Kara Chasteen

Dec 22, 2020

Statement to the Burnet County Commissioner's Court

Good Morning and thank you for the opportunity to speak. We have all been through a rough year and I know each of you are probably exhausted. I know and respect all of you and consider you friends. You are the leaders of our county. You are the leaders we look to for guidance when there is an emergency. You are the ones we trust. When this virus first stated to take its tole on our country, I think we were all a little confused. No one knew which path to follow. No one wants to make a mistake and lead people in the wrong direction, so many just did nothing. Then it happened...the dirty politicians on both sides saw and opportunity to make some money. Good common-sense medicine that might have saved many lives were thrown out the window, we were put on lock down, we were told to mask up and socially distance, we locked our elderly up in the care facilities and let them die alone, we skipped family events, we canceled all our fairs and reunions, but still the virus raged on. There were some doctors that started treating people with drugs that had been on the market for 50 to 80 years. These were drugs they had used for years. Off label use of many drugs has been accepted for years. It is not new or uncommon, but all of the sudden that was not allowed. We don't know what the long-term side effects will be, they said! Really, a drug that has been on the market for 80 years? We know what the side effects are! We are since found out that the long-term side effects of having Covid-19 can be devastating. Given the option of being treated with a well-known drug or just taking my chances with Covid-19, I'm going to take the medicine. The problem is...most people were not even given that option. The rug was jerked out from under doctors and they were threatened and intimidate and told not to prescribe these drugs! Tell you patients to go home and isolate with fluids and Tylenol. Come back when you can't breathe and you are so sick that you require hospitalization, most likely ICU and a ventilator! That is the most insane thing I have heard in my life. I have raised animals my whole life and if there is one thing I know; it is that you never let an illness get ahead of you. You treat immediately. In a healthy person the immune system is the first line of defense. When the immune system fails to do its job, you step in and help asap, not when the person is one their death bed.

When this first started, I spoke. I said this is insane! Treat these people! I was met with much opposition by people that had been brain washed and mislead by the media and government. They had managed to scare people into submission. Instead of going to work on the problem and figuring out, like Americans do, we were hiding in our homes. This is not the American way.

There are doctors in this county that have successfully treated many and are willing to share what they know with you. The problem is they have not been asked. They are been scolded for speaking out. One local doctor has over 250 people on preventative treatment with only 2 getting the illness, both of whom recovered without serious illness. This has gone on long enough! People are dying and becoming disabled because they are being denied the treatments that could easily save most of them. We cannot sit idly by and allow this to continue. I am here today to ask you to override the health authority and make your own decisions. Invite these doctors in and speak to them. I know that many of you have

personal experience with this disease and you know what I am telling you is the truth. I realize that you cannot tell doctors how to treat their patients, but you can seek advise from a panel of doctors and not just one! You can be heroes in this time. Take charge and be the leaders we depend on you to be.

Thank you for your time.

12-14-15

RESOLUTION:

Be it resolved that the Burnet County Executive Committee strongly recommends the following to the Burnet County Commissioners:

The Burnet County Commissioners make known the list of therapeutics attached which have been proven to have positive outcomes in COVID-19 patients, when used in a timely manner.

The Burnet County Commissioners highly recommend that these therapeutics shall be offered to treat COVID-19 cases in Burnet County.

The Burnet County Commissioners notify by registered letter every medical doctor and medical facility in the county of the above decision.

PREMISE:

Treatments (therapeutics) for COVID-19 have been suppressed by federal government doctors, the CDC, the NIH and the Burnet County Health Authority. Indeed the Main Stream Media and Social Media companies are censoring and suppressing known life-saving benefits of these medicines.

FACTS:

Uganda - 11-13-2020	Population 42 million	15,217 cases	143 deaths
Texas - 11-18-2020	Population 29 million	1.1 million cases	20,100 deaths.

The famous LANCET medical publication in Great Britain had to **retract** an article which stated Hydroxychloroquine was dangerous. (HCQ has been used for 82 years!)

In Texas, doctors prescribing HCQ and related therapeutics on patients were/are being harassed by the Texas Pharmaceutical and Medical Boards.

Dr. Vladimir Zelenko a New York doctor has successfully treated 699 patients (info from March 30, 2020) with Hydroxychloroquine. No deaths. No hospitalizations.

SUMMARY:

COVID 19 and the seasonal FLU are RNA viruses. Thousands of front line doctors know that the four therapeutic drugs listed **successfully treat** CV-19. It may even work as a treatment for the FLU.

CV-19 THERAPEUTIC DRUGS

--Budesonide Ampul (generic) – **PRIMACORT** (brand name) Ampul – Inhalant Nebulizing Machine (found in every pharmacy in America)

--**HYDROXYCHOLORQUINE** – ZINC SULFATE – ZPAK (treatment cost $ 20)

--**IVERMECTIN** – ZINC SULFATE – DOXYCYCLINE (treatment cost twelve cents per pill)

--**REGENERON** – Anti-body cocktail (IV required) Hospitalization for 3-4 days.

CONCLUSION:

Burnet County should lead Texas out of this insanity and require doctors to provide their patients sufficient information, including information regarding HCQ and related medications, so that they have informed consent regarding the full scope of their treatment options.

Burnet County has approximately 48,500 citizens and has had 20 deaths from CV-19.

Burnet County resident has a **.0004%** chance of dying from this disease.

Despite this low incidence, a patient's right to choose their treatment is meaningless without full informed consent.

Dear Senators Kolkhorst and Hall,

I treated my first patient with active COVID-19 in March 16, 2020, based on international data that I had read about a week before reporting that hydroxychloroquine and zinc showed promise. At that time, I did not hesitate to use these since there was nothing else that I was aware of that might help. (I might also add that this treatment was not controversial at that time.)

That patient and one later that week, (age 53 and the other age 64 with co-morbidities), did well. It was the beginning of the pandemic in our community and I just wanted to help my patients.

Subsequently, my practice has treated 203 patients, and we have 225 on preventative regimens. We currently are following 31 active cases. Although I have seen deaths from patients who have called requesting treatment from us when it was too late to treat and the patient needed to go the hospital, NOT ONE SINGLE PATIENT has died among those that we have treated. Four of those we have treated have had to be hospitalized but ALL were LATE presenters. They all had a short stay for oxygen support and were discharged. No one who got treated in our group required ICU care or ventilatory support.

With these outcomes, it is criminal that the message from our medical leadership is NOT to treat with the tools we have at this time.

I have primarily followed the same type of protocols that have been published by Drs. McCullough and Zelenko for treatment and prophylaxis. I have even shared these protocols with my local medical society (about 89 doctors) and one ER doctor responded with "RESPONSE TO AMY OFFUTT" which essentially told the whole group that these regimens being shared was inappropriate. A local pulmonologist supported the ER doctor's discouragement. Even the local TDH doctor sent an email back in the group to all of the doctors stating that I should not spread this information as I should "first do no harm." I share this information because there are so many authorities against treating and I do not understand that approach. Why wouldn't I treat my patients?

Through prayer and the love of my family as well as the amazing teamwork of my practice staff, we continue to focus on our patients and leave the opinions of anti-treatment vocalists outside of the office.

My prayer at this time is for our leadership to awaken to the reason, logic, and compassion that is at their fingertips and grab it, promote it, and save the lives of millions who are left to remain in fear at the possibility of their deaths from this nasty disease.

Please let me know if there is anything I can do to support the implementation of mass treatment and prevention regimens for our state and country.

Stay well,

Amy Offutt, M.D.
Sent from my iPhone

It was inevitable that the Coronavirus pandemic would be politicized, and it is a tragedy that it was. From the start, I knew it was impossible to have a perfect response. We were facing a new virus that caused an entirely new disease. No one wanted to under react, and as a result, I feared the tendency would be to overreact and create unrealistic expectations regarding our ability to stop a highly contagious pathogen.

The challenges facing us were daunting. Our national strategic stockpile had been reduced during the H1N1 pandemic and had not been replenished. It took time to develop a reliable test, and even more time to scale up production to meet the demand. The fact that a large percentage of people that become infected exhibit no symptoms made the Coronavirus even more difficult to detect and contain.

I have tried not to criticize elected officials that had the responsibility to make very tough decisions with limited and highly imperfect information. Others have not been so reluctant. Perhaps my background in manufacturing taught me to be more understanding of those forced to deal with difficult situations.

The members of this committee have had front row seats to government's response - at both the federal and state level. We participated in dozens of conference calls and multiple hearings with agency officials that worked 24/7 to respond to an unprecedented event. It is always easy to criticize, but I for one, have been sympathetic with the challenges they faced and highly appreciative of their efforts.

As we are all aware, the Coronavirus is not going away. Even though it appears an effective vaccine may be developed and available in record time, people will continue to become infected and sick for months to come. We still need to develop effective therapies, particularly in the very early stages of the disease.

It is on this point that I have been, and will continue to be, highly critical of our collective dereliction in not robustly exploring therapies designed to stop viral replication and halt the progression of the disease. We are all aware that Tamiflu is only effective when prescribed early enough to stop the flu virus from replicating and before the patient becomes too sick. Why haven't federal agencies and the medical community applied the same logic and approach to the Coronavirus?

This question has baffled me since March, and there probably is not a single explanation. We do know the Coronavirus was politicized and used as an effective weapon in the presidential election. We also know some of the suggested therapies included off the shelf supplements and "off label" uses of widely prescribed drugs. The cost of these therapies is well under $50 versus a brand new drug, Remdesivir, that costs over $3,000 and can only be used in-hospital, and therefore does not prevent hospitalization in the first place. Could big PHARMA have played a role in discouraging less costly alternatives? The answer seems obvious, even though their methods will no doubt remain obscured.

This hearing is not about promoting any one particular therapy over others. But the absence of any serious NIH study or consideration of Hydroxychloroquine - either by itself or in combination with other drugs and supplements - is worth discussing. This is a drug that has been safely and effectively used to prevent Malaria and treat Lupus and Rheumatoid Arthritis for decades.

Yet doctors who have had the courage to follow the Hippocratic oath and use their "off label" prescription rights to treat their patients using hydroxychloroquine have been scorned and state medical boards have threatened to withdraw their licenses. The same has happened to pharmacists filling prescriptions for the drug in some states. Will those using Ivermectin and other off the shelf drugs being used "off label" to treat COVID patients suffer the same fate?

Since the onset of this pandemic, I have publicly advocated for allowing doctors to be doctors - to practice medicine, explore different therapies, and share their knowledge within the medical community, and with the public. I believe international, federal and state medical agencies and institutions have let us down. I fear too many have been closed minded bureaucrats, potentially driven by conflicting interests and agendas. Tragically, media and social media have failed to ask the right questions and censored what they do not understand.

My public advocacy has connected me to doctors who care and are trying to compassionately help their patients in spite of the bureaucratic roadblocks they have encountered. Over the last month, I have been included in an email group comprising over 250 practicing physicians from all over the world sharing their knowledge and experience. Three members of that group are here today.

