasing the relevance and perceived value of the message (Esposito, Hornsey, and Spoor 2013). Separately, Nair, Manchanda, and Bhatia (2010) report that

physicians are influenced by opinion leaders who are research active i.e.,- “in-group” leaders. Note that, empirically, our “in-group” measure of susceptibility, support for Trump, is indistinguishable from political affiliation and is highly correlated with demographic characteristics such as race, age, income and education (see Appendix A3). However, political affiliation may be only relevant in particular contexts (Enders et al. 2022) and may mask lazy thinking (Pennycook and Rand 2019) or response to incentives offered by social media (Ceylan, Anderson, and Wood 2023). The evidence for the association of demographic characteristics with susceptibility to misinformation is also mixed (Pennycook and Rand 2019; Roozenbeek et al. 2020; Scherer et al. 2021). Consequently, following the principle of parsimony, we interpret Trump support as an in-group measure, as opposed to say political leaning or a proxy for other demographic characteristics. Interpreting Trump support as an in-group measure is less restrictive and recognizes that susceptibility to misinformation of a demographic may not be absolute, and possibly varies across contexts. Second, we extend the literature on misinformation to explicitly examine the moderating role of the degree of susceptibility on the net effect of misinformation and its countermeasures.

In summary, the current paper extends the work on countermeasures to misinformation in four ways. First, it focuses on the persistence of misinformation effects on actual physician decisions, in a context where the stakes are very high. It examines misinformation effects over the medium term, as we observe physician decisions up to eighteen months after definitive evidence countering misinformation is available. In contrast, experimental studies on misinformation typically examine the short term impact only. Second, the paper explicitly examines whether susceptibility moderates the effect of

countermeasures. Third, we examine the incremental effect of definitive scientific evidence against the use of HCQ and IVM on prescription claims. Fourth, we contrast the efficacy of different types of countermeasures (informative and restrictive) on physician prescription decisions.

Data

In our analysis, we use three data sources: data on prescription claims, data on Covid-19 cases, and vote share for the presidential candidates in the 2016 US presidential election. We discuss each in detail next.

Prescription Claims Data We obtained state level weekly prescription claims at the drug name level from GoodRx. There are three aspects that are important to note. First, prescription claims fulfilled in a hospital setting are not in our data. This is important as HCQ did temporarily receive emergency use authorization (EUA) from the FDA in hospital settings and for clinical trials. In other words, all of our prescriptions require experts i.e. physicians to agree to the course of treatment outside of a hospital setting; a setting not covered by the EUA. Second, the data is at the drug name level, so we can identify Hydroxychloroquine prescription claims in our data. Third, our data spans the years 2019 to 2021 (inclusive). We can observe prescription claim behaviors well after scientific evidence shows that HCQ is not a treatment for Covid-19, and there is a viable vaccine alternative. The data is at the state level to protect patient confidentiality.

Covid-19 Cases Data We rely on data collected by the New York Times (The New York Times 2021) on Covid cases.

Support for Donald J. Trump We rely on state level results from the 2016 U.S. presidential election⁸.

⁸ <https://www.nytimes.com/elections/2016/results/president>

Our focal measure of interest is the total prescription claims for HCQ. To address data privacy concerns, the claims are indexed before conducting the analysis. The indexing is constructed by multiplying an arbitrary scaling factor for all values before any modeling. This masks the actual magnitude but preserves relative magnitudes.

Institutional Details and Model Free Evidence

Chou, Oh, and Klein (2018) define *health* misinformation as a health-related claim of fact that is currently false due to a lack of scientific evidence. By this standard, the promotion of HCQ and IVM as a treatment for Covid-19 in the absence of scientific evidence constitutes health misinformation. We discuss each in detail.

Hydroxychloroquine Health misinformation statements on the efficacy of HCQ against Covid-19 first originated on February 25, 2020 when Didier Raoult posted a video online (IHU Méditerranée-Infection 2020). In that video, Raoult overstates the potential of HCQ for treating Covid-19 given the scientific knowledge available at that point. President Donald J. Trump drew far more significant attention to HCQ on March 19 and 20, 2020, when he endorsed HCQ as a potential remedy for Covid-19. Dr. Anthony Fauci, the director of the National Institute of Allergy and Infectious Diseases, refuted HCQ-related claims by President Trump on March 19, 2020, and March 20, 2020 within twenty-four hours (Rev 2020). Other institutions at the federal and state level responded with countermeasures to HCQ misinformation, imposing a range of restrictions on OLDU of HCQ. On April 24, 2020 the FDA explicitly cautioned against the use of HCQ outside of the hospital setting or a clinical trial.⁹ At no stage was HCQ approved for Covid-19 treatment outside of the hospital setting or as a prophylactic/preventive measure. By June 15, 2020 there was

⁹<https://www.fda.gov/safety/medical-product-safety-information/hydroxychloroquine-or-chloroquine-covid-19-drug-safety-communication-fda-cautions-against-use>

definitive evidence from randomized clinical trials and observational studies that HCQ was ineffective as a measure against Covid-19 (see online Appendix A1 for details).

Consequently, the National Institutes of Health (NIH) and the Infectious Diseases Society of American issued guidelines against HCQ use to treat Covid-19.^{10,11} In contrast, evidence in favor of HCQ had been discredited (Vinetz 2020). Further, the FDA rescinded its limited emergency use authorization (EUA) on June 15, 2020 and “concluded that, based on this new information and other information discussed in the attached memorandum, it is no longer reasonable to believe that oral formulations of HCQ and CQ may be effective in treating COVID-19, nor is it reasonable to believe that the known and potential benefits of these products outweigh their known and potential risks”.¹² Nevertheless, misinformation regarding the efficacy of HCQ to treat and prevent Covid-19 continued to gain traction (Estes 2020). Table 1 provides a summary timeline of HCQ related events. Online Appendix 1 provides the details of the timeline of the spread of HCQ-related misinformation and the response at the federal level.

¹⁰ <https://web.archive.org/web/20200619023829/https://www.covid19treatmentguidelines.nih.gov/whats-new/>

¹¹ <https://www.idsociety.org/globalassets/idsa/practice-guidelines/covid-19/treatment/idsa-covid-19-gl-tx-and-mgmt-v2.0.0.pdf>

¹² FDA’s HCQ EUA for Covid-19 treatment was issued on March 28, 2020. There was no EUA for preventive/prophylactic use. The FDA stated, “Given the uncertainty regarding the potential benefits and risks for COVID-19, it is critical to first have evidence from clinical trials”.

Table 1: Timeline of HCQ related events

Date	Event
02/25/2020	Dr. Raoult Initiates HCQ Misinformation
3/19/2020	President Trump Endorses HCQ
3/20/2020	President Trump Endorses HCQ. Dr. Fauci Counters Trump's Claims
4/14/2020	By now, 35 States Impose Restrictions on HCQ use
<i>06/21/2020</i>	<i>HCQ Debunked: FDA declares HCQ is no longer under EUA, NIH stops HCQ trials.*</i>
08/25/2020	By now, 9 states reverse restrictions
07/04/2021	67% of Adults in the US receive at least one dose of vaccine.
12/31/2021	End of Analysis Period in our data

*Signifies when there is definitive scientific evidence against HCQ use emerged.

At the state level, thirty-five states issued statements/ orders regarding some kind of policy on HCQ prescribing practices in response to HCQ misinformation. In effect these countermeasures placed restrictions on off-label drug use (OLDU) of HCQ for Covid-19 treatment. We extract several relevant dimensions of the policies (see Online Appendix 2 for details). Based on the state pharmacy board's / health department's response, we classify each state into a) Weak Policy - no statement or mere suggestion on HCQ use with no particulars, b) advisory - recommendations for requiring Covid-19 diagnosis only, not enforceable, c) partial ban - prohibits prophylactic use, but allows therapeutic use with documentation and d) full ban - prohibits prophylactic and therapeutic use outside the hospital/clinical trial settings. Note, weak and advisory policies are informative policies, whereas partial ban and full ban are restrictive policies. For each state, we document the effective date of the policy. 11 of these states also reversed their policies (4 states reversed bans, and 7 reversed partial bans). Table 2 summarizes the number of states by policy and Trump support.

Table 2: A breakdown of the number of states
by HCQ countermeasures and Trump Support

	Against Trump	Pro Trump
Ban	3	1
Ban Subsequently Reversed	4	0
Partial Ban	3	4
Partial Ban Subsequently Reversed	1	6
Advisory	4	9
Weak Policy	5	10
Total States	20	30