To me, it is obvious that we should robustly explore every possible treatment to combat this pandemic at every stage of the disease. Why has there been such resistance to low cost, off the shelf therapies that might stop the progression of COVID-19 and help keep people out of hospitals and intensive care?

I hope today's hearing can answer that question and provide direction on how to correct this glaring blunder that has cost far too many lives.

Dr. McCullough Senate Testimony

Thank you Chairman Johnson, Ranking Member Peters, and the members of the Committee for the opportunity to speak to you today about the need for more government attention and support for the early treatment of COVID-19.

As we sit here today the COVID-19 outbreak has the greatest number of currently infected persons, highest hospital census, and all epidemic curves are pointing straight up. We face public panic, hospital over-runs, and significantly higher mortality in the months to come. The highly contagious infection starts out like a cold and takes about two weeks to either resolve or worsen into serious pneumonia. Thus, urgent pandemic response can be viewed as having four pillars as shown on the first chart: the four pillars are: Contagion Control; Early Home Treatment; Late Stage Treatment; and Vaccination. To date, we have tragically ignored the second pillar, Early Treatment, so I am glad today's hearing is focused on it.

Doctors and researchers around the world have learned much about the virus from more than 75,000 scientific reports and 54 million cases where the disease process in three phases a shown on the second chart: first phase is early viral replication, followed by the second phase cytokine storm and the third phase blood clotting . They have innovated with the use of established medications used in various combinations to lessen the intensity and duration of symptoms, cut hospitalizations, and avoid death. I led a team of US and Italian physicians to synthesize what had been learned from this progress and published the first sequenced multidrug protocol for early COVID-19 at home in the August 7 issue of the *American Journal of Medicine*.

What inspired me and my physician colleagues was the need for an immediate compassionate response. Patients wait in fear at home after testing positive, logically thinking they would face a terrifying hospitalization, isolation, and at worse--death. Innovative and courageous physicians knew they had to rapidly use clinical judgment and learn from all sources of evidence to come up with a treatment plan for at-home patients. Protocols focussed on newly diagnosed COVID-19 patients at high risk for hospitalization and death and used over the counter supplements and available generic medications. Telemedicine became the backbone of monitoring, helping track symptoms and adjust treatment.

Our paper drew considerable attention and became a beacon for more innovation and rapid research that have led to subsequent refinement and application to practice.

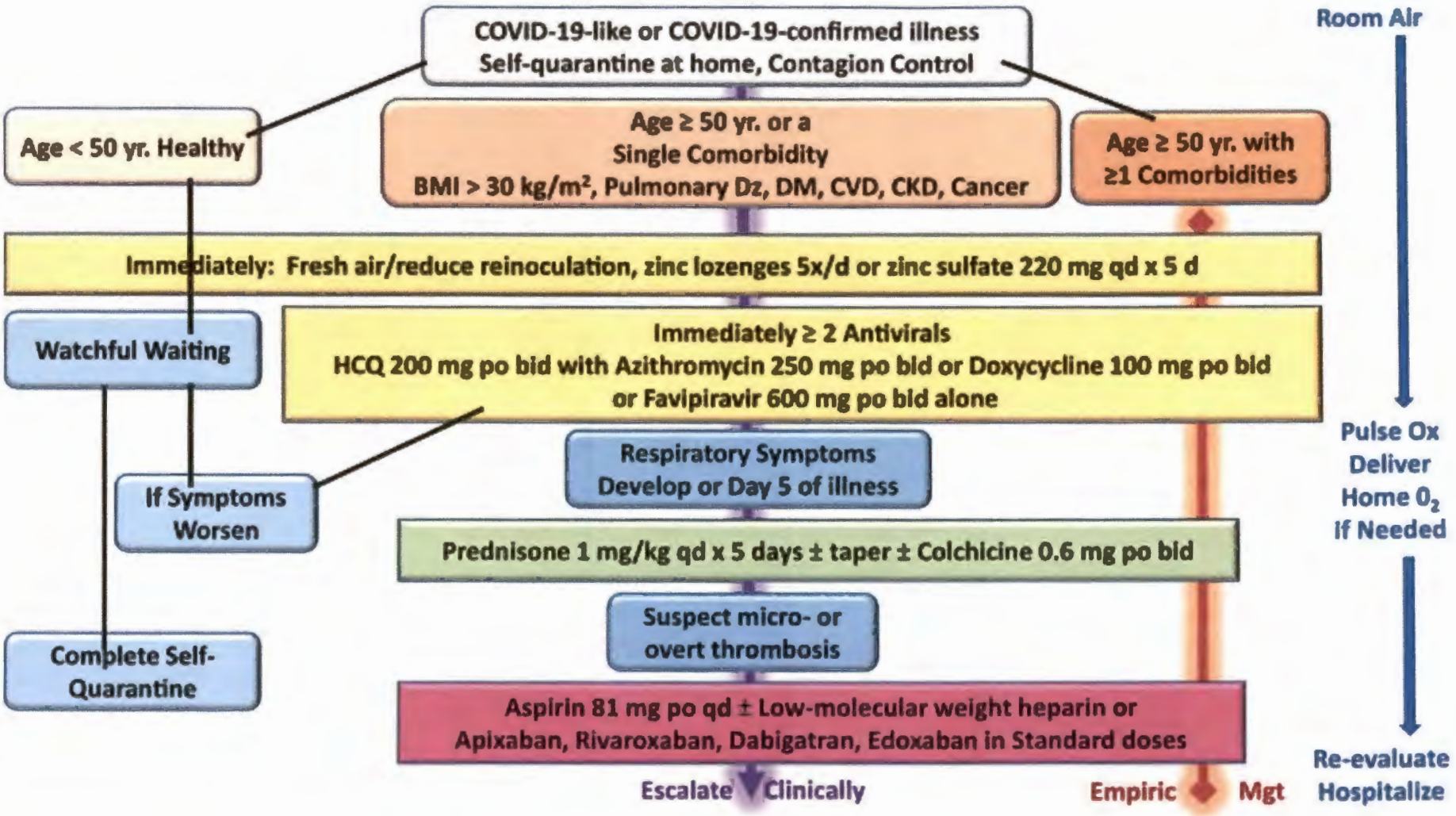
Unfortunately, the government has not always been very supportive of practicing physicians. Regulatory barriers have blocked access to generic drugs in at-home treatment protocols, and as a result, doctors have been forced to create endless workarounds to get medicine quickly before the virus spirals out of control in their vulnerable patients. Government agencies and medical organizations have admonished doctors for responding to COVID-19 patients outside of the hospital and have actively discouraged attempts to treat patients. Sadly, this has resulted in few patients getting early treatment and no chance of avoiding a hospitalization.

Astonishingly, The National Institutes of Health, in its October 9, 2020, COVID-19 Treatment Guidelines directs doctors to let even high-risk COVID-19 patients, sicken at home for two weeks or

more, and when finally gasping and choking for air, place them in hospital isolation. NIH says that a COVID-19 patient may receive their first medical treatment only if oxygen is given. While the NIH, agency representatives, and academicians stand behind this document as "best science" many practicing physicians, patients, and community leaders view this as medically irresponsible and humanely unconscionable.

I have managed COVID-19 over the spectrum of illness, and I can tell you that I would never allow a high-risk COVID-19 patient to go without treatment, become progressively panicked and unable to breathe, and force them to the hospital, possibly never to see their loved ones again. By the time a patient is that sick, the chances of lung, heart, and organ damage is far too high. Hospital administered medications cannot save all the patients or stop the torrent of hospital complications. Administration of intravenous drugs at earlier stages of COVID exposes others to the virus and is not scalable. The use of oral sequenced multi-drug treatment at home as a national strategy has a reasonable chance of success with acceptable safety. Competent physicians and providers who are called by their patients should be supported by all stakeholders in their efforts to provide compassionate care, reduce the spread of infection, and avoid hospitalization and death.

In summary, I urge the Committee to ask all responsible government agencies to prioritize an "early treatment initiative." I believe this is the only viable strategy to avoid catastrophic loss of life before natural immunity and vaccination can bring this crisis to a close.


COVID-19-like or COVID-19-confirmed illness
Self-quarantine at home, Contagion Control
Room Air
Age < 50 yr. Healthy
Age ≥ 50 yr. or a
Single Comorbidity
BMI > 30 kg/m², Pulmonary Dz, DM, CVD, CKD, Cancer
Age ≥ 50 yr. with
≥1 Comorbidities
Immediately: Fresh air/reduce reinoculation, zinc lozenges 5x/d or zinc sulfate 220 mg qd x 5 d
Watchful Waiting
Immediately ≥ 2 Antivirals
HCQ 200 mg po bid with Azithromycin 250 mg po bid or Doxycycline 100 mg po bid
or Favipiravir 600 mg po bid alone
Pulse Ox
Deliver
Home 0_2
If Needed
Respiratory Symptoms
Develop or Day 5 of illness
If Symptoms
Worsen
Prednisone 1 mg/kg qd x 5 days ± taper ± Colchicine 0.6 mg po bid
Suspect micro- or
overt thrombosis
Complete Self-
Quarantine
Aspirin 81 mg po qd ± Low-molecular weight heparin or
Apixaban, Rivaroxaban, Dabigatran, Edoxaban in Standard doses
Re-evaluate
Hospitalize
Escalate Clinically
Empiric Mgt

Statement of George Fareed, M.D. for Senate Hearing, November 19, 2020

I have a background in virology from a research standpoint from work at the NIAID (NIH) and as a Professor performing research at Harvard Medical School (after I graduated from Harvard Medical School in 1970 I became a professor there) and at UCLA School of Medicine. I have had ***30 Years of Clinical experience****, treating HIV and other infectious diseases as well as practicing primary care medicine.*

· I have experience treating **COVID patients both in the flu stage as outpatients**, but also as hospitalized inpatients, even in the ICU

· *Like everything else in medicine, the goal is to treat early-- COVID patients are* ***difficult to treat when they get very sick***

· The Imperial Valley where I work became the COVID epicenter for California in June and July.

Since early March both in my Brawley clinic and Dr. Brian Tyson's The All Valley Urgent Care Clinic in El Centro (where I also work), over 25,000 fearful people were screened, over two thousand four hundred were COVID-19 positive and we treated successfully many hundreds of the high risk and symptomatic ones.

· *We have always used a* ***triple HCQ cocktail****: HCQ (3200 mg over 5 days), azithromycin or doxycycline and* ***especially zinc****, which is often left out in the studies. The cocktail is best given early* ***within the first 5 to 7 days*** *while the patient is in the flu stage (I have had success treating even as late as 14 days when patients have been sent home untreated from the ER). The timing of the drug is when the virus is in the* ***period of maximal replication in the upper respiratory tract*** *My goal is to prevent hospitalization which was achieved by reevaluating high risk patients every 2-3 days. I blend in corticosteroids and prolong the HCQ treatment for 5 to 30 more days if symptoms warrant but they generally do not. I use it especially in* ***high risk individuals*** *(over 60 or with co-morbidities and anyone with moderate to severe flu symptoms)---the healthy do not need the treatment.*

I used this regimen to successfully treat 31 elderly nursing home residents in an outbreak in June and 29 recovered fully.

· *The drug works mechanistically through multiple actions: the* ***ionophore HCQ (the "gun") and zinc ("the bullet"), HCQ blocks the sigma 1 receptor and has several other direct antiviral effects****---the antibiotic also has anti-viral effect and potentiates the action of the HCQ and zinc. As additional anti-covid agents become available they can be added to this regimen to enhance its efficacy. I am routinely now combining Ivermectin in a* ***quadruple HCQ/IVM cocktail*** *with excellent results since Ivermectin is safe and has a different anti-covid action. Monoclonal antibodies from Regeneron and Lilly will be suitable also when readily available.*

· *The results are consistently good, often dramatic, with improvement within 48 hours*

· *I have seen very few hospitalizations, and only a few deaths in patients that were sick to begin with and received the medication late while hospitalized.*

· ***I have not seen a single negative cardiac event and few other side effects, despite what we hear in the media***

My experience is in-line *with all the studies regarding* ***early use of the HCQ cocktail***

LET ME BE CLEAR: THIS IS ONLY ABOUT THE SCIENCE----THE SCIENCE OF VIRAL REPLICATION, THE SCIENCE OF THE STAGES OF COVID, AND THE SCIENCE WHY EARLY TREATMENT WORKS.

· *AND THE SCIENCE TELLS US THAT EARLY treatment would be an effective strategy to use on a national level, which motivated me and a few of my colleagues to write a letter to the President, a letter to my congressman, a letter to California health department, an Open Letter to Dr. Fauci, and a National Plan for COVID-19.*

This is not about an opinion of an "expert"- this is about science and data.

· *As we describe in the National Plan, this approach would be* ***the solution to the pandemic****---protect the vulnerable, and if high risk individuals get sick, there is a solution for them with early treatment with the antiviral cocktail.*

If early treatment was available, people would be much more confident going back to work and sending their kids back to school.

Statement of Harvey A. Risch, MD, PhD
Professor of Epidemiology, Yale School of Public Health

Senators and colleagues: thank you for convening this hearing. We all understand the endemic disease that we are facing, that we have to face it head-on and not hide from it hoping that it will go away. I want to give you my perspective.

In May of this year I observed that results of studies of a drug suggested to treat Covid, hydroxychloroquine, were being misrepresented by what I thought at the time was sloppy reporting. We have heard from Dr. McCullough how Covid disease progresses in phases, from viral replication, to florid pneumonia to multi-organ attack. Viral replication is an outpatient condition, but the pneumonia that fills the lungs with immune-system debris is hospitalizable and potentially life-threatening. We have also heard how each phase, each pathologic aspect of the disease, has to have its own specific treatments that apply to its own biologic mechanisms. Thus, I was frankly astounded that studies of hospital treatments were being represented as applying to outpatients, in violation of what I learned in medical school about how to treat patients.

We are now finally coming to address why over the last six months, our government research institutions have invested billions of dollars in expensive patent medication and vaccine development but almost nothing in early outpatient treatment, the first line of response to managing the pandemic. It is not that we lacked candidate medications to study, we have had a number of promising agents. But I believe that the early-on conflation of hospital with outpatient disease served to imply that treatment of outpatient disease had been studied and found ineffective. This illogical premise motivated me to look at the evidence for outpatient treatment.

I reiterate: we are considering the evidence for early treatment of high-risk outpatients to prevent hospitalization and mortality. That is it. Treatment starting in the first five days or so after the onset of symptoms. Treatment of older patients or patients with chronic conditions such as diabetes, obesity, heart diseases, lung diseases, kidney diseases, immune-system diseases, survivors of cancer etc. These are the people most likely to die from Covid, and they are the people most needing protection. I have sought to obtain reports of every study of every medication pertaining to early treatment of high-risk outpatients. I monitor the literature daily. And what I have found is actually quite remarkable. What I have observed is that while there have been positive reports about a number of drugs, every study of outpatient use of one drug, hydroxychloroquine, with or without accompanying agents, has shown substantial benefit in reducing risks of hospitalization and mortality.

These studies break down into two major types. The first is double-blinded, randomized controlled trials, and the second is non-randomized but still controlled trials. You have heard from various government and scientific personalities that randomized controlled trials provide the strongest form of evidence. Many of these people have also claimed that randomized trials

provide the only trustworthy form of evidence. There is some truth in these assertions, but there is also lots of falsehood. We know for example that the great majority of drugs used to treat heart diseases were established with non-randomized trials. Cholesterol-lowering drugs were in widespread use before randomized trials were ever done. Azithromycin, the most commonly used antibiotic in children, was not established by randomized trials. The idea that only randomized trials provide trustworthy evidence is a simplistic notion that may sound good in theory, but the comparison between randomized and non-randomized trials is something that has actually been extensively studied in the medical literature. I am an epidemiologist because even though I love biological theories, I develop them all the time to study how nature works, but it is from the human empirical data that we learn how indeed nature works.

And we have huge amounts of empirical data to show that randomized trials and their corresponding non-randomized trials give the same answers. Dr. Tom Frieden, previously Director of the CDC, in 2017 wrote an extensive essay in the New England Journal of Medicine showing that non-randomized trials can provide fully compelling evidence, especially when they are done carefully to account for reasons why patients received the drugs, and importantly, when circumstances are such that the cost of waiting for randomized trials involves major sickness and mortality as we have been experiencing this year. But Dr. Frieden's essay, as authoritative as it is, provides only snapshots of the empirical evidence for his observations. The real evidence comes from a meta-analysis of meta-analyses done by the Cochrane Library Consortium, a British international organization formed to organize medical research findings to facilitate evidence-based choices about health interventions. The Cochrane investigators examined what involve tens of thousands of comparisons between randomized trials and their non-randomized counterparts and found that the two types of studies arrived at virtually identical conclusions. This is the real evidence about why good non-randomized trials comprise evidence every bit as important as randomized trials. Large amounts of consistent empirical data are the evidence, not plausible but simplistic assumptions, no matter who says them.

So what did I find about hydroxychloroquine in early use among high-risk outpatients? The first thing is that hydroxychloroquine is exceedingly safe. Common sense tells us this, that a medication safely used for 65 years by hundreds of millions of people in tens of billions of doses worldwide, prescribed without routine screening EKGs, given to adults, children, pregnant women and nursing mothers, must be safe when used in the initial viral-replication phase of an illness that is similar at that point to colds or flu. In fact, a study by researchers at the University of Oxford showed that in 14 large international medical-records databases of older rheumatoid arthritis patients, no significant differences were seen in all-cause mortality for patients who did or did not use hydroxychloroquine. The Oxford investigators also looked at cardiac arrhythmias and found no increase for hydroxychloroquine users. This was in more than 900,000 hydroxychloroquine users. This is examined at length in my paper in the American Journal of Epidemiology in May. Now, the FDA posted a warning on July 1 on its website about hydroxychloroquine used in outpatients, but we can discuss this later; the FDA

has had no systematic evidence in outpatients and erroneously extrapolated from hospital inpatients to outpatients, what I said earlier was invalid.

About studies of hydroxychloroquine early use in high-risk outpatients, every one of them, and there are now seven studies, has shown significant benefit: 636 outpatients in São Paulo, Brazil; 199 clinic patients in Marseille, France; 717 patients across a large HMO network in Brazil; 226 nursing-home patients in Marseille; 1,247 outpatients in New Jersey; 100 long-term care institution patients in Andorra (between France and Spain); and 7,892 patients across Saudi Arabia. All these studies pertain to the early treatment of high-risk outpatients—and all showed about 50 percent or greater reductions in hospitalization or death. The Saudi study was a national study and showed 5-fold reduction in mortality for hydroxychloroquine plus zinc vs zinc alone. Not a single fatal cardiac arrhythmia was reported among these thousands of patients attributable to the hydroxychloroquine. These are the non-randomized but controlled trials that have been published.

Now we also know that all of the outpatient randomized controlled trials this year also together show statistically significant benefit. These six studies comprised generally much younger patients, only a fraction of whom were at high risk, so they individually had too few hospitalizations or deaths to be statistically significant. But they all suggested lower risks with hydroxychloroquine use, and when they were analyzed together in meta-analysis as my colleagues and I found, this lower risk was statistically significant across the studies.

We have spent the last six months with formal government policies and warnings against early outpatient treatment, with large government investments in vaccines and expensive new treatments yet to be proven and almost no support of inexpensive but useful medications, and a quarter of a million Americans have died from this mismanaged approach. Even with newly promising vaccines, we have almost no information about how they will perform in older and high-risk patients, in whom respiratory virus vaccines are known to have weak efficacy; it will be a number of months before they become widely available; and we don't know how long vaccine immunity will last, or even if the vaccines will work for the newly increasing mutant strains of the virus. As I have said on many occasions, the evidence for benefit of hydroxychloroquine used early in high-risk outpatients is extremely strong, and the evidence against harm is also equally strong. This body of evidence dramatically outweighs the risk/benefit evidence for remdesivir, monoclonal antibodies or the difficult to use bamlanivimab that the FDA has approved for emergency use authorizations while denying the emergency use authorization for hydroxychloroquine. This egregious double standard for hydroxychloroquine needs to be overturned immediately and its emergency use authorization application approved. This is how we will get on the road to early outpatient treatment and the major curtailment of mortality. Thank you.

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COVID-19 Fact Sheet

Risks to you and your family

In Burnet County, as of December 21st, 2020, there is a 29% risk that one person in a group of 15 is actively COVID-19-infectious.

- In Llano County, this risk is 40%.

Quarantine and Isolation

Isolation: 10 day period at a minimum, starting on the date of symptom onset.

- Individual must have minimal to no symptoms at the end of isolation
- Must be fever-free (and off of all fever-reducing medications) for at least 24 hours.

Quarantine: 14 day period starting on the date of last exposure to the case, testing recommended 5-9 days after exposure. The CDC still recommends the 14-day quarantine, even with these updated options:

- 7-day quarantine possible if the individual continues to be asymptomatic and is tested within 48 hours of the 7th day of isolation (i.e. on day 5 or day 6).
  - Likelihood of transmission still 5-12%
- 10-day quarantine possible if the individual continues to be asymptomatic but cannot be tested for some reason.
  - Likelihood of transmission still 1-10%

Asymptomatic Infections

20-40% of cases of COVID-19 may be asymptomatic, meaning the individual has no symptoms to indicate that they are sick. Asymptomatic cases may be contagious for longer than those who are symptomatic and are more likely to be younger adults.

Testing

Antigen tests (also known as rapid tests) have much higher false negativity rates (ranging from 10-25%) than PCR (diagnostic) testing but provide quicker results. For active infection, both the FDA and CDC still recommend PCR testing or antigen testing followed by PCR testing.

- PCR tests are more likely to detect early or pre-symptomatic infection due to increased sensitivity.