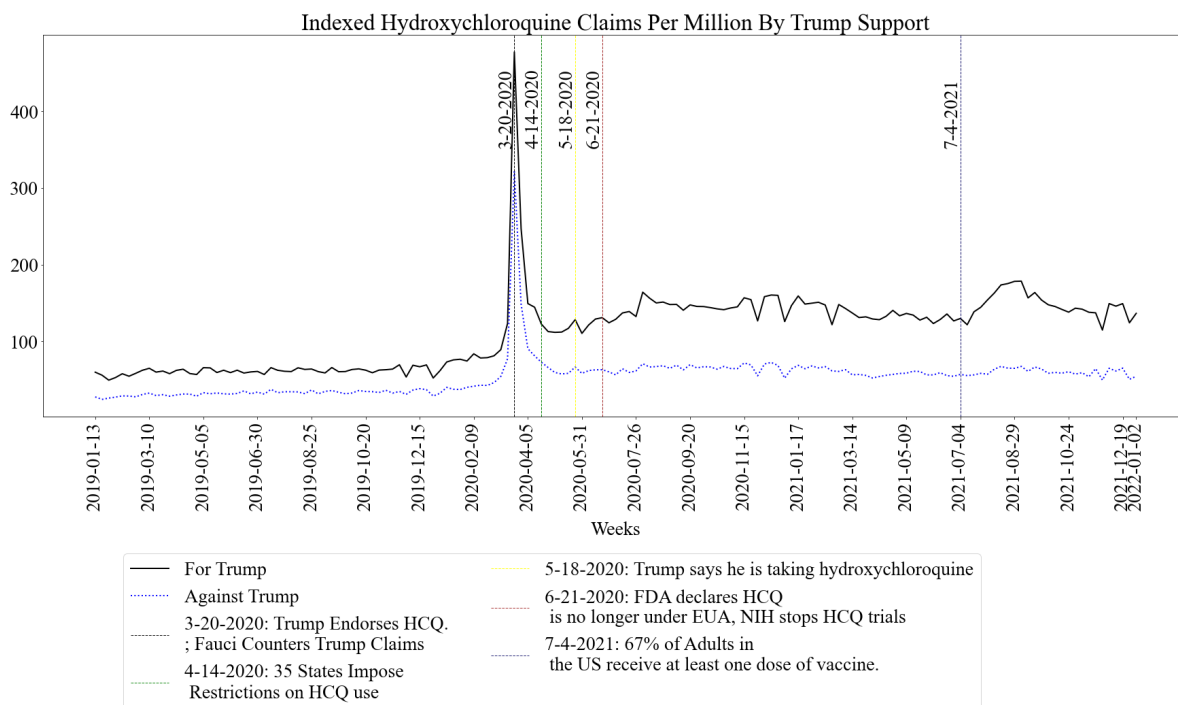
Figure 1(a) provides model-free evidence for the effect that the misinformation campaign had on the market of prescription claims for HCQ. Figure 1(a) shows that HCQ claims peaked during Trump's announcement week (note the announcement was on a Thursday), and declined to about baseline within four weeks after the announcement. This replicates findings in (Vaduganathan et al. 2020). The graph suggests that the number of prescription claims was higher in 2020 than in 2019. Figures 1(a) and 1(b) together suggest that increases in Covid cases per capita were not necessarily associated with an increase in HCQ claims.

Countermeasures were introduced between March 19th, 2020, and April 14th, 2020, by 35 states. Figure 1(a) shows that even after the FDA revoked the EUA for HCQ, we see increases in HCQ claims, with the gap between Trump supporting states and Trump opposing states increasing after the FDA's announcement, possibly due to rising Covid cases. Note the FDA's repeal of the HCQ EUA coincides with emergence of definitive proof

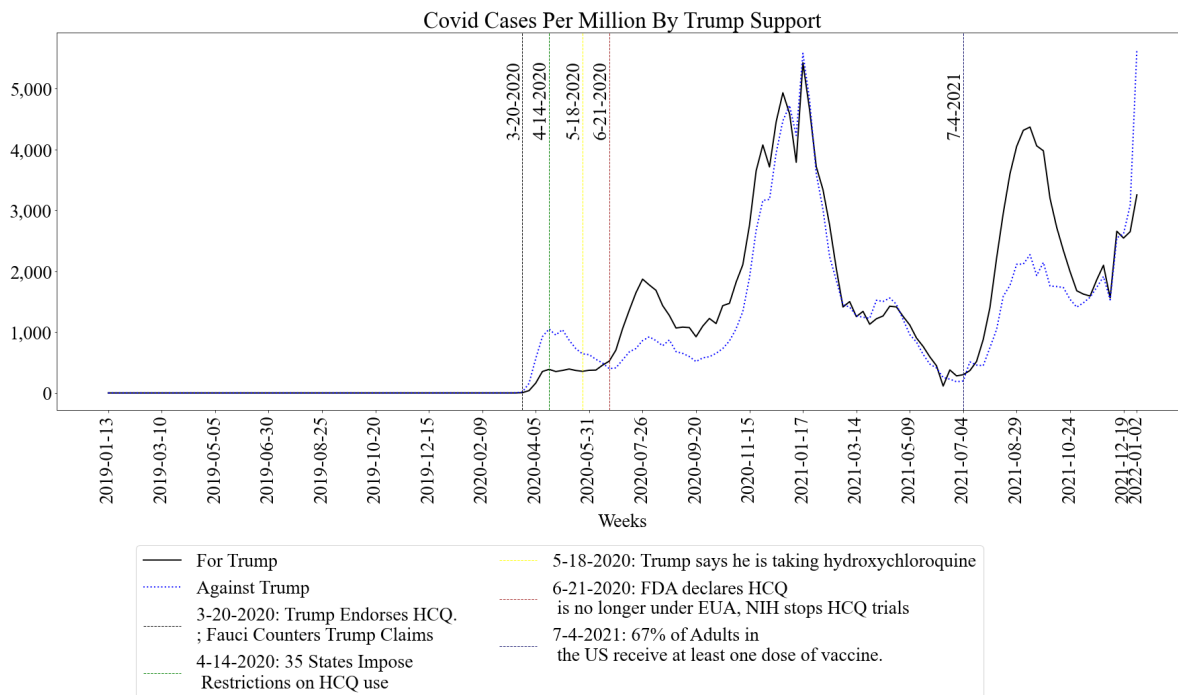
that HCQ was not useful to treat Covid-19 and the removal of HCQ from the FDA's drug shortage list (Iowa Board of Medicine et al. 2020).

Figure 1 Hydroxychloroquine National Level Aggregates

1(a) Claims Per Million People



1(b) Covid Cases Per Million People



Ivermectin Even though Ivermectin in the context of Covid first received scientific attention in April, 2020 from a study that was subsequently retracted, Ivermectin was not widely known outside the scientific community at this time. Ivermectin (IVM) gained significant attention as a potential treatment for Covid-19, particularly after Dr. Pierre Kory's testimony at the Senate hearing, where he advocated for its use on December 8, 2020.¹³ Subsequently, Ivermectin gain considerable attention in the conservative media, and from celebrities¹⁴. Similar to HCQ, the initial evidence for IVM was weak to begin with, and was eventually discredited. While Hydroxychloroquine (HCQ) countermeasures included both informative and restrictive measures, the countermeasures for IVM were primarily informative, with no imposed restrictions on its prescription for Covid-19 treatment. However, similar to HCQ, subsequent evidence emerged indicating the ineffectiveness of IVM against Covid-19, and several studies that brought Ivermectin into limelight for Covid-19 were discredited by July, 2021(Hill et al. 2022).

Table 3: Timeline of IVM related events

Date	Event
04/01/2020	Australian Study Suggests Ivermectin Could be a Treatment for Covid-19
2/4/2021	Merck Issues a warning against Ivermectin Use
12/8/2020	Dr. Kory testifies in favor of Ivermectin in a Senate Committee
<i>1/14/2021</i>	<i>NIH: Not enough Data to say Ivermectin works</i>
03/05/2021	FDA warns against Ivermectin use.
07/04/2021	67% of Adults in the US receive at least one dose of vaccine.
<i>07/15/2021</i>	<i>Key Studies that drew attention to Ivermectin Discredited.*</i>
08/26/2021	CDC Issues Warning on IVM use
12/31/2021	End of Analysis Period

*Signifies when the evidence that led to interest in IVM were discredited.

¹³ <https://www.hsgac.senate.gov/wp-content/uploads/imo/media/doc/Testimony-Kory-2020-12-08.pdf>

¹⁴

<https://www.npr.org/sections/health-shots/2021/09/19/1038369557/ivermectin-anti-vaccine-movement-culture-wars>

We present the model free evidence in Figure 2. Even though an early Australian study offered some preliminary evidence favoring IVM use against Covid-19 in April, 2020, prescription claims increased substantially only in December, 2020. This was when a senate hearing was held to explore alternative treatment strategies. There is some evidence that this hearing was politically motivated and was held at the request of conservative interests^{15,16}. We also note that there was an announcement by the CDC on August 26, 2020.

However, prescription claims begin to rise again toward the end of 2021, with the rise in Covid cases. It is also interesting that IVM claims peaked before Covid cases, suggesting that some patients and physicians viewed IVM as a prophylactic. Further, there is a difference in relative increase of prescription claims between Trump supporting states and the rest of the states. This difference cannot be explained by Covid case count between December 1, 2020 and July 4, 2021. But the subsequent difference after July 4, 2021 could be due to differential Covid case rates. Overall, the patterns for IVM substantially mimic the patterns for HCQ claims.

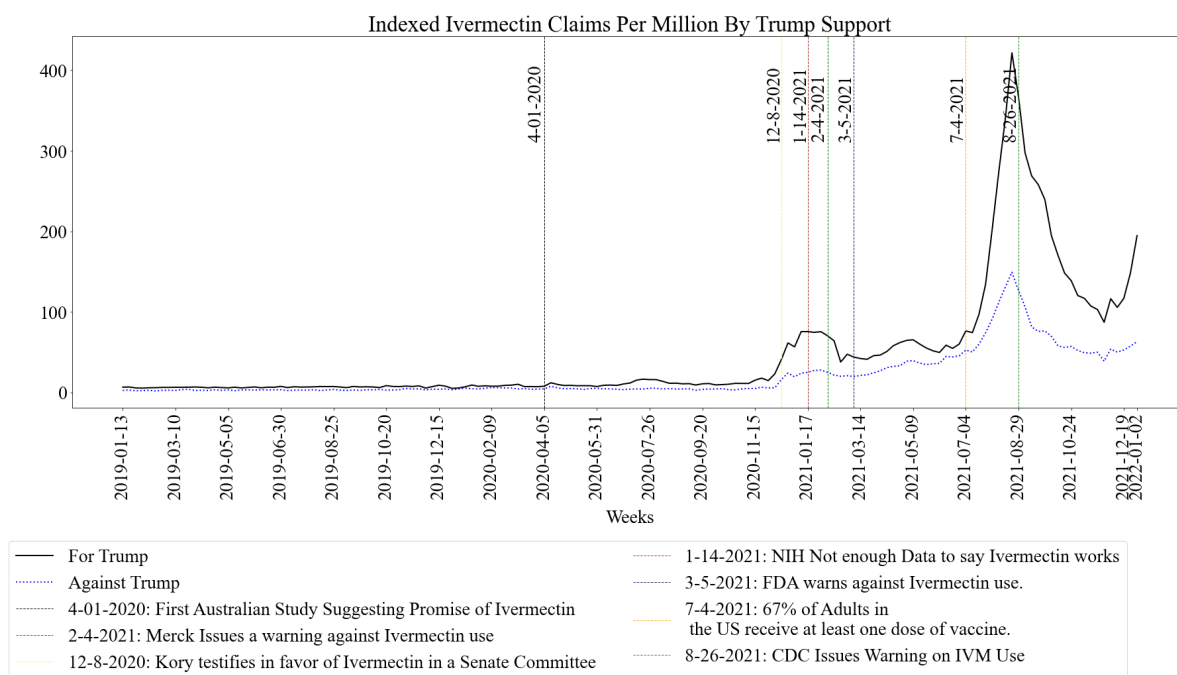
¹⁵

<https://local12.com/health/medical-edge-reports/senate-hearing-to-discuss-therapies-to-fight-covid-19-turns-political-cincinnati>