Review of Medications Proposed for Use in COVID-19 Patients

Outpatient Care and/or Mild Cases

Monoclonal antibodies: Indicated for patients at high risk for developing severe disease, but not yet progressing to the point of hospitalization (given emergency use authorization by the FDA for non-hospitalized patients with comorbidities like obesity and diabetes).

- Bamlanivmab[1]
- Casirivimab and Imdevimab[2]
- Greater decrease in SARS-CoV-2 viral load, lower hospitalization rate

Hydroxychloroquine: Randomized trial of patients with mild cases of COVID-19 showed no real reduction in viral load, hospitalization rates, or time to symptom resolution.[3] WHO recently indicated that it strongly recommends against the use of HCQ.

Ivermectin: Data on benefits like decreased time to symptom resolution, lower mortality, or decreased viral load are largely from low-quality studies.

- Most prominent study on the effect of ivermectin on hospitalized patients suffered from methodological issues, with the group receiving Ivermectin also more likely to receive corticosteroids.[4]
- Usage recommended only in the context of clinical trials.

Acetaminophen: WHO rolled back its recommendations that only acetaminophen be used (instead of ibuprofen) as a fever-reducer and pain-reliever, but most clinical recommendations still have acetaminophen as the first choice antipyretic over NSAIDs.[5]

Vitamin D: Reliable data comes only from studies that looked at the impact of Vitamin D deficiency on COVID-19 outcomes, indicating that those with severe COVID-19 were more likely to be deficient in Vitamin D.[6] Evidence towards the administration of Vitamin D to otherwise healthy individuals with COVID-19 is not convincing. Prophylactic administration for the purposes of preventing COVID-19 is not recommended unless the patient has a documented deficiency.

Vitamin C: Paralleling evidence towards Vitamin D, COVID-19 patients are more likely to be deficient in Vitamin C, and deficiency is more likely to occur during infection due to increased consumption to combat increased oxidative stress.[7] Prophylactic administration for the purposes of preventing COVID-19 is not recommended unless the patient has a documented deficiency.

Zinc: Pre-print research shows similar evidence about the link between zinc and COVID-19 as with Vitamin C and D. Serum zinc levels tend to be lower in patients admitted with more severe COVID-19 and low zinc levels are associated with viral proliferation in cells.[8] Prophylactic administration for the purposes of preventing COVID-19 is not recommended unless the patient has a documented deficiency.

Inpatient Care

Dexamethasone: Significantly reduced 28-day mortality in hospitalized patients on some kind of oxygen or ventilatory support, not recommended for those hospitalized but independently breathing.[9]

- Any kind of corticosteroid is not recommended for non-hospitalized patients with mild-to-moderate cases.[10]

Remdesivir: May reduce mortality in those receiving supplemental oxygen, but data is not convincing and the benefit seems to be marginal. Insufficient evidence to indicate efficacy in any group except in the context of a clinical trial.[10]

Hydroxychloroquine: WHO recently indicated that it strongly recommends against the use of HCQ. No clear reduction in mortality or hospital stay and side effects like diarrhea and nausea/vomiting can be concerning in seriously ill patients.[10]

Lopinavir/Ritonavir: WHO recently indicated that it strongly recommends against the use of these antivirals. No real differential effect for seriously ill patients, no provision of benefits like reduced mortality, reduced time spent on a ventilator, or reduced hospital stay.[10]

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Thank you for allowing me to speak today. My name is Tammy Hullum and my immediate family as well as my sister-in-law, brother-in-law, and 90 and 91 year-old mother-in-law and father-in-law recently came down with covid 19. If not for medicines available, I believe several of my family members would not be on the road to recovery today. We were all diagnosed on December 1. I understand the word was to not gather for Thanksgiving and now we are hearing this for Christmas. Family means a lot to me as well as my elderly in-laws. There is no guarantee of how many days or holidays we will be together so this is not an option. We had read all the information on treatment of Covid and chose this route to prevent hospitalization if anyone came down with Covid 19. I know personally 5 people who went into the hospital on doctor's orders. Only 2 are out, 1 is still battling, and 2 have died. Avoiding hospitalization was 1st on our list. We called my father-in-law's doctor in Georgetown when his fever was 101 for 3 days straight, continued with headaches, oxygen levels were low and he had no energy. He was told to continue to take Tylenol and drink lots of fluids. If he got worse, take him to the emergency room. My husband's doctor had Covid in March. He posted information on social media about medicines he was taking which included Hydroxicloroquin. When asked if he would prescribe this for his patients, his reply was yes. We called the office and were told no, he won't prescribe it and to take Tylenol and drink fluids. If it got worse he was to go to the hospital. My daughter continued to have headaches for many days and her chest began to hurt. She has had pneumonia many times in the past and I was worried about this going to her lungs. I contacted Baylor Scott and White. After a $40 co pay we were told for her to use her inhaler and if it got worse to go to the emergency room. I was contacted by a friend and told a doctor in Marble Falls would prescribe the needed medicine but she doesn't take insurance. The cost would be $150 a person (which would still be cheaper and less dangerous than a hospital stay). Many of you, maybe not Damon for obvious reasons, know my father-in-law, Thomas the town barber. He has operated Hullum's barbershop for over 70 years. At $12 a haircut he hasn't become a millionaire and for him to have to put up $300 for he and his wife in addition to medicines would be a lot. It was then I found another doctor that is a teladoctor from San Angelo. She talked with each family member, took information on background, medicines taking, and symptoms. She prescribed the needed medicines for each member which included hydroxochloroquin, steroids, z-packs, and budesonide along with a nebulizer and individual mask/tubes for all. The final cost would be $540 for all 8 family members. The only problem was the medicines would have to be picked up in San Angelo since they knew the pharmacist there and she would be able to call them in for us. Thanks to my background of being a teacher and not getting many restroom breaks, I was able to travel to the pharmacy, get the medicines curb-side, and travel back to Burnet in just over 5 hours without having to stop for the restroom. Within 12 hours of starting the medicines, every person's headaches stopped, oxygen levels came up, and 24 hours into treatments, we were having a difficult time keeping my father-in-law down. It was amazing at the turn-around these medicines caused. Their cost was $30 each for the medicines for my in-laws. These medicines are not costly but for possible political reasons the doctors have their hands tied. One person told me the doctor at the minor emergency would have liked to prescribe the medicine but the large pharmaceutical companies are not allowing it. I do realize the vaccines will be available soon but there isn't enough information to show possible long-term side effects but the medicines we took have been used for years and could

Zinc, D3, Vitamin C since March

save lives. These medicines are available and can be picked up at larger as well as smaller pharmacies if needed. I'm not sure who is to blame for not being able to get the medicines but causing the public fear is not the answer when there are proven medicines. We should have the choice of medicines over vaccines. Every pharmacy will not be able to install a $25,000 freezer to keep the vaccines so power will continue to be in larger pharmacies hands when vaccines are available. I'm asking you to talk with whoever is in charge in Burnet County to help get these medicines to the citizens. They do work. And thank you to the Texas Health Department that called us 1 week after being diagnosed and told us to stay in our houses and not leave When I mentioned food and medicine was needed, she told me there are available organizations that could help with food. It would be nice to have known this earlier.

What Is Right To Try?

On May 30, 2018, President Donald Trump signed S.204, the Trickett Wendler, Frank Mongiello, Jordan McLinn and Matthew Bellina Right to Try Act. Right to Try opens a new pathway for terminally ill patients who have exhausted their government-approved options and can't get into a clinical trial to access treatments. Although 41 states have passed Right to Try laws, the signing of S.204 makes Right to Try the law of the land, creating a

To be eligible for right to try, a patient must meet the following criteria:

- Be diagnosed with a life-threatening disease or condition;
- Have exhausted approved treatment options;
- Be unable to participate in a clinical trial involving the eligible investigational drug, as certified by a doctor, who is in good standing with her licensing organization and will not be compensated directly by the manufacturer for so certifying; and
- Give written informed consent regarding the risks associated with taking the investigational treatment.

What is a life-threatening disease or condition?

Federal law defines a life-threatening disease or condition as: "Diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted" (21 CFR 312.81).

What drugs or treatments qualify for Right to Try?

The treatments available under the law must meet the following conditions:

- Have completed an FDA-approved Phase 1 clinical trial;
- Be in an active clinical trial intended to form the basis of an application for approval or be the subject of an application for approval that has been filed with the FDA; and
- Be in ongoing active development or production and not discontinued

treatment meet the qualifications of the federal law, Right to Try applies, regardless of whether the patient's state adopted Right to Try.

Does medical cannabis qualify?

Right to Try only applies to treatments that have completed an FDA-approved Phase 1 clinical trial and remain under study in an active clinical trial. If there is a Phase 2 or 3 clinical trial for medical cannabis as a treatment of an underlying terminal condition, it may qualify.

Does a treatment that is already FDA-approved for something else qualify for Right to Try?

Doctors may already prescribe treatments 'off-label.' Off-label means prescribing an FDA approved treatment for a condition, dose, or population other than what the FDA approved. Therefore, no special permission is needed for a physician to prescribe treatments that are approved for other conditions. Right to Try applies to treatments that are being given to patients in clinical trials but are not already FDA approved.

What can companies charge for treatments?

Federal law bans companies from making a profit on any drug or treatment that has not been approved by the FDA, but the law does allow companies to recover the costs that are directly related to providing an

This means that a patient could be charged for the direct costs of providing their individual treatment, but the company cannot make a profit.

How will payment work?

Just like with the FDA's existing Expanded Access program, insurance companies and taxpayer-funded healthcare programs like Medicaid or Medicare are not required to cover the cost of investigational treatments, but they may choose to do so. Some insurance companies have covered the costs of investigational treatments used by patients under state Right to Try laws, but others have not. Each patient's cost situation will be different and determined by their individual insurance company or program and their own financial resources.

How do I initiate a request?

The patient, the patient's representative, or physician should send a letter to the drug manufacturer's director of compassionate use or other designated representative to discuss options for access. A sample letter is provided here.

Where can I find a list of potential treatments?

If your physician is not yet aware of investigational treatments, there are several websites that can assist in locating potential treatments:

No. Drug companies are not required to provide treatments to patients under Right to Try laws. It would not be appropriate to force companies to provide treatments that they do not think are the right fit for a patient or if they do not have enough supply to provide the treatment outside of its clinical trial.

Can I make my doctor submit a request for a treatment I want to try?

No. Doctors have a responsibility to ensure that patients are given treatments that they believe, in their professional opinion, could help them. A doctor who does not think a treatment will help is not obligated to make a request for the treatment. In addition, doctors who pursue treatments under Right to Try must be in good standing with their state licensing or certifying board, and they cannot be compensated for certifying that patients qualify for Right to Try.

How will a company decide if they will give me the treatment?

Each company will develop its own process and procedures for approving Right to Try requests.

Download the Federal Right to Try FAQ as a PDF.


to


to

VIDEO: EVERYONE DESERVES THE RIGHT TO TRY

Fax: 602-256-7045
RightToTry@goldwaterinstitute.org

Treatments Your Healthcare Provider Might Recommend if You Are Sick

Updated Dec. 8, 2020 Print

Treatments used for COVID-19 should be prescribed by your healthcare provider. People have been seriously harmed and even died after taking products not approved for COVID-19, even products approved or prescribed for other uses.

Drugs Approved or Authorized for Use

- The Food and Drug Administration (FDA) has approved one drug, remdesivir (Veklury), to treat COVID-19.
- The FDA can also issue emergency use authorizations (EUAs) to allow healthcare providers to use products that are not yet approved, or that are approved for other uses, to treat patients with COVID-19 if certain legal requirements are met.
- The National Institutes of Health (NIH) has developed and regularly updates Treatment Guidelines to help guide healthcare providers caring for patients with COVID-19, including when clinicians might consider using one of the products under an EUA.

Treatment Outside of the Hospital

If you receive a positive test result for COVID-19 and are more likely to get very sick from COVID-19, your healthcare provider may recommend that you receive treatment.

- **For people at high risk of disease progression.** The FDA has issued EUAs for two investigational monoclonal antibodies that can attach to parts of the virus. These antibodies could help the immune system recognize and respond more effectively to the virus.
  - Bamlanivimab and casirivimab plus imdevimab are available under FDA EUAs for patients at high risk of disease progression and severe illness. Preliminary data suggest that some outpatients may benefit from receiving anti-SARS-CoV-2 monoclonal antibodies early in the course of infection. The NIH COVID-19 Treatment Guidelines find that, to date, there are insufficient data from clinical trials to recommend for or against these treatments and these treatments should not be considered standard of care.

Your healthcare provider also may recommend the following to relieve symptoms and support your body's natural defenses.

- Taking medications, like acetaminophen or ibuprofen, to reduce fever.
- Drinking water or receiving intravenous fluids to stay hydrated.
- Getting plenty of rest to help the body fight the virus.

Treatment in the Hospital

Your healthcare provider will decide on what approach to take for your treatment. There are drugs that have shown some benefit in reducing the severity of illness or risk of death for patients in the hospital by:

- **Slowing the virus.** Antiviral medications reduce the ability of the virus to multiply and spread through the body.
  - Remdesivir (Veklury) is an antiviral medication approved by FDA to treat COVID-19. The current NIH COVID-19 Treatment Guidelines recommend remdesivir for certain patients who are hospitalized with COVID-19. Remdesivir is given to patients by infusion through their veins.
- **Reducing an overactive immune response.** In patients with severe COVID-19, the body's immune system may overreact to the threat of the virus, worsening the disease. This can cause damage to the body's organs and tissues. Some treatments can help reduce this overactive immune response.
  - Dexamethasone is a steroid medication, similar to a natural hormone produced by the body. The NIH COVID-19 Treatment Guidelines recommend dexamethasone, or a similar medication, to prevent or reduce injury to the body for some hospitalized patients with severe COVID-19. Dexamethasone is recommended for patients who need supplemental oxygen.
- **Treating complications.** COVID-19 can damage the heart, blood vessels, kidneys, brain, skin, eyes, and gastrointestinal organs. It also can cause other complications. Depending on the complications, additional treatments might be used for severely ill hospitalized patients, such as blood thinners to prevent or treat blood clots.
- **Supporting the body's immune function.** Plasma from patients who have recovered from COVID-19—called convalescent plasma—can contain antibodies to the virus. This could help the immune system recognize and respond more effectively to the virus, but currently the NIH COVID-19 Treatment Guidelines find there is not enough evidence to recommend these treatments.

Slow the spread of COVID-19

The best way to protect yourself is to avoid getting or spreading COVID-19.

- Stay 6 feet from others who don't live in your household
- Wear a mask over your nose and mouth.
- Avoid crowds and poorly ventilated places.
- Wash your hands often.
- Cover your coughs and sneezes.
- Clean and disinfect frequently touched surfaces.
- Monitor your health daily.

Getting a flu vaccine is more important than ever this flu season to protect yourself, your family and your community from flu. A flu vaccine can also help reduce the burden on our healthcare systems responding to the COVID-19 pandemic and save medical resources for care of COVID-19 patients.

If you think you may have been exposed to a person with COVID-19, contact your healthcare provider.

- Stay home and away from the people you live with to prevent the spread of COVID-19 in your home.
- Consider getting tested.
- Monitor your symptoms.
- If someone is showing emergency warning signs, get medical care immediately. Emergency warning signs include:
  - Trouble breathing
  - Persistent pain or pressure in the chest
  - New confusion
  - Inability to wake or stay awake
  - Bluish lips or face.

Additional Resources

Combat COVID: Information about Clinical Trials

Texas

Right To Try signed into law by Governor Greg Abbott on June 12, 2015.

WHAT IS RIGHT TO TRY? / WHY WE NEEDED RIGHT TO TRY / GETTING TREATMENT / TREATING A PATIENT / FAQ / RIGHT TO TRY IS WORKING / NEWS / CONTACT

Ivermectin

Last Updated: August 27, 2020

Ivermectin is a Food and Drug Administration (FDA)-approved antiparasitic drug that is used to treat several neglected tropical diseases, including onchocerciasis, helminthiases, and scabies.[1] It is also being evaluated for its potential to reduce the rate of malaria transmission by killing mosquitoes that feed on treated humans and livestock.[2] For these indications, ivermectin has been widely used and has demonstrated an excellent safety profile.[1]

Proposed Mechanism of Action and Rationale for Use in Patients With COVID-19

Ivermectin acts by inhibiting the host importin alpha/beta-1 nuclear transport proteins, which are part of a key intracellular transport process that viruses hijack to enhance infection by suppressing the host antiviral response.[3] Ivermectin is therefore a host-directed agent, which is likely the basis for its broad-spectrum activity *in vitro* against the viruses that cause dengue, Zika, HIV, and yellow fever.[3-6]

Recommendation

- The COVID-19 Treatment Guidelines Panel **recommends against** the use of **ivermectin** for the treatment of COVID-19, except in a clinical trial **(AIII)**.

Rationale

Ivermectin has been shown to inhibit the replication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in cell cultures.[7] However, pharmacokinetic and pharmacodynamic studies suggest that achieving the plasma concentrations necessary for the antiviral efficacy detected *in vitro* would require administration of doses up to 100-fold higher than those approved for use in humans.[8,9] Even though ivermectin appears to accumulate in the lung tissue, predicted systemic plasma and lung tissue concentrations are much lower than 2 μM, the half-maximal inhibitory concentration (IC_{50}) against SARS-CoV-2 *in vitro*.[10,11]

Ivermectin is not approved for the treatment of any viral infection, including SARS-CoV-2 infection. The FDA issued a warning in April 2020 that ivermectin intended for use in animals should not be used to treat COVID-19 in humans.

Clinical Data in Patients With COVID-19

The available clinical data on the use of ivermectin to treat COVID-19 are limited.

Retrospective Analysis of Using Ivermectin in Patients With COVID-19

This study has not been peer reviewed.

This retrospective analysis of consecutive patients with confirmed SARS-CoV-2 infection (27% with severe COVID-19) who were admitted to four Florida hospitals compared patients who received at least one dose of ivermectin (n = 173) to those who received "usual care" (n = 103). The primary outcome was all-cause, in-hospital mortality. The secondary outcomes included mortality in patients with severe disease (defined as "need for either FiO_2 ≥50% or noninvasive or invasive mechanical ventilation") and extubation rates in those who were mechanically ventilated.[12]

Results

- Ivermectin administration was reportedly consistent with hospital guidelines: a single dose of 200 µg/kg, with repeat dosing on Day 7 if the patient was still hospitalized (13 patients received a second dose). Ninety percent of the ivermectin group and 97% of the usual care group received hydroxychloroquine (the majority received hydroxychloroquine in conjunction with azithromycin).
- All-cause mortality was lower among the patients in the ivermectin group than among patients in the usual care group (OR 0.27; $P = 0.03$). The mortality benefit appeared to be limited to the subgroup of patients with severe disease.
- There was no difference between the groups for the median length of hospital stay (7 days in both groups) or the proportion of mechanically ventilated patients who were successfully extubated (36% in the ivermectin group vs. 15% in the usual care group; $P = 0.07$).

Limitations

- This was a retrospective analysis.
- The study included little or no information on oxygen saturation or radiographic findings. It was also unclear whether therapeutic interventions other than hydroxychloroquine, such as remdesivir or dexamethasone, were used in the study.
- The timing of therapeutic interventions was not standardized; if the timing is not accounted for, it can bias the survival comparison.
- The analyses of the durations of ventilation and hospitalization do not appear to account for death as a competing risk.
- No virologic assessments were performed.

Interpretation

The limitations of this retrospective analysis make it difficult to draw conclusions about the efficacy of using ivermectin to treat patients with COVID-19.

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Therapeutic Management of Patients with COVID-19

Last Updated: December 3, 2020

Executive Summary

Two main processes are thought to drive the pathogenesis of COVID-19. Early in the course of the infection, the disease is primarily driven by replication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Later in the course of infection, the disease is driven by an exaggerated immune/inflammatory response to the virus that leads to tissue damage. Based on this understanding, it is anticipated that antiviral therapies would have the greatest effect early in the course of disease, while immunosuppressive/anti-inflammatory therapies are likely to be more beneficial in the later stages of COVID-19.

In the earliest stages of infection, before the host has mounted an effective immune response, anti-SARS-CoV-2 antibody-based therapies may have their greatest likelihood of having an effect. In this regard, although there are insufficient data from clinical trials to recommend either for or against the use of any specific therapy in this setting, preliminary data suggests that outpatients may benefit from receiving anti-SARS-CoV-2 monoclonal antibodies early in the course of infection. The anti-SARS-CoV-2 monoclonal antibodies bamlanivimab and casirivimab plus imdevimab are available through Emergency Use Authorizations for outpatients who are at high risk for disease progression.