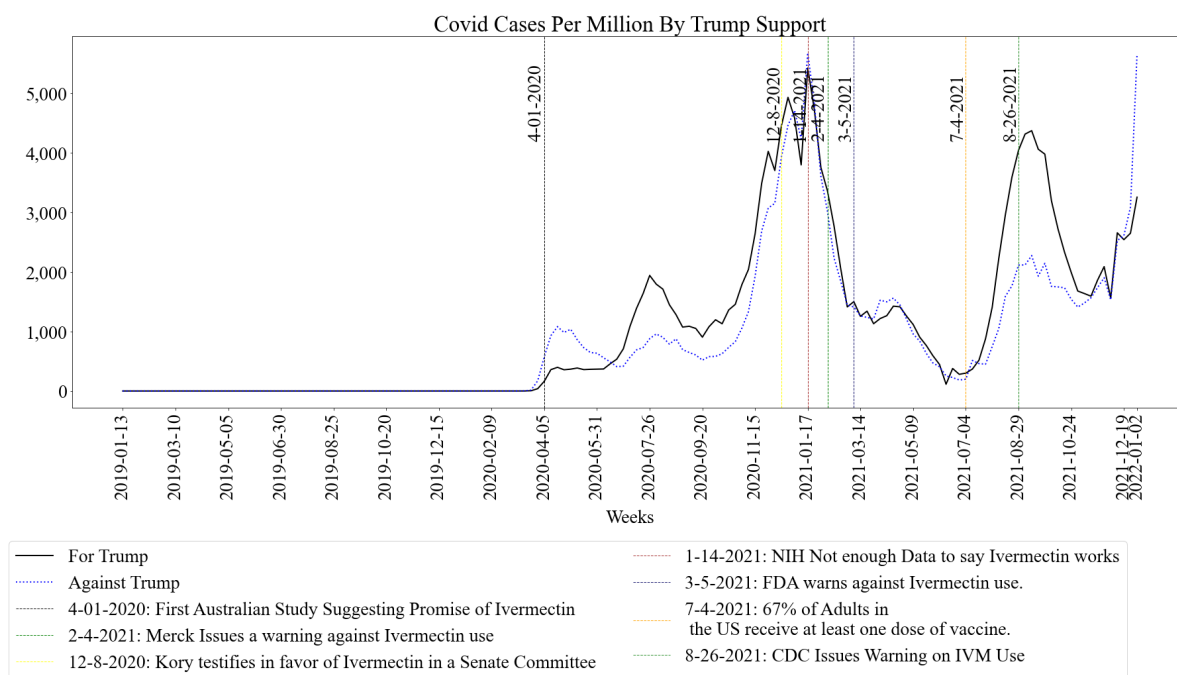
¹⁶ <https://www.ronjohnson.senate.gov/2021/2/youtube-cancels-the-u-s-senat>

Figure 2 Ivermectin National Level Aggregates

2(a) Claims Per Million People



2(b) Covid Cases Per Million People



Empirical Approach

Our empirical approach is aligned with each of our four research questions. We discuss our approach for each question for clarity.

Persistence of Misinformation after Countermeasures (Persistence Analysis):

We previously defined net effect as the incremental HCQ claims attributable jointly to misinformation and its countermeasures. We seek causal estimates or the average treatment net effect on the treated (ATT) of misinformation and its countermeasures on prescription claims at the national level. The national level causal estimates offer an aggregate view. We describe our identification strategy to arrive at causal estimates, followed by a description of our synthetic control approach.

Identification Strategy We aim to draw causal inferences from observational data by employing a quasi-experimental framework. We detail our approach for HCQ; the analysis for IVM proceeds in a similar fashion. Specifically, the treatment date for HCQ is represented by the date of Raoult's video and its subsequent virality, which are exogenous to the previous demand for HCQ. Thus, we designate the treatment date as February 25, 2020, corresponding to the publication of Raoult and colleagues' YouTube video.

For national level ATTs, we assess the extent to which the increase in actual HCQ claims can be attributed to misinformation and its countermeasures, by constructing a synthetic control from a control group. The control group consists of all other drugs in our database, excluding IVM and Chloroquine (CQ), which were subjected to misinformation during the pandemic. By utilizing other drugs as control units, we implicitly control for various confounding factors. These factors include platform-specific effects (e.g., market penetration for GoodRx), seasonality, trends, and Covid-related measures such as

shelter-in-place orders, indoor mask mandates, and travel restrictions. We make the reasonable assumption that these Covid measures affect all drug claims similarly, except in cases where patients can reasonably be safe without the prescription medication. Moreover, as the discussion predominantly centered around HCQ within our analysis window and did not spill over to other drugs, we can reasonably assume that these other drugs are not influenced by misinformation regarding HCQ or its countermeasures. We investigate the use of Covid-19 related drugs as controls in the robustness section.

However, with thousands of drugs in our database ¹⁷, we face the challenge of the “small N, large P” problem as our dataset includes only 52 weeks of pre-treatment data. To overcome this issue, we adopt the Bayesian Synthetic controls methodology proposed by Kim, Lee, and Gupta (2020), described in detail in the next subsection. However, to ensure model convergence, we reduce the number of control units. Specifically, we include the top 100 drugs by volume of claims as control units. Additionally, to include all prescription drugs as controls, we aggregate claims across other drugs at the generic product identifier or GPI2 level. The GPI2 level allows for grouping similar drugs together. There are 100 GPI2 codes that cover all drugs. We exclude claims from the top 100 drugs by claim volume from the GPI2 aggregation to prevent duplication. As a result, our final control group comprises 200 control units, including top 100 drugs by volume and all 100 GPI2 categories.

To estimate the counterfactual or baseline, we estimate a Bayesian synthetic control model that captures the relationship between the focal HCQ and the control units during the pre-treatment period. The measure of interest in this analysis is the incremental HCQ claims, which is defined as the difference between actual HCQ claims and the counterfactual estimate. We discuss our synthetic control approach next.

¹⁷ We are not able to disclose the exact number due to privacy concerns.

Synthetic Control Approach We apply the Bayesian synthetic control model introduced in (Kim, Lee, and Gupta 2020) to estimate the counterfactual number of claims for HCQ over time in case the misinformation campaign would not have taken place and compare it to the actual number of claims. This model overcomes several issues of the difference-in-differences model (Card and Krueger 1993) and the frequentist synthetic control approaches (Abadie, Diamond, and Hainmueller 2010). The difference-in-differences approach would require us to pick one control drug that satisfies all the necessary assumptions including parallel trend assumption from the entire set of potential controls, which significantly reduces the flexibility of the model. An advantage of the Bayesian approach over frequentist synthetic control methods is straightforward statistical inference, and therefore, it facilitates hypothesis testing (Kim, Lee, and Gupta 2020). Most importantly, by using sparse priors, it naturally lends itself to addressing the “small N, large P” problem.

We follow very closely to the notation introduced in (Kim, Lee, and Gupta 2020). We describe the model for a particular state. Let us denote each drug or GPI2 category by j , $j = 0, 1, \dots, J$, where the 0 corresponds to HCQ, and the indices $1, \dots, J$ correspond to the control drugs/ GPI2 groups. Note that we exclude other Covid treatment drug groups, including antivirals, from this group of controls. We denote each week by t , $t = 1, 2, \dots, T$. The treatment date, in our context, is the first time HCQ is publicly touted as an effective treatment with insufficient scientific evidence. The treatment occurs during the week $T_1 + 1 < T$, so we have T_1 pre-treatment weeks and $(T - T_1)$ post-treatment weeks. Note, 0 indicates treatment unit, and T_1 the treatment date. We want to estimate Y_{0t} (the counterfactual) using control units where, Y indicates outcome of interest, and $t \geq T_1$ as

follows: $Y_{0t} = \beta_0 + \sum_{j=1}^J \beta_j Y_{jt} + \epsilon_{0t}$, where $t < T_1$, j references control drugs or GPI2 groups, ϵ_{0t} is the treatment unit specific shock in time t .

We estimate $\hat{\beta} = \underset{\beta}{argmin} \sum_{t=1}^{T_0} (Y_{0t} - \beta_0 - \sum_{j=1}^J \beta_j Y_{jt})^2$, where the parameters are estimated using the spike and slab prior (Thomson et al. 2019). Results are robust to an alternate prior, the horseshoe, introduced in the context of synthetic controls in (Kim, Lee, and Gupta 2020), although in some instances the horseshoe prior based model did not converge. The critical and untestable assumption is that the relationship between the focal drug and the control drugs/GPI2 categories in the pre-treatment period would continue to hold in the absence of treatment.

Moderating Effect of Degree of Susceptibility on the Effect of Misinformation (Susceptibility Analysis):

We exploit the variation in state-level Trump support in the 2016 elections, to assess how state level's ATTs vary with degree of susceptibility. However, to do so, we require state level ATT estimates. Consequently, using the same identification and synthetic control approach as outlined for the persistence analysis, we estimate state level synthetic control models. We estimate the ATT from the synthetic controls model, using February 25, 2020 as the treatment date for HCQ; the date Raoult posted his video online.