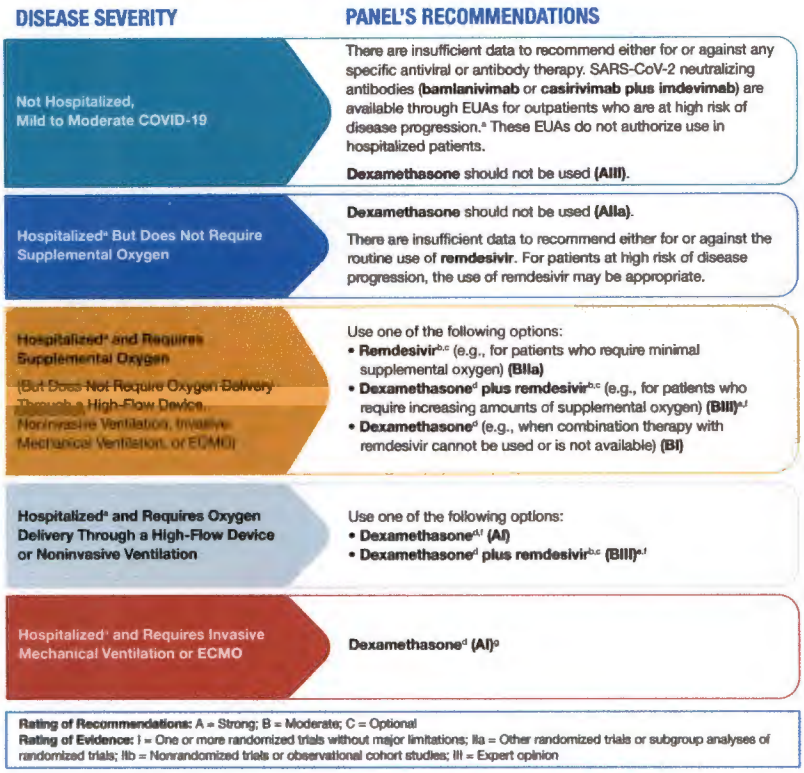
Remdesivir, an antiviral agent, is currently the only drug that is approved by the Food and Drug Administration for the treatment of COVID-19. It is recommended for use in hospitalized patients who require supplemental oxygen. However, it is not routinely recommended for patients who require mechanical ventilation due to the lack of data showing benefit at this advanced stage of the disease.[1-4]

Dexamethasone, a corticosteroid, has been found to improve survival in hospitalized patients who require supplemental oxygen, with the greatest effect observed in patients who require mechanical ventilation. Therefore, the use of dexamethasone is strongly recommended in this setting.[5-8]

The COVID-19 Treatment Guidelines Panel (the Panel) continues to review the most recent clinical data to provide up-to-date treatment recommendations for clinicians who are caring for patients with COVID-19. Figure 1 summarizes the Panel's recommendations for managing patients with varying severities of disease. A comprehensive summary of the clinical data for the drugs that are being investigated for the treatment of COVID-19 can be found in the Antiviral Therapy, Immune-Based Therapy, and Adjunctive Therapy sections of these Guidelines.

Figure 1. Pharmacologic Management of Patients with COVID-19 Based on Disease Severity

Doses and durations are listed in the footnote.



[a] See the Panel's statements on the FDA EUAs for bamlanivimab and casirivimab plus imdevimab. These EUAs do not authorize use in hospitalized patients.

[b] The remdesivir dose is 200 mg IV for one dose, followed by 100 mg IV once daily for 4 days or until hospital discharge (unless the patient is in a health care setting that can provide acute care that is similar to inpatient hospital care). Treatment duration may be extended to up to 10 days if there is no substantial clinical improvement by Day 5.

[c] For patients who are receiving remdesivir but progress to requiring oxygen through a high-flow device, noninvasive ventilation, invasive mechanical ventilation, or ECMO, remdesivir should be continued until the treatment course is completed.

[d] The dexamethasone dose is 6 mg IV or PO once daily for 10 days or until hospital discharge. If dexamethasone is not available, equivalent doses of other corticosteroids, such as prednisone, methylprednisolone, or hydrocortisone, may be used. See the Corticosteroids section for more information.

[e] The combination of dexamethasone and remdesivir has not been studied in clinical trials.

[f] In the rare circumstances where corticosteroids cannot be used, baricitinib plus remdesivir can be used (BIIa). The FDA has issued an EUA for baricitinib use in combination with remdesivir. The dose for baricitinib is 4 mg PO once daily for 14 days or until hospital discharge.

[g] The combination of dexamethasone and remdesivir may be considered for patients who have recently been intubated (CIII). Remdesivir alone is not recommended.

Key: ECMO = extracorporeal membrane oxygenation; EUA = Emergency Use Authorization; FDA = Food and Drug Administration; IV = intravenous; the Panel = the COVID-19 Treatment Guidelines Panel; PO = orally; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

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CDC Centers for Disease Control and Prevention

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Summary

What is already known about this topic?

Hydroxychloroquine and chloroquine are approved to treat autoimmune diseases and to prevent and treat malaria. Earlier this year, they were widely reported to be of potential benefit in the prevention and treatment of COVID-19; however, current data indicate that the potential benefits of these drugs do not outweigh their risks.

What is added by the report?

New prescriptions by specialists who did not typically prescribe these medications (defined as specialties accounting for ≤2% of new prescriptions before 2020) increased from 1,143 prescriptions in February 2020 to 75,569 in March 2020, an 80-fold increase from March 2019.

What are the implications for public health practice?

Attention to updated clinical guidance, especially by nonroutine prescribers, will help safeguard supplies and ensure safe use of hydroxychloroquine and chloroquine for patients with approved indications.

Hydroxychloroquine and chloroquine, primarily used to treat autoimmune diseases and to prevent and treat malaria, received national attention in early March 2020, as potential treatment and prophylaxis for coronavirus disease 2019 (COVID-19) (*1*). On March 20, the Food and Drug Administration (FDA) issued an emergency use authorization (EUA) for chloroquine phosphate and hydroxychloroquine sulfate in the Strategic National Stockpile to be used by licensed health care providers to treat patients hospitalized with COVID-19 when the providers determine the potential benefit outweighs the potential risk to the patient.* Following reports of cardiac and other adverse events in patients receiving hydroxychloroquine for COVID-19 (*2*), on April 24, 2020, FDA issued a caution against its use† and on June 15, rescinded its EUA for hydroxychloroquine from the Strategic National Stockpile.§ Following the FDA's issuance of caution and EUA rescindment, on May 12 and June 16, the federal COVID-19 Treatment Guidelines Panel issued recommendations against the use of hydroxychloroquine or chloroquine to treat COVID-19; the panel also noted that at that time no medication could be recommended for COVID-19 pre- or postexposure prophylaxis outside the setting of a clinical trial (*3*). However, public discussion concerning the effectiveness of these drugs on outcomes of COVID-19 (*4,5*), and clinical trials of hydroxychloroquine for prophylaxis of COVID-19 continue.¶ In response to recent reports of notable increases in prescriptions for hydroxychloroquine or chloroquine (*6*), CDC analyzed outpatient retail pharmacy transaction data to identify potential differences in prescriptions dispensed by provider type during January–June 2020 compared with the same period in 2019. Before 2020, primary care providers and specialists who routinely prescribed hydroxychloroquine, such as rheumatologists and dermatologists, accounted for approximately 97% of new prescriptions. New prescriptions by specialists who did not typically prescribe these medications (defined as specialties accounting for ≤2% of new prescriptions before 2020) increased from 1,143 prescriptions in February 2020 to 75,569 in March 2020, an 80-fold increase from March 2019. Although dispensing trends are returning to prepandemic levels, continued adherence to current clinical guidelines for the indicated use of these medications will ensure

their availability and benefit to patients for whom their use is indicated (*3*,*4*), because current data on treatment and pre- or postexposure prophylaxis for COVID-19 indicate that the potential benefits of these drugs do not appear to outweigh their risks.

Hydroxychloroquine and chloroquine prescriptions dispensed through outpatient retail pharmacies in the United States during January–June 2019 and January–June 2020 were examined using deidentified pharmacy transactions from the IQVIA National Prescription Audit database.** This database includes 92% of all outpatient retail prescriptions dispensed in the United States; prescription estimates were projected by IQVIA to represent all retail outpatient medication dispensing at the state and national levels.

New prescriptions for hydroxychloroquine and chloroquine were defined as those dispensed to a patient without a history of prescription for these medications in the preceding 12 months. Hydroxychloroquine accounted for approximately 99% of prescriptions dispensed during the study period. Refill/switch prescriptions were defined as those dispensed either as a refill of a previous prescription or as a new prescription with a change in medication strength or brand or switches between medications within the same therapeutic category (i.e., bidirectional switches of hydroxychloroquine and chloroquine). New and refill/switch prescriptions dispensed before reports of potential benefit on medication use for COVID-19 (during January–June 2019) were compared with new and refill/switch prescriptions during January–June 2020. Fold changes in the numbers of new prescriptions were calculated and defined as the ratio between the estimated number of prescriptions in March, April, May, and June 2020, with respect to the same months in 2019. The percentage of total dispensed prescriptions by specialty group was calculated using the total number of dispensed prescriptions by specialty group, divided by the overall total number of dispensed prescriptions for the month; the percentage of new prescriptions by a specialty group was calculated by dividing the new prescriptions dispensed for the specialty group by the total prescriptions for the specialty group. The percentage of new prescriptions dispensed to males was calculated as the number of new prescriptions for males divided by the total number of new prescriptions.

Prescriptions were not included if they were dispensed by mail order; mail-dispensed prescriptions accounted for <7.5% of dispensed hydroxychloroquine and chloroquine. Prescriptions by veterinarians were also excluded.

Prescriptions included information on the prescriber's medical specialty, as defined by the American Medical Association (AMA) self-designated practice specialties.†† For this study, clinicians prescribing hydroxychloroquine or chloroquine were categorized based on the frequency of prescribing of hydroxychloroquine or chloroquine before the COVID-19 pandemic. Specialists from rheumatology, dermatology, allergy, and nephrology, who might have had experience using these drugs for indicated medical conditions within their specialty before the pandemic (collectively termed routine prescribers) were responsible for 62% of new hydroxychloroquine or chloroquine prescriptions in 2019. Allopathic and osteopathic physicians, who included internal medicine, family practice, general practice, and pediatrics, and nurse practitioners, physician assistants, and prescribers with unspecified specialty (per AMA classification) were grouped for this study into primary care prescribers; this group provided 35% of the new prescriptions in 2019. Other specialists were considered nonroutine prescribers§§ if, in 2019, their specialty prescribed ≤2% of hydroxychloroquine or chloroquine prescriptions. Nonroutine prescribing specialties are less likely under normal circumstances to directly manage patients with autoimmune disorders or provide prescriptions for malaria prophylaxis.

The overall estimated number of hydroxychloroquine or chloroquine prescriptions dispensed in March and April 2020 increased from 819,906 in 2019 to 1,312,859 in 2020 (Table). In 2019, 92% of prescriptions were refill/switch prescriptions. Refill/switch prescriptions increased 1.4-fold, from 377,222 in March 2019 to 536,804 in March 2020, and remained elevated in April (456,489; 1.2-fold higher than in April 2019) (Figure 1). New prescriptions for hydroxychloroquine or chloroquine in March 2020 (222,382) were 7.2-fold higher than the 30,737 prescriptions in March 2019; in April, the number of new prescriptions (106,184) was 3.3-fold higher than the 31,748 in April 2019 (Table).

Overall, 54% of new prescriptions in March and April 2020 were written by primary care prescribers. In March 2020, primary care prescribers wrote more new prescriptions than did routine prescribers, writing 10,350 dispensed prescriptions in 2019 compared with 108,705 in 2020, a 10.5-fold increase (Figure 2). Primary care prescribers continued to be the largest source of new prescriptions in April 2020, writing 67,055 prescriptions (63% of total new prescriptions).

During March and April 2020, nonroutine prescribers accounted for the largest percentage increase in new prescriptions compared with the same period in 2019 (81.3-fold and 18.1-fold increases in March and April, respectively). The nonroutine prescribing specialties with the highest prescribing volume and growth in March 2020 were ophthalmology, anesthesiology, and cardiology.

During March and April 2019, most new prescriptions were dispensed to females (81%). In 2020, the estimated number of total new prescriptions for males was 93,776 in March (16.1-fold higher than March 2019), and 40,055 in April (6.8-fold higher than April 2019), accounting for 42% and 38% of all new prescriptions in March and April, respectively.

In May and June 2020, refill/switch prescriptions declined but remained elevated: 436,823 in May (1.1-fold higher than May 2019) and 461,670 in June (1.3-fold higher than June 2019). New prescriptions in May 2020 declined to 37,537 (7.9%) of all dispensed hydroxychloroquine or chloroquine prescriptions, with a similar number of dispensed prescriptions (38,803; 7.8%) in June 2020. In May 2020, the percentage of new prescriptions by those in nonroutine prescribing specialties declined to 18.5% from 82.5% in March and 54.2% in April.

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Discussion

In the United States, during March and April 2020, monthly hydroxychloroquine and chloroquine outpatient prescribing was higher than it was during the previous year. These medications are routinely prescribed for lupus and rheumatoid arthritis (hydroxychloroquine) and for antimalarial prophylaxis malaria treatment (chloroquine), and the annual rate of prescribing has not varied substantially from year to year (*6*). In contrast, new prescriptions written by primary care prescribers and nonroutine prescribing specialists increased significantly in 2020. Primary care prescribers provided 54% of new prescriptions dispensed at outpatient retail pharmacies during March–April 2020; the largest percentage increase in new prescriptions compared with the same period in 2019 was among nonroutine prescribers.

A large increase in new prescriptions occurred for adult males (16.1-fold increase in March 2020 compared with March 2019). This increase in hydroxychloroquine prescribing for males is notable given that females are historically more likely to receive a new hydroxychloroquine prescription for autoimmune disease, consistent with described prevalence of autoimmune disorders among females (78%) (*7*). By May and June 2020, the numbers of new prescriptions and the number of new prescriptions from nonroutine prescribing specialties had declined and were approaching those of 2019. These declines might have been influenced by publication of additional studies indicating that the medications were not found to be effective for treatment of COVID-19 and by FDA safety warning (*8*).

The findings in this report are subject to at least four limitations. First, mail-order prescriptions were not included in the study, nor were prescriptions given in inpatient settings, so data do not indicate total medication use nationwide. However, the data are weighted to be nationally representative, although they are based on a sample of 92% of outpatient prescriptions. Second, because specialty information was lacking for nurse practitioners, physician assistants, and unspecified specialties, these prescribers were categorized as primary care; however, it is possible that these providers were working in routine or nonroutine prescriber practices. In addition, allopathic and osteopathic physicians with internal medicine and subspecialty training potentially were not classified by subspecialty. Third, among patients receiving prescriptions, clinical indications, patients' underlying medical conditions, and concurrent medications were unknown. Finally, no information was available to confirm whether the medication was taken or stored for future use or if any adverse events occurred.

If prescribing or prescribed these drugs, providers and patients should be familiar with the potential for drug interactions and adverse events associated with hydroxychloroquine or chloroquine use (*8,9*). The importance of obtaining a patient's complete medical and medication history to evaluate risks should be emphasized to nonroutine prescribers of hydroxychloroquine or chloroquine. In the setting of polypharmacy and comorbid conditions, such as preexisting heart conditions, performing an electrocardiogram to evaluate the QT interval before starting these medications is advisable, because hydroxychloroquine or chloroquine can prolong the QT interval, leading to malignant arrhythmias such as torsade de pointes or ventricular fibrillation (*9*). Because of the long-terminal half-life of hydroxychloroquine (>40 days) (*10*), patients could continue to be at risk for drug interactions and adverse cardiac events after the course of therapy is completed.

Although federal guidelines now recommend against using hydroxychloroquine or chloroquine for the treatment or prevention of COVID-19, dispensing policies and restrictions vary significantly by state (*8*). Policies by boards of pharmacy in some states, such as New Jersey, require hydroxychloroquine prescriptions to include a diagnosis, documentation of a positive diagnostic test, and be limited to a 14-day supply.¶¶ In Texas, similar restrictions instituted in May expired in July.*** Several other states advise caution in prescribing hydroxychloroquine or chloroquine for COVID-19, while allowing for clinical judgement without policy limitations. Although dispensing of hydroxychloroquine or chloroquine prescriptions has been declining since March 2020, continued attention to updated clinical guidance (*3,4*), especially by nonroutine prescribers, will help safeguard supplies and ensure safe use of these medications for patients with approved indications.†††

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* https://www.fda.gov/media/136534/download .

† https://www.fda.gov/drugs/drug-safety-and-availability/fda-cautions-against-use-hydroxychloroquine-or-chloroquine-covid-19-outside-hospital-setting-or .

§ https://www.fda.gov/media/138945/download .

¶ https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7330261/ .

** IQVIA projected prescription estimates using proprietary methods and information internal to the company. https://www.iqvia.com/locations/united-states/solutions/commercial-operations/essential-information/prescription-information .

†† http://www.dmddata.com/2009_05_sdps.pdf .

§§ Nonroutine specialties included addiction medicine, allergy/immunology, anesthesiology, cardiology, cardiothoracic surgery, cardiovascular surgery, clinical neurophysiology, clinical pharmacology, colon and rectal surgery, critical care, critical care medicine, dentistry, dermatopathology, diagnostic laboratory, diagnostic laboratory immunology, emergency medicine, endocrinology, gastroenterology, general preventive medicine, general surgery, genetics, geriatric psychiatry, geriatrics, hematology, hepatology, hospice and palliative medicine, infectious disease, medical microbiology, naturopathic doctor, neurologic surgery, neurology, neurosurgery-critical care, nuclear medicine, nutrition, obstetrics/gynecology, obstetrics/gynecology-critical care, occupational medicine, oncology, ophthalmology, optometry, orthopedic surgery, orthopedic surgery of spine, other, other surgery, otolaryngology, otology, pain medicine, pathology, pediatric critical care, pediatric neurosurgery, pharmacist, physical medicine and rehab, plastic surgery, podiatry, psychiatry, psychology, pulmonary critical care, pulmonary diseases, radiology, sleep medicine, sports medicine, surgery, thoracic surgery, and urology.

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TABLE. Estimated hydroxychloroquine or chloroquine retail dispensing, by prescriber category — United and 2020*

Specialty/Prescription characteristic	2019 Jan	Feb	Mar	Apr	May	June	2020 Jan	Feb	Mar
All providers (routine, primary care or unspecified, and nonroutine)									
No. of total prescriptions.	414,278	373,985	407,959	411,947	420,901	396,620	413,345	383,435	759,186
Refill/Switch prescriptions†	383,105	345,244	377,222	380,199	387,761	366,750	381,260	352,959	536,804
Fold change in refill/switch prescriptions from 2019	—	—	—	—	—	—	1.0	1.0	1.4
New prescriptions, no. (% of total)	31,173 (7.5)	28,741 (7.7)	30,737 (7.5)	31,748 (7.7)	33,140 (7.9)	29,871 (7.5)	32,085 (7.8)	30,476 (7.9)	222,382 (29.3)
New prescriptions for males, no. (% new)	6,049 (19.4)	5,495 (19.1)	5,834 (19.0)	5,960 (18.8)	6,393 (19.3)	5808 (19.4)	5,791 (18)	5,664 (18.6)	93,776 (42.2)
Fold change new prescriptions from 2019	—	—	—	—	—	—	1.0	1.1	7.2
% New prescriptions from combined primary care or routine specialty	96.9	97.0	97.0	97.1	96.8	96.9	97.4	96.2	66.0
Routine prescribers**									

Specialty/Prescription characteristic	2019 Jan	Feb	Mar	Apr	May	June	2020 Jan	Feb	Mar
% of total prescriptions	64.1	64.2	64.6	64.7	64.9	64.9	64.2	64.1	49.7
No. of prescriptions	265,495	240,259	263,559	266,599	273,155	257,508	265,571	245,842	377,271
Refill/Switch prescriptions[†]	246,518	222,477	244,101	246,401	252,400	238,899	245,640	227,261	339,163
Fold change in refill/switch prescriptions from 2019	—	—	—	—	—	—	1.0	1.0	1.4
New prescriptions, no. (% in-group total)	18,977 (7.1)	17,782 (7.4)	19,458 (7.4)	20,198 (7.6)	20,755 (7.6)	18,609 (7.2)	19,931 (7.5)	18,581 (7.6)	38,108 (10.1)
New prescriptions for males, no. (% new)	3,279 (17.3)	3,074 (17.3)	3,398 (17.5)	3,488 (17.3)	3,590 (17.3)	3290 (17.7)	3,276 (16.4)	3,067 (16.5)	9,559 (25.1)
Fold change in new prescriptions from 2019	—	—	—	—	—	—	1.1	1.0	2.0
Primary care or unspecified specialty prescribers[¶]									
% of total prescriptions	33.9	33.7	33.4	33.3	33.1	33.1	33.9	33.9	38.2
No. of prescriptions	140,386	126,216	136,376	137,242	139,124	131,153	140,090	130,024	290,277
Refill/switch prescriptions[†]	129,164	116,131	126,026	126,616	127,805	120,830	128,768	119,272	181,572
Fold change in refill/switch prescriptions from 2019	—	—	—	—	—	—	1.0	1.0	1.4
New prescriptions, no. (% in-group total)	11,222 (8.0)	10,085 (8.0)	10,350 (7.6)	10,626 (7.7)	11,319 (8.1)	10,323 (7.4)	11,322 (8.1)	10,752 (8.3)	108,705 (37.4)
New prescriptions for males, no. (% new)	2,494 (22.2)	2,189 (21.7)	2,194 (21.2)	2,239 (21.1)	2,486 (22.0)	2256 (21.8)	2,322 (20.5)	2,211 (20.6)	48,283 (44.4)
Fold change in new prescriptions from 2019	—	—	—	—	—	—	1.0	1.1	10.5
Nonroutine prescribers[§]									
% of total prescriptions	2.0	2.0	2.0	2.0	2.1	2.0	1.9	2.0	12.1
No. of prescriptions	8,397	7,510	8,024	8,107	8,622	7,960	7,684	7,569	91,639

Specialty/Prescription characteristic	2019						2020		
	Jan	Feb	Mar	Apr	May	June	Jan	Feb	Mar
Refill/Switch prescriptions†	7,423	6,636	7,095	7,183	7,556	7,021	6,852	6,426	16,070
Fold change in refill/switch prescriptions from 2019	—	—	—	—	—	—	0.9	1.0	2.3
New prescriptions, no. (% in-group total)	974 (11.6)	874 (11.6)	929 (11.6)	924 (11.4)	1,066 (12.4)	939 (11.8)	832 (10.8)	1,143 (15.1)	75,569 (82.5)
New prescriptions for males, no. (% new)	275 (28.2)	232 (26.5)	242 (26.0)	233 (25.2)	317 (29.7)	263 (28.0)	193 (23.2)	386 (33.8)	35,934 (47.6)
Fold change in new prescriptions from 2019	—	—	—	—	—	—	0.9	1.3	81.3

* Prescription data for 2017 and 2018 were also examined but found consistent with 2019, without remarkable month to month variation.