Our approach to analyzing the heterogeneity in state-week ATTs is similar to meta-analysis (Grewal, Puccinelli, and Monroe 2018; Szymanski and Henard 2001). Specifically, the state level synthetic control approach provides us with both a point estimate of the incremental estimate as well as the posterior distribution of the incremental effect for each state-week combination (Kim, Lee, and Gupta 2020). The standard deviation of each

posterior distribution serves as an estimate of measurement error. We incorporate the square of this measurement error as weights in a weighted least squares regression (Bezawada and Pauwels 2013). Our model specification is as follows.

$$ATT\ Per\ Capita_{it} = constant + \alpha ProTrump_i + \sum_t \theta_t week_t + \gamma covid\ cases\ per\ capita_{it} + \epsilon_{it} \quad (eq\ 1)$$

Here, $ATT\ Per\ Capita_{it}$ is the ATT for state i in week t divided by the population (in Millions) of the state. By controlling for population, we control for population size differences across states. Our focal variable of interest in this regression is $ProTrump_i$. We measure the variable $ProTrump_i$ as the ratio of votes won by President Trump in 2016 divided by the votes from the nearest competitor in that state. By definition, $ProTrump_i$ values equal to or exceeding (below) 1 indicates that Trump won (lost) that state in 2016. This measure corresponds to the degree of susceptibility, unlike a simple binary categorization of states won or lost by President Trump. To account for common shocks, we include week-specific fixed effects. We include the Covid case count per capita (in Millions) to account for possible time-varying differences in Covid prevalence across states, where γ is the corresponding coefficient.

We estimate the model described in eq 1 over four different time periods. The first is the immediate period after Raoult's posting of the HCQ video (March 22, 2020 and April 14, 2020). We report results for the intermediate period-after countermeasures were implemented (April 14, 2020) and before the FDA revoked the EUA for HCQ (June 21, 2020). Definitive evidence against the use of HCQ culminated in the FDA's revocation of

the EUA for HCQ on June 21, 2020. We report results after this revocation up to the end of 2020. We also report results for 2021.

The Effect of Definitive Evidence on Incremental Prescription Claims (Event Study):

In the case of HCQ, the scientific establishment had formally discredited HCQ resulting in the FDA's withdrawal of its emergency use authorization for HCQ on June 21, 2020. We investigate whether this additional evidence had an effect on the effect size due to misinformation. We separately estimate an event study model for the date when the FDA revoked the EUA for HCQ (June 21, 2020). We report results for 4 weeks and 8 weeks before and after the FDA's revocation. Note, we are interested in the additional incremental effect of HCQ being discredited. Consequently, our event study analysis must control for different state level countermeasures in place. We also control for Covid cases per capita, and Trump support. As before, we use weighted least squares to incorporate the measurement error estimates from the state level synthetic control models. The synthetic control approach accounts for state-specific time-invariant effects, so we do not additionally control for state-specific effects in this regression. We also exclude states that changed HCQ policies in the event study analysis window.

$$\begin{aligned}
 ATT\ Per\ Capita_{it} = & \text{constant} + \delta_0 Post\ FDA_t + \alpha ProTrump_i + \sum_j \beta_j policy_{ijt} \\
 & + \gamma covid\ cases\ per\ capita_{it} + \epsilon_{it}
 \end{aligned}
 \tag{eq 2}$$

Here, our focal variable of interest is $Post\ FDA_t$. It takes value 1 for the period after the FDA's revocation and 0 otherwise. $policy_{ijt}$ indicates whether the state i has under the j^{th} policy in week t . The reference policy is the weak policy. We cluster errors by policy, to control for similarity within a policy.

We also report results , where we include the interactions between Trump support and the different policies, as shown in equation 3. The intuition is that there is heterogeneity in how policies are implemented, based on the state's support for Trump. We cluster errors by policy, to control for similarity within a policy.

$$\begin{aligned}
 ATT\ Per\ Capita_{it} = & \text{constant} + \delta_0 Post\ FDA_t + \alpha ProTrump_i + \sum_j \beta_j policy_{ijt} \\
 & + \sum_j \delta_j policy_{ijt} \times ProTrump_i \\
 & + \gamma covid\ cases\ per\ capita_{it} + \epsilon_{it}
 \end{aligned}
 \tag{eq 3}$$

Our approach for IVM is similar, except all countermeasures regarding Ivermectin use are federal informative policies and state level weak policies, so we do not control for policies in any of the IVM models.

Comparison of Countermeasures:

To compare and contrast countermeasures, we estimate the following equation using weighted least squares, with errors clustered by policy.

$$\begin{aligned}
 ATT\ Per\ Capita_{it} = & \text{constant} + \sum_t \theta_t week_t + \alpha ProTrump_i + \sum_j \beta_j policy_{ijt} \\
 & + \sum_j \delta_j policy_{ijt} \times ProTrump_i \\
 & + \gamma covid\ cases\ per\ capita_{it} + \epsilon_{it}
 \end{aligned}
 \tag{eq 4}$$

All of the terms in equation 4 have been introduced earlier. The reference policy is the weak policy, and we exclude states that reversed policies from our analysis. We estimate the model described in eq 4 over four different time periods for each countermeasure similar to our susceptibility analysis. We cluster errors by policy.

This also serves as an alternate specification and a robustness check to our analysis on the moderating effect of Trump support. Specifically, in examining the moderating of Trump support, we did not control for state level countermeasures. To the extent countermeasures are correlated with Trump support, our earlier analysis is correct. Alternatively, countermeasures were implemented due to state-specific time-invariant factors such as the state's healthcare leadership (Kim, Lee, and Gupta 2020; Seiler, Tuchman, and Yao 2021). Consequently, controlling for these countermeasures as shown in equation 4 serves as a robustness test. We can also then interpret the interactions between Trump support and the different policies as the moderating effect of Trump support on countermeasures.

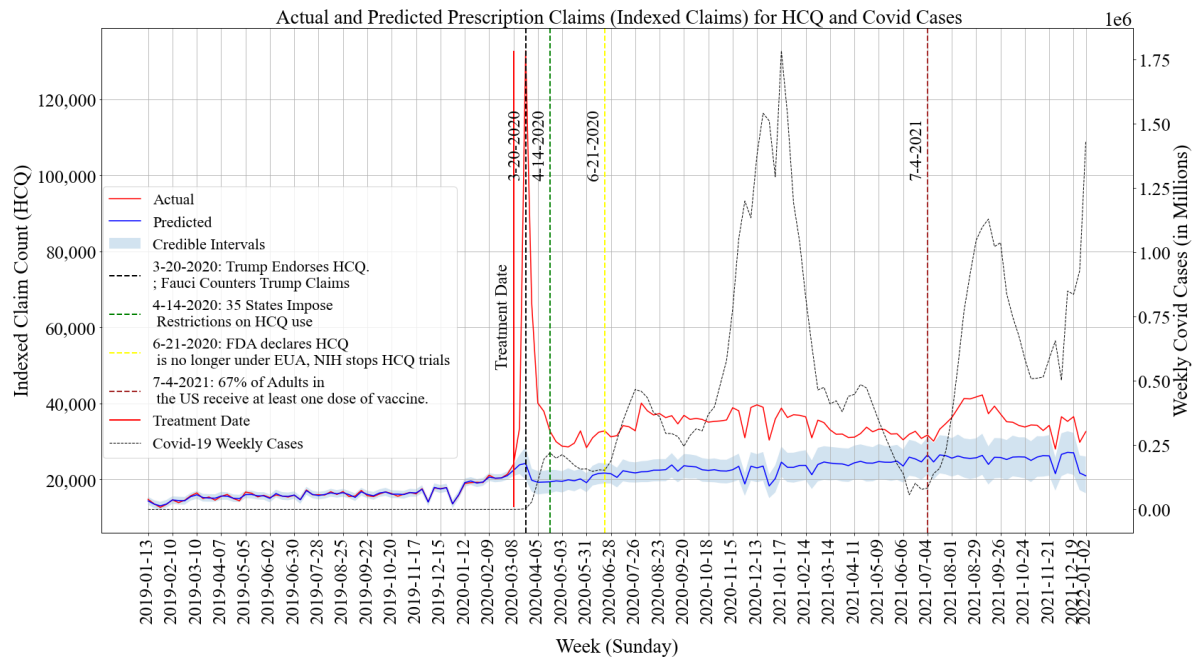
Note, we do not examine state level countermeasures for IVM, as all states had a weak policy.

HCQ Results

We first present results for HCQ, and then separately present the corresponding results for IVM.

Persistence of Misinformation after Countermeasures (Persistence Analysis): Figure 3, plots the actual and counterfactual indexed HCQ prescription claims over time, based on the estimates from the national level synthetic control model. The plot indicates the HCQ actual claims (black line), the estimated baseline number of claims (blue line), and the estimated credible intervals of the baseline (grey filled area) over time. Figure 3 suggests that the total number of claims levels off after the initial spike.

FIGURE 3 Total Hydroxychloroquine Claims over Time Nationwide



We also report percentage increase in HCQ claims using the raw unindexed data in Table 4. From June 15th, 2020 till the end of the year (medium term), there is a significant 57.73% increase in HCQ claims (see Table 4). This is after a) significant evidence against the use of HCQ was available, b) evidence favoring HCQ was discredited or weak compared to the evidence against HCQ, c) the FDA revoked its EUA and d) when shortages had ended (Iowa Board of Medicine et al. 2020). Claims remain elevated averaging a 51.87% increase in 2021.

Table 4: Percentage Change in incremental HCQ claims over time

	Percentage ATT Increase
Trump Announcement (Week of 3/22/2020)	482.44%
Immediate (3/22/2020 - 4/14/2020)	137.59%
Intermediate (4/14/2020 -6/21/2020)	53.57%
After FDA Revocation till end of 2020	68.42%
2021	51.87%
Overall After FDA Revocation till end of 2021	57.73%

It is possible that federal statements issued by Dr.Fauci and healthcare institutions led to a decline in prescription claims right after the immediate spike from President Trump's comments. We observe a similar decline in states with no countermeasures (results available on request). Nevertheless, even at the end of 2021, HCQ claims remain elevated (51.87% above counterfactual). This is evidence for the persistence of the effect of misinformation of physician prescribing behavior in the medium term.

Moderating Effect of Degree of Susceptibility on the Effect of Misinformation

(Susceptibility Analysis): Next we examine the role of susceptibility in moderating the effects of misinformation. Figure 4 presents the indexed ATT Per Capita estimates from the synthetic control models aggregated into two groups - for and against Trump states. We plot these effects over time. It is clear that there are systematic differences between the two types of states, with higher ATT per capita in pro-Trump states.

Figure 4: Moderating Effect of Susceptibility (Trump Support) on HCQ Claims

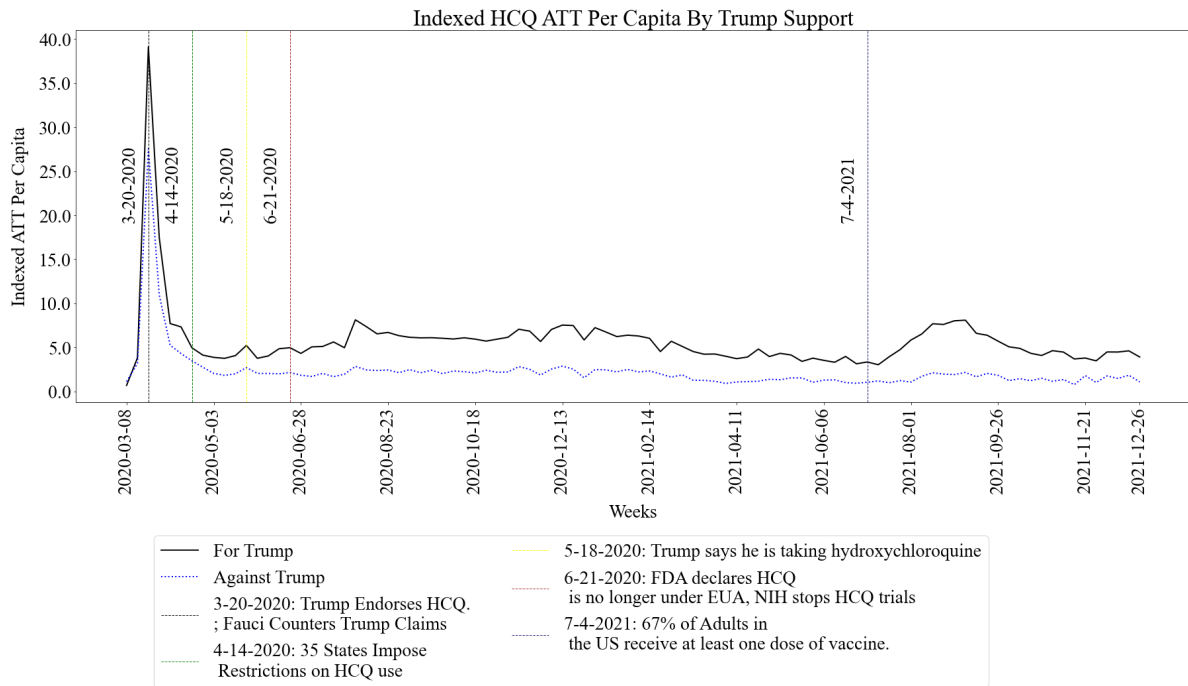


Table 5 presents results from the analysis proposed in equation 1 for the different time periods. In the immediate aftermath of Trump’s announcement, we see no statistical difference across states that Trump won and lost in the 2016 elections. Overall, the results suggest that “in group” susceptibility to misinformation can blunt the effect of federal and state countermeasures. Consistent with the graphical representation in figure 4, the differences between pro-Trump and anti-Trump states persists after the FDA revoked the EUA for HCQ use, and also in 2021. This is evidence that degree of susceptibility moderates the net effect of misinformation on experts.

Table 5: Moderating Effect of Susceptibility (Trump Support)

<i>Dependent Variable:</i>				
Indexed Incremental HCQ Claims Per Capita				
	Immediate 3/22/2020-4/14/2020	Intermediate 4/14/2020-6/21/2020	After FDA Revocation 6/21/2020 - 12/31/ 2020	Year 2021
Constant	0.946 (0.974)	-0.434 (0.362)	-0.219 (0.303)	-0.747 (0.531)
Cases Per Capita	-2.981 (1.625)	0.009*** (0.002)	0.002* (0.001)	0.004*** (0.001)
Pro Trump	0.002 (1.039)	2.126*** (0.194)	3.063*** (0.181)	2.277*** (0.132)
Observations	150	600	1,300	2,500
R ²	0.790	0.288	0.306	0.249
Adjusted R ²	0.784	0.272	0.291	0.233
Residual Std. Error	5.525 (df = 145)	1.684 (df = 586)	2.112 (df = 1272)	1.654 (df = 2448)
F Statistic	135.979*** (df = 4; 145)	18.206*** (df = 13; 586)	20.752*** (df = 27; 1272)	15.879*** (df = 51; 2448)
<i>Note:</i>	*p<0.05; ** p<0.01; *** p<0.001 Weighted Least Squares Estimation, Week Fixed Effects			

The Effect of Definitive Evidence on Incremental Prescription Claims (Event Study):

We examine the effect of FDA's revocation of its End User Authorization for HCQ use in hospital settings. The date of the FDA's revocation coincides with the emergence of definitive evidence that HCQ was not useful in the context of Covid-19.

Figure 3 suggests that there are no discernible change in trends for effect sizes after the FDA's revocation. As a formal test, we control for differences in policy across states and include interactions with Trump support, using equations 2 and 3. Table 6 documents the results and indicates a small short term effect in the 4 week window (M= -0.531, SD =0.150), and a null effect in the 8 week window (M= -0.011, SD = 0.171). This suggests that the incremental effect of definitive information, if any, was short lived. Separately, given the persistence of the incremental claims in 2021, suggests the medium term effect of the definitive evidence was modest.

Table 6: Effect of FDA Revocation on HCQ Claims

<i>Dependent Variable:</i>				
Indexed Incremental HCQ Claims Per Capita				
	+/- 4 Weeks		+/- 8 Weeks	
	(1)	(2)	(3)	(4)
Constant	0.756* (0.366)	1.084*** (0.091)	0.455 (0.416)	0.776*** (0.210)
Cases (in 1000s)	0.012*** (0.003)	0.013*** (0.003)	0.012*** (0.003)	0.013*** (0.003)
Partial Ban	1.341** (0.460)	0.349 (0.356)	1.526 (0.789)	0.428 (0.250)
Advisory	0.679*** (0.062)	0.068 (0.101)	0.734*** (0.085)	0.252* (0.124)
Ban	-0.515*** (0.153)	-2.156*** (0.347)	-0.473*** (0.113)	-1.870*** (0.279)
Pro Trump	1.214*** (0.338)	0.438*** (0.130)	1.407*** (0.332)	0.807*** (0.158)
Pro Trump x Ban		2.697*** (0.427)		2.173*** (0.469)
Pro Trump x Partial Ban		1.279 (0.765)		1.211 (0.996)
Pro Trump x Advisory		0.960*** (0.085)		0.682*** (0.128)
Pro Trump x Weak/No Policy		0.658*** (0.033)		0.379* (0.148)
Post FDA	-0.475*** (0.123)	-0.531*** (0.150)	0.017 (0.142)	-0.011 (0.171)
Observations	368	368	736	736
R ²	0.369	0.401	0.354	0.370
Adjusted R ²	0.358	0.384	0.348	0.361
Residual Std. Error	1.472 (df = 361)	1.442 (df = 357)	1.673 (df = 729)	1.656 (df = 725)
F Statistic	35.164*** (df = 6; 361)	23.903*** (df = 10; 357)	66.484*** (df = 6; 729)	42.582*** (df = 10; 725)
<i>Note:</i> *p<0.05; **p<0.01; ***p<0.001				
1. All models exclude Idaho, Oregon, New York, and Texas , as they changed policies in the analysis window.				
2. Includes 46 states				
3. Weighted Least Squares Estimation, Clustered Errors By Policy where Applicable				

Comparison of Countermeasures: We report the results of the regression proposed in equation 4 in Table 7.

Table 7: Comparison of Countermeasures

<i>Dependent Variable:</i>				
	Indexed Incremental HCQ Claims Per Capita			
	Immediate 3/22/2020-4/14/2020	Intermediate 4/14/2020-6/21/2020	After FDA Revocation 6/21/2020 - 12/31/ 2020	Year 2021
Constant	1.079* (0.539)	0.435 (0.457)	1.026*** (0.165)	0.175 (0.328)
Cases (in 1000s)	-1.454** (0.478)	0.009*** (0.003)	0.003*** (0.0004)	0.003** (0.001)
Partial Ban		-2.113*** (0.139)	-2.642*** (0.033)	-2.898*** (0.046)
Advisory		0.419*** (0.074)	-0.931*** (0.005)	-0.593*** (0.025)
Ban		-1.004*** (0.044)	-1.583*** (0.059)	-1.485*** (0.062)
Pro Trump	-0.203 (0.670)	0.926*** (0.010)	0.656*** (0.075)	0.604*** (0.042)
Pro Trump x Ban		1.270*** (0.109)	2.459*** (0.087)	2.502*** (0.122)
Pro Trump x Partial Ban		4.019*** (0.100)	6.172*** (0.007)	5.524*** (0.006)
Pro Trump x Advisory		0.433*** (0.034)	2.323*** (0.034)	1.589*** (0.008)
Pro Trump x Weak/No Policy		0.358*** (0.011)	1.054*** (0.028)	0.655*** (0.001)
Observations	113	468	1,014	1,950
R ²	0.778	0.392	0.436	0.346
Adjusted R ²	0.770	0.365	0.417	0.326
Residual Std. Error	5.754 (df = 108)	1.482 (df = 447)	1.744 (df = 979)	1.479 (df = 1891)
F Statistic	94.883*** (df = 4; 108)	14.435*** (df = 20; 447)	22.299*** (df = 34; 979)	17.268*** (df = 58; 1891)
<i>Note:</i>				
*p<0.05; **p<0.01; ***p<0.001				
1. The model covering the immediate period after HCQ gained prominence is restricted to 33 states with no policies till 3/22/2020. Inclusion of all 50 states does not substantively affect the results.				
2. We exclude states that changed policies during the pandemic.				
3. Includes Week Fixed Effects				
4. Weighted Least Squares Estimation, Clustered Errors By Policy where Applicable				

Note that we use states with weak policies as the base line. The coefficients of the policies can be interpreted as the effect of each policy type in comparison to weak policies, in states with zero support for Trump. Any action in the form of advisories, partial bans or bans appears to be better than a weak policy, when Trump support is negligible. Restrictive

policies (bans and partial bans) reduce claims more than informative measures (advisories and weak policies). This is true across time windows. However, we observe that the main effect of Trump support and the interactions between Trump support and policies are all positive and significant. This suggests that bans, partial bans, advisory policies and weak policies were less effective in states Trump won. We see a similar result across time periods. This serves as a robustness check for our susceptibility analysis as well.

Ivermectin Results

Persistence Analysis We follow the same procedures for our synthetic control analysis as for HCQ, except the treatment date is April 1, 2020, the date the first study on IVM was published online. Table 8 reports the percentage increase in claims over varying time periods. The highest percentage increase, on average, is after 67% of the US population had received at least one dose of the Covid-19 vaccine.

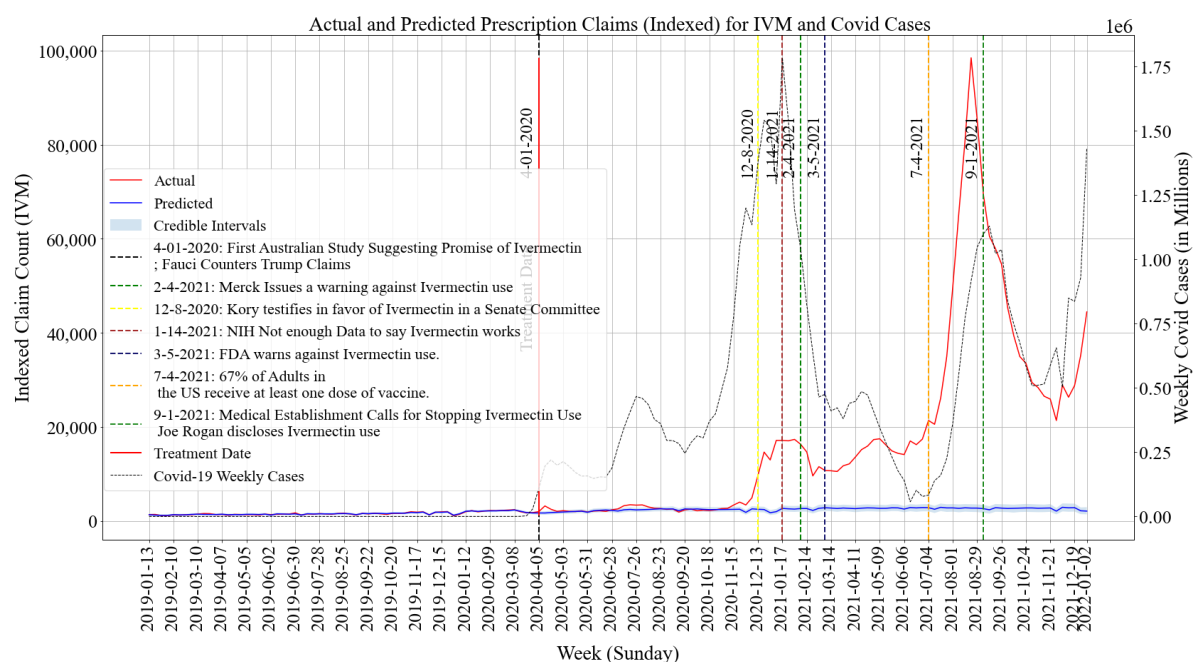
Table 8: Percentage Change in incremental HCQ claims over time

	Percentage ATT Increase
Immediate (Dr. Kory's Senate Testimony) 12/8/2020-1/14/2021	615.36%
After NIH Refutes IVM 1/21/2021-7/4/2021	451.59%
After July 4, 2021 1/21/2021-12/31/2021	1617.64 %

Figure 5 offers more insight into the time varying treatment effects. We observe a small, short-lived increase in prescription claims in relation to the counterfactual on April 1, 2020, but the major increase does not occur till December 8, 2020, when Dr. Kory testified for the senate committee. This increase sustains till the end of 2021, with a substantial increase in 2021 coincident with an increase in Covid cases. In other words, much like our

finding for HCQ, we observe a persistent effect of misinformation for IVM, despite federal and state level informative countermeasures.

Figure 5: Total Ivermectin Claims over Time Nationwide

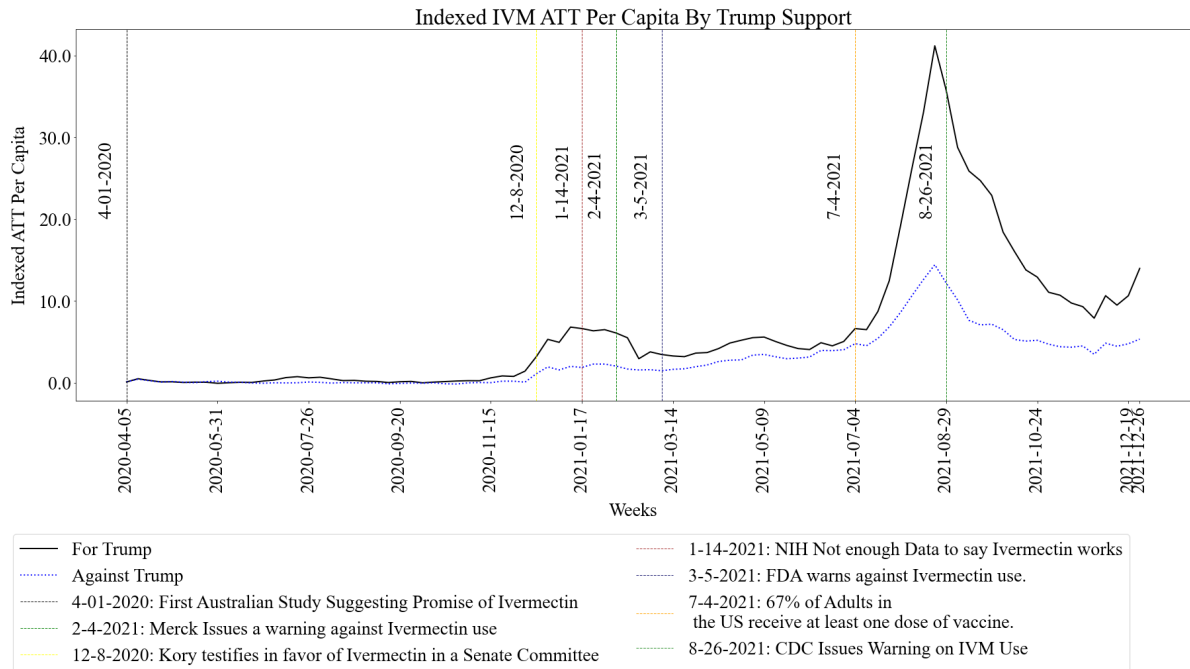


Susceptibility Analysis: Similar to figure 4, we plot the ATT per capita for Trump supporting and opposing states in figure 6. The difference between the two regions emerged more sharply after July 4, 2021, the date when 67% of the US population had received at least one dose of the vaccine. This increase could be due to several celebrities drawing greater attention to IVM, including the appearance of Dr. Kory on the Joe Rogan experience show on June 21, 2021¹⁸. There is a significant overlap in the audience of Joe Rogan, a podcast celebrity, and President Trump¹⁹.

¹⁸ <https://www.jreodcast.com/episode/joe-rogan-experience-1671-bret-weinstein-dr-pierre-kory/>

¹⁹ <https://pro.morningconsult.com/trend-setters/joe-rogan-fans-demographics-political-messaging-persuasion>

Figure 6: Moderating Effect of Susceptibility (Trump Support) on IVM Claims



We formally test this in a regression framework, using equation 1 and report the results in Table 9.

Table 9: Ivermectin Prescription Claims

Dependent Variable:			
Indexed Incremental IVM Claims Per Capita			
	Immediate 12/8/2020-1/7/2021	After NIH Refutes IVM 1/14/2021-7/4/2021	After July 4, 2021 7/4/2021-12/31/2021
Constant	-1.085 (0.773)	0.868 (0.588)	1.628* (0.742)
Cases Per Capita	0.007*** (0.002)	0.007*** (0.002)	0.022*** (0.002)
Pro Trump	0.600 (0.400)	0.039 (0.129)	2.199** (0.473)
Observations	150	1,100	1,250
R ²	0.127	0.106	0.318
Adjusted R ²	0.103	0.087	0.303
Residual Std. Error	3.367 (df = 145)	2.616 (df = 1076)	8.899 (df = 1223)
F Statistic	5.269*** (df = 4; 145)	5.531*** (df = 23; 1076)	21.927*** (df = 26; 1223)
Note:	*p<0.05; **p<0.01; ***p<0.001		
Weighted Least Squares Estimation, Week Fixed Effects			

Definitive Evidence: By July 15, 2021 the initial studies that reported that IVM could help with Covid-19, were discredited. The CDC made an announcement on August 26, 2021 discrediting IVM was effective, reducing prescription claims. However, we observe a subsequent increase in prescription claims at the end of the year (see figure 5). This suggests that even if the definitive evidence were effective, this was only for a short duration, and not sufficient to drive IVM prescriptions to zero. This corresponds to our finding for HCQ.

Summary of Findings From our study of HCQ claims, we find that the initial countermeasures likely reduced but did not eliminate prescriptions for HCQ immediately after Trump's endorsement. HCQ claim remained elevated till the end of 2021, providing evidence of persistence of misinformation effects among experts, even after countermeasures at the federal and state level were imposed. This increase was higher in states that Trump won in the 2016 election, providing evidence that susceptibility has a role to play. HCQ claims remain substantially elevated and persisted for 18 months even after the publication of credible HCQ studies along with the withdrawal of the FDA's EUA for HCQ by June 15th, 2020. Consequently, the emergence of definitive evidence was not sufficient to curtail HCQ prescriptions. While countermeasures were more effective in comparison to weak policies, restrictive policies (bans and partial bans) were more effective than informative policies (advisories and weak policies). Further, the effect of both informative and restrictive countermeasures were moderated by Trump support, and did not eliminate HCQ prescribing behavior altogether. This moderating effect sustained even after Covid vaccines were widely available. We observe similar medium term effects for Ivermectin. Even after the studies that provoked initial interest in IVM as a treatment option were discredited, IVM continued to be prescribed at high levels. In particular, IVM averages

an astounding 1617.64 % increase in prescriptions after Covid-19 vaccines become widely available.

Robustness Checks

Our robustness checks broadly fall into two types : data/model related and alternative explanations for our observed effects. We discuss these next.

Data/ Model Related Robustness Checks

Single Platform Data Our data is sourced from a single platform, GoodRx. We view our analysis as an index of claim patterns in the market. As a data check, we sourced HCQ and IVM claims at the national level from another data supplier, who wishes to be anonymous. The anonymous data supplier is a hub for an extensive pharmacy network, routing real-time Rx claims transactions between pharmacies and PBMs. This connectivity offers broad coverage of pharmacies, prescribing providers, and pharmacy benefit managers (PBMs) sourced as a part of the business platform. Coverage includes specialty pharmacy claims, general distribution prescription drugs, and durable medical equipment claims filled via pharmacy. The data supply is 1st party and deliverable on a t+1 basis from the claims submission date. The Pearson correlation between GoodRx data and the data supplier data for HCQ and IVM claims are 0.88 and 0.9 respectively.

Placebo Test As a falsification test, we assume that the treatment occurred at the beginning of 2020. We conduct a synthetic control analysis, where we assume that the misinformation started 6 months prior to Raoult's video, that is in the week of September 2, 2019. As can be seen from the national-level model in Figure 6, the model predicts no effect right up to February 25, 2020 when Raoult posted his video. We observe no incremental HCQ claims prior to February 25, 2020. This suggests that our model specification is

appropriate and indicates that there was no stockpiling in anticipation of shortages before March 19, 2020. We conduct a similar analysis for IVM (see Figure 7) with similar results.

Figure 6: Placebo Test (HCQ)

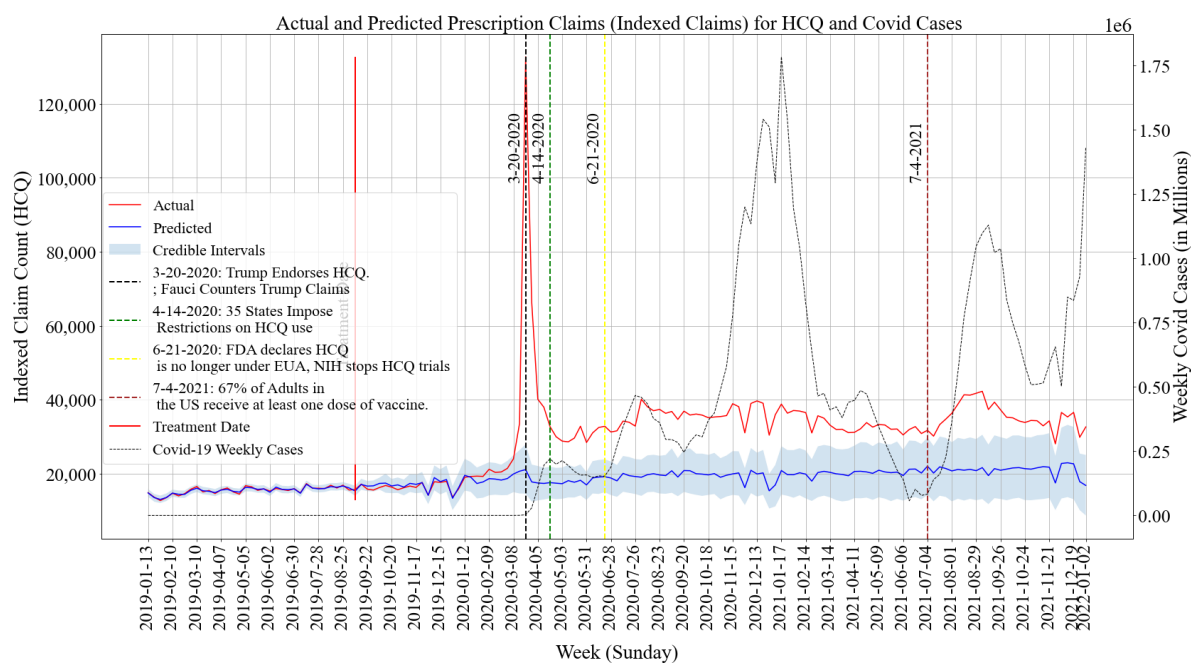
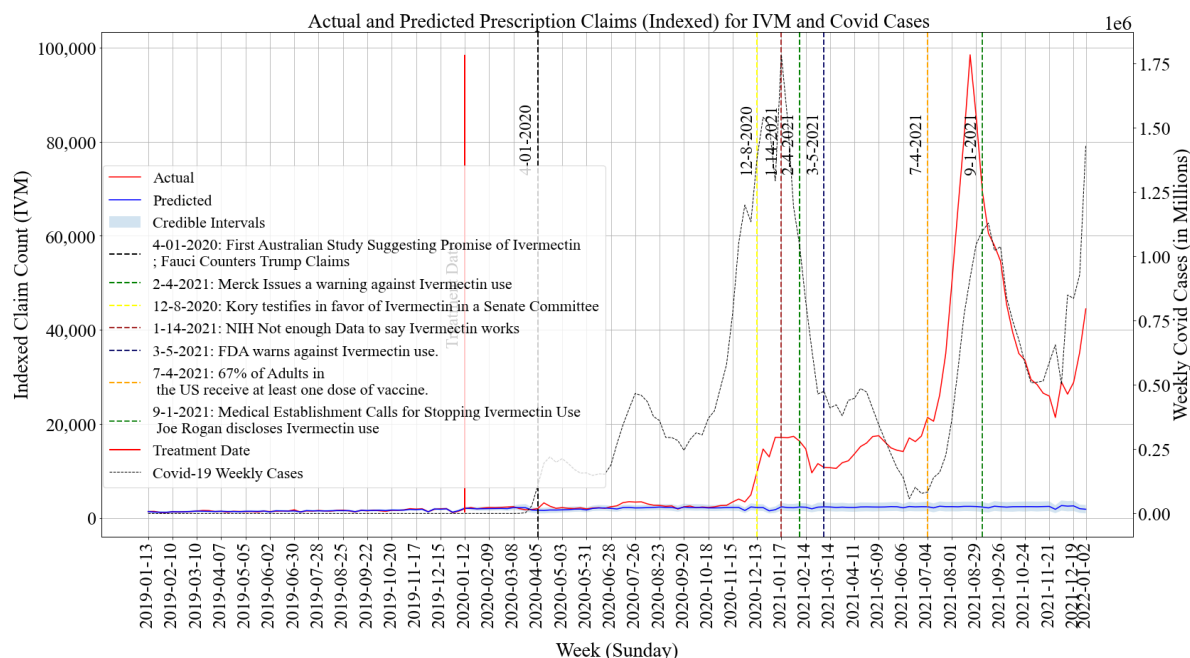


Figure 7: Placebo Test (IVM)



Covid Cases Inclusion of covid death rates in place of case rates does not substantially alter our results. An alternative source of covid data (Reinhart et al. 2021) also does not significantly affect our results.

Choice of Controls We use top 100 drugs by volume and aggregate GPI2 categories as controls. Results substantively remain the same if we use a) top 200 drugs by volume or b) use a random sampling of 200 drugs. Further, HCQ is considered as a maintenance drug. Restricting controls to only include maintenance drugs also does not substantially alter our findings.

In another specification, we estimated models with other drugs that were used to treat Covid-19 and available at pharmacies along with aggregate GPI2 categories as controls. We identified drugs used for Covid-19 treatment from the NIH's treatment advisories between April 21, 2020 and December 30, 2021 (inclusive) for Covid-19.²⁰ Our

²⁰ <https://www.covid19treatmentguidelines.nih.gov/about-the-guidelines/guidelines-archive/>

treatment effect estimates are larger, and less conservative (see Table 10 and contrast with Table 5). The regression results are also substantively the same (Table 11).

Table 10: Percentage Change in incremental HCQ claims over time Using Other Covide Drugs, and GPI2 categories as controls.

	Percentage ATT Increase
Trump Announcement (Week of 3/22/2020)	513.59%
Immediate (3/22/2020 - 4/14/2020)	147.21%
Intermediate (4/14/2020 -6/21/2020)	56.72%
After FDA Revocation till end of 2020	74.87%
2021	63.56%
Overall After FDA Revocation till end of 2021	67.57%

Table 11: Moderating Effect of Susceptibility (Trump Support)

<i>Dependent Variable:</i>				
	Indexed Incremental HCQ Claims Per Capita			
	Immediate 3/22/2020-4/14/2020	Intermediate 4/14/2020-6/21/2020	After FDA Revocation 6/21/2020 - 12/31/ 2020	Year 2021
Constant	0.502 (1.208)	-0.224 (0.375)	-0.150 (0.313)	-0.321 (0.518)
Cases Per Capita	-3.354 (1.810)	0.008*** (0.002)	0.001 (0.001)	0.002*** (0.001)
Pro Trump	0.801 (1.309)	2.546*** (0.226)	3.567*** (0.202)	3.022*** (0.163)
Observations	150	600	1,300	2,500
R ²	0.786	0.319	0.354	0.297
Adjusted R ²	0.780	0.303	0.341	0.282
Residual Std. Error	7.459 (df = 145)	1.999 (df = 586)	2.527 (df = 1272)	2.186 (df = 2448)
F Statistic	133.334*** (df = 4; 145)	21.074*** (df = 13; 586)	25.848*** (df = 27; 1272)	20.275*** (df = 51; 2448)
<i>Note:</i>	*p<0.05; ** p<0.01; *** p<0.001			
	Weighted Least Squares Estimation, Week Fixed Effects			

Another alternative specification for the state level countermeasures analysis is to simply use states with no countermeasures (Weak Policy) as controls. Note that this specification does not account for differences in time-varying and state specific growth of the GoodRx platform, whereas our approach addresses this concern.

Self Selection into HCQ Countermeasures by States It is possible that states with higher susceptibility to misinformation select weaker countermeasures. So countermeasures serve merely as a proxy for the level of misinformation in a given state. There are a few arguments against this possibility. First, the countermeasures were introduced within a very short time after HCQ claims gained substantial momentum from celebrity attention in the third week of March; within less than 10 days of Trump's announcement in most of the 35 states, and in many cases within a day or two of Trump's announcement, primarily by state level regulatory bodies with the exception of two states where the governor introduced the countermeasure. Second, the initial response to celebrity support for HCQ, before any countermeasures were introduced, could serve as a proxy for support for HCQ. In additional analysis, we investigate whether a) the short term spike around Trump's announcement, b) covid cases per capita, and c) vote share favoring Trump in the 2016 elections explains the type of policy selected, using a multinomial logistic regression analysis. The only significant coefficient was vote share favoring Trump reduced the likelihood of selecting bans. Coefficients for the spike measures and covid cases are insignificant and available on request. Nevertheless, if we view these countermeasures as proxies for misinformation, the analysis remains useful as countermeasures adopted by states serve as a flag for policymakers on states where misinformation may be more damaging, and state/federal level countermeasures less effective.

Another concern regarding our countermeasures analysis is that states have time varying differences in misinformation levels. So our results are not about differences in countermeasures, but differences in misinformation levels or a combination of countermeasures and misinformation. While we cannot definitively rule out this possibility,

we note that there are at least 4 states in each countermeasure category, and our estimates are averaged over states adopting a particular policy. We note that our previous arguments suggest that it is unlikely (but not impossible) that misinformation levels and choice of countermeasures are themselves correlated. Consequently, time varying misinformation levels are less likely to be driving our results. Our analysis and results also remain relevant in the event that the results are driven primarily due to misinformation levels (and countermeasures have no effect altogether), as it offers a point of reference to policy makers on potential areas to focus on during future misinformation outbreaks.

Alternative Explanations

Misinformation Regarding Chloroquine Phosphate Chloroquine Phosphate (CQ) was also mentioned by President Trump on March 19, 2020. There was only a short lived increase in prescription claims (see Appendix A4). It is unclear whether this is the result of a lack of sustained misinformation regarding CQ, or simply because HCQ seemed more plausible, and people focused on HCQ. We measure interest using google trends. While not definitive, it does appear that there was only a short lived interest in CQ.

Differential Media Coverage of Countermeasures across states It is quite possible that the media covered countermeasures differently across states. This could mitigate the effect of countermeasures. However, our study focuses on prescription claims - where physicians have to sign off on the prescription. Ideally, experts like physicians should be able to directly access updated information outside of media sources.

Role of Shortages of HCQ One alternative account for our findings is that the increases in claims are from the existing patients who use HCQ for FDA-approved conditions in response to HCQ shortages - and not from patients seeking HCQ for Covid-19

treatment. This is unlikely for the following reasons. First, HCQ was added to the FDA's shortage list on March 31, 2020 and removed from the drug shortage list by June 26, 2020 (Iowa Board of Medicine et al. 2020). If our results are due to adjustment for the shortages, we would see a sharp increase in HCQ claims at this point in time as supply eased, which we don't. Second, there is no reported increase in Lupus or malaria cases based on our review of Factiva and news articles. Consequently, we interpret any incremental HCQ claims as attributable to the net effect of misinformation and countermeasures.

Substitutes for HCQ and IVM There are no over-the-counter (OTC) substitutes for HCQ and HCQ purchase requires a prescription. Therefore, differential access to over-the-counter substitutes does not explain our results. The same is true for IVM. Some consumers used animal formulations of IVM, but this is not pertinent to our study as such consumption does not include physician decisions.

Discussion

The findings in this paper indicate that the effects of misinformation persist in the medium term, despite the implementation of informative and restrictive countermeasures. While countermeasures do provide benefits, the residual impact of misinformation remains substantial. Furthermore, susceptibility to misinformation plays a significant role in its impact. States with higher levels of support for former President Trump exhibited larger treatment effects per capita compared to states where Trump lost, on average. Moreover, countermeasures were found to be less effective in these Trump-supporting states. We also find that the emergence of definitive evidence has at best a modest effect in reducing the misinformation effect. Finally, we also find that restrictive countermeasures are more effective than informative countermeasures.

The substantive implications of these findings are as follows. First, while countermeasures do provide benefits, the residual impact of misinformation remains substantial. Importantly, misinformation can persist well after countermeasures are in place. This adds to the existing literature on the persistence of misinformation (Ecker et al. 2022; Ecker, Lewandowsky, and Tang 2010; Lewandowsky et al. 2012), and shows that such persistence impacts decisions by experts such as physicians. Second, our findings suggest that debunking of misinformation by regulators may not always be effective. It is possible that they are perceived as out-group by some recipients, such as Trump supporters, and hence less trustworthy. This finding complements prior work by Fong, Guo, and Rao (2022) that debunking of misinformation by regulators can be effective as regulators are viewed as trustworthy. Our results suggest that the effectiveness of regulators in debunking misinformation may be context dependent. Policymakers and future researchers may wish to examine whether engaging with communities and leveraging in-group members could more effectively counter misinformation in the healthcare market. Interestingly, it also surfaces the possibility that certain influential in-group members can mischievously exploit public health emergencies. Third, these findings alert policymakers and firms to an important issue - physicians' off-label use of medication. It is possible that, in the absence of recommended alternatives, well-meaning physicians exercise OLDU privileges to prescribe HCQ (Wittich, Burkle, and Lanier 2012). This highlights the need for more effective communication to physicians on the attendant risk of such prescriptions. Alternatively, if patients demanded these medicines from physicians, then it highlights the need for more effective patient education, and tools to enable physicians to respond effectively. In either case (or likely a mix of the two), our results suggest that the scientific

arguments were not completely successful in countering arguments supported by poor/discredited evidence. This poses a communications challenge for both policymakers and firms seeking to influence physicians and patients. Fourth, while strong measures such as bans may communicate the importance of curbing misinformed off-label use, even bans are moderated by susceptibility. It is possible that bans on paper were not enforced as strictly in Trump supporting states than in other states. Further, it remains unclear if such restrictions are feasible in the future with some states pushing legislation to protect doctors who prescribe Ivermectin²¹. Further, the finding that misinformation regarding Ivermectin (IVM) had a significant impact on prescription claims, even after the evidence and experience of HCQ, indicates the strength of persistence among physicians. This highlights that curtailing misinformation for one drug does not guarantee success in combating misinformation related to other drugs amongst physicians. These combined findings re-emphasize the importance of engaging in-group experts when deciding how best to communicate scientific information.

Our findings indicate a need for policy makers and scholars to investigate how to develop credible in-group communication strategies to avoid a clash between physician - patient privileges and science based practice of healthcare (Cacciatore 2021). These findings are all the more relevant as a recent survey by the Federation of State Medical Boards showed that 2 out of 3 medical boards reported increased complaints about misinformation spread by licensees in 2021 (Chaudhry 2021).

This study has some limitations as well that offer new avenues of research. First, our data is from a single platform, GoodRx. There could be systematic differences in overall

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<https://www.usatoday.com/story/news/health/2022/03/10/covid-ivermectin-bill-dozens-states-push-laws-protect-doctors/9356967002/?gnt-cfr=1>

physician-patient behavior and physician-patient behavior on this platform. Our causal framework controls for platform specific effects, but we cannot rule out the possibility that a selected group of patients migrate to GoodRx. However, we note that the incremental prescription claims still capture prescribing behaviors resulting from misinformation. Nevertheless, examination across other data sources and experiments regarding expert decisions is a promising area of study. Second, our analysis cannot distinguish patient pressure from physician choice in prescribing HCQ and IVM. It is likely that both play a role. Careful studies that disentangle the effects of each can help finetune misinformation countermeasures for patient and physician communities. Third, we cannot rule out the possibility that our measure of susceptibility reflects political affiliation or underlying demographic characteristics. This does not detract from the present study, however, it points to a possible fruitful line of inquiry that disentangles different sources of susceptibility, including susceptibility to “in group” leaders. Fourth, this study does not examine why some types of misinformation persist. For example, Chloroquine Phosphate (CQ) was also mentioned by President Trump on March 19, 2020. There was only a short-lived increase in prescription claims (see Appendix A4). This finding is consistent with Google trends data (see Appendix A4) , that indicates that for some reason CQ did not catch on. Investigating the virality of misinformation presents another interesting line of work. Fifth, this paper does not investigate the persuasiveness vs informativeness of misinformation content itself, a promising avenue of future research. Despite these limitations, this study underscores the enduring influence of misinformation on the public and experts, and the role of susceptibility in moderating countermeasures.

Financial and Competing Interests

Two authors are/were employees of the data provider. The other authors have no financial or competing interests to declare.

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