† Refill/switch prescriptions include dispensed prescriptions that were either a refill or a new prescription for a different dose or a switch in brand.

§ Nonroutine = addiction medicine, allergy/immunology, anesthesiology, cardiology, cardiothoracic surgery, cardiovascular surgery, clinical neurophysiology, clinical pharmacology, colon and rectal surgery, critical care, critical care medicine, dentistry, dermatopathology, diagnostic laboratory, diagnostic laboratory immunology, emergency medicine, endocrinology, gastroenterology, general preventive medicine, general surgery, genetics, geriatric psychiatry, geriatrics, hematology, hepatology, hospice and palliative medicine, infectious disease, medical microbiology, naturopathic doctor, neurologic surgery, neurology, neurosurgery-critical care, nuclear medicine, nutrition, obstetrics/gynecology, obstetrics/gynecology-critical care, occupational medicine, oncology, ophthalmology, optometry, orthopedic surgery, orthopedic surgery of spine, other, other surgery, otolaryngology, otology, pain medicine, pathology, pediatric critical care, pediatric neurosurgery, pharmacist, physical medicine and rehab, plastic surgery, podiatry, psychiatry, psychology, pulmonary critical care, pulmonary diseases, radiology, sleep medicine, sports medicine, surgery, thoracic surgery, and urology.

¶ Primary care/unspecified = family practice, general practice, internal medicine, internal medicine/pediatrics, nurse practitioner, osteopathic medicine, pediatrics, physician assistant, and specialty unspecified.

** Routine = allergy, dermatology, nephrology, and rheumatology.

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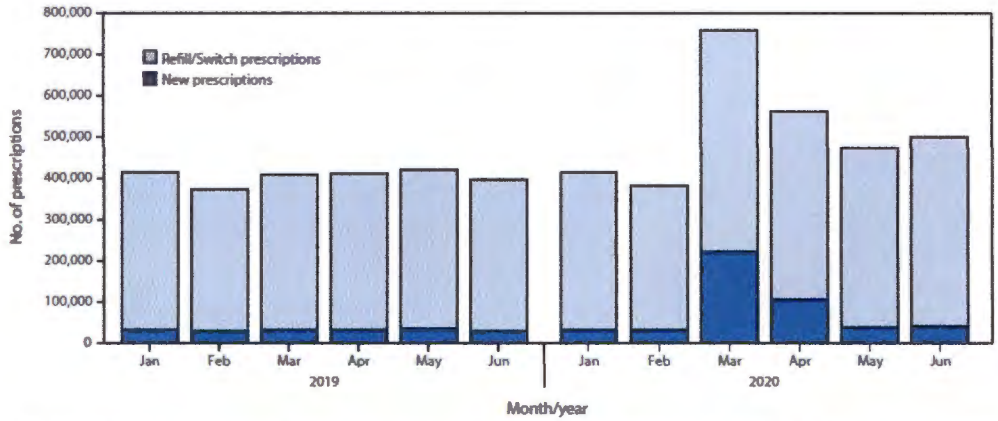
FIGURE 1. Estimated refill/switch* and new retail prescriptions for hydroxychloroquine or chloroquine dispensed in the United States — January–June, 2019–2020



* Refill/switch prescriptions include dispensed prescriptions that were either a refill of an existing prescription or a new prescription for a different dose or a brand switch.

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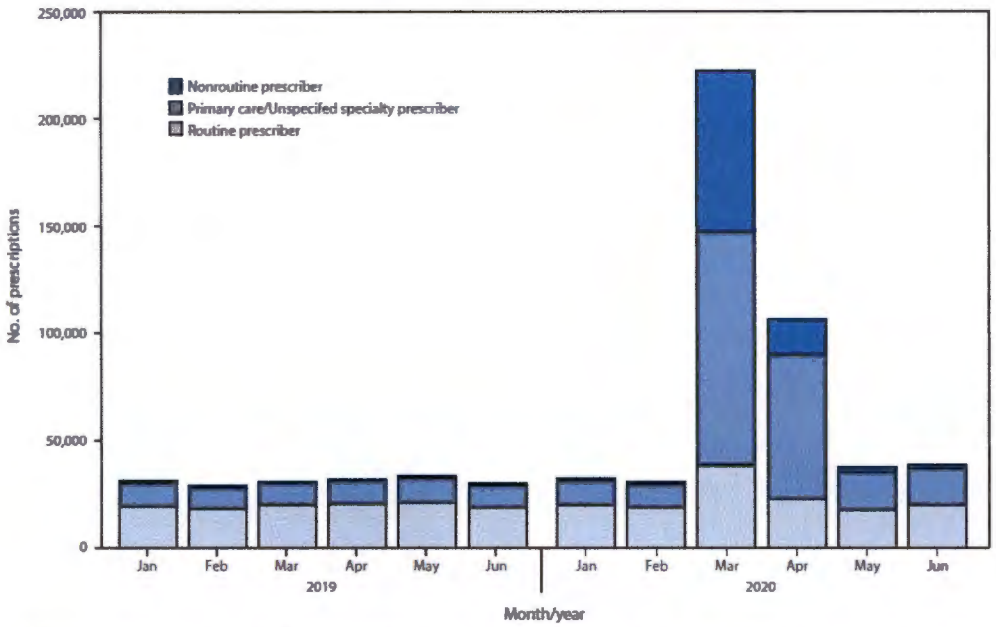
FIGURE 2. Estimated new retail prescriptions of hydroxychloroquine or chloroquine dispensed, by prescriber category* — United States, January–June, 2019–2020



* *Nonroutine prescribers* = addiction medicine, allergy/immunology, anesthesiology, cardiology, cardiothoracic surgery, cardiovascular surgery, clinical neurophysiology, clinical pharmacology, colon and rectal surgery, critical care, critical care medicine, dentistry, dermatopathology, diagnostic laboratory, diagnostic laboratory immunology, emergency medicine, endocrinology, gastroenterology, general preventive medicine, general surgery, genetics, geriatric psychiatry, geriatrics, hematology, hepatology, hospice and palliative medicine, infectious disease, medical microbiology, naturopathic doctor, neurological surgery, neurology, neurosurgery-critical care, nuclear medicine, nutrition, obstetrics/gynecology, obstetrics/gynecology-critical care, occupational medicine, oncology, ophthalmology, optometry, orthopedic surgery, orthopedic surgery of spine, other, other surgery, otolaryngology, otology, pain medicine, pathology, pediatric critical care, pediatric neurosurgery, pharmacist, physical medicine and rehab, plastic surgery, podiatry, psychiatry, psychology, pulmonary critical care, pulmonary diseases, radiology, sleep medicine, sports medicine, surgery, thoracic surgery, and urology. *Primary care/unspecified prescribers* = family practice, general practice, internal medicine, internal medicine/pediatrics, nurse practitioner, osteopathic medicine, pediatrics, physician assistant, and specialty unspecified. *Routine prescribers* = allergy, dermatology, nephrology, and rheumatology.

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Chloroquine or Hydroxychloroquine With or Without Azithromycin

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Chloroquine is an antimalarial drug that was developed in 1934. Hydroxychloroquine, an analogue of chloroquine, was developed in 1946. Hydroxychloroquine is used to treat autoimmune diseases, such as systemic lupus erythematosus (SLE) and rheumatoid arthritis, in addition to malaria. In general, hydroxychloroquine has fewer and less severe toxicities (including less propensity to prolong the QTc interval) and fewer drug-drug interactions than chloroquine.

Both chloroquine and hydroxychloroquine increase the endosomal pH, inhibiting fusion of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the host cell membranes.[1] Chloroquine inhibits glycosylation of the cellular angiotensin-converting enzyme 2 receptor, which may interfere with binding of severe acute respiratory syndrome-associated coronavirus (SARS-CoV) to the cell receptor.[2] In vitro studies have suggested that both chloroquine and hydroxychloroquine may block the transport of SARS-CoV-2 from early endosomes to endolysosomes, possibly preventing the release of the viral genome.[3] Both chloroquine and hydroxychloroquine also have immunomodulatory effects. It has been hypothesized that these effects are other potential mechanisms of action for the treatment of COVID-19. However, despite demonstrating antiviral activity in some in vitro systems, hydroxychloroquine with or without azithromycin did not reduce upper or lower respiratory tract viral loads or demonstrate clinical efficacy in a rhesus macaque model.[4]

Chloroquine and hydroxychloroquine, with or without azithromycin, have been studied in multiple clinical trials for the treatment of COVID-19. The recommendations below are based on an assessment of the collective evidence from these studies.

Recommendations

- The COVID-19 Treatment Guidelines Panel (the Panel) **recommends against** the use of **chloroquine** or **hydroxychloroquine** with or without azithromycin for the treatment of COVID-19 in hospitalized patients **(AI)**.
- In nonhospitalized patients, the Panel **recommends against** the use of **chloroquine** or **hydroxychloroquine** with or without **azithromycin** for the treatment of COVID-19, except in a clinical trial **(AI)**.
- The Panel **recommends against** the use of **high-dose chloroquine** (600 mg twice daily for 10 days) for the treatment of COVID-19 **(AI)**.

Rationale

The safety and efficacy of chloroquine and hydroxychloroquine with or without azithromycin have been evaluated in randomized clinical trials, observational studies, and single-arm studies. Please see Chloroquine or Hydroxychloroquine With or Without Azithromycin: Selected Clinical Data for more information.

In a large randomized controlled trial of hospitalized patients in the United Kingdom, hydroxychloroquine did not decrease 28-day mortality when compared to the usual standard of care. Participants who were randomized to receive hydroxychloroquine had a longer median hospital stay than those who received the standard of care. In addition, among patients who

were not on invasive mechanical ventilation at the time of randomization, those who received hydroxychloroquine were more likely to subsequently require intubation or die during hospitalization than those who received the standard of care.[5]

In another randomized controlled trial that was conducted in Brazil, neither hydroxychloroquine alone nor hydroxychloroquine plus azithromycin improved clinical outcomes among hospitalized patients with mild to moderate COVID-19. More adverse events occurred among patients who received hydroxychloroquine or hydroxychloroquine plus azithromycin than among those who received the standard of care.[6] Data from another randomized study of hospitalized patients with severe COVID-19 do not support using hydroxychloroquine plus azithromycin over hydroxychloroquine alone.[7]

In addition to these randomized trials, data from large retrospective observational studies do not consistently show evidence of a benefit for hydroxychloroquine with or without azithromycin in hospitalized patients with COVID-19. For example, in a large retrospective observational study of patients who were hospitalized with COVID-19, hydroxychloroquine use was not associated with a reduced risk of death or mechanical ventilation.[8] Another multicenter retrospective observational study evaluated the use of hydroxychloroquine with and without azithromycin in a random sample of a large cohort of hospitalized patients with COVID-19.[9] Patients who received hydroxychloroquine with or without azithromycin did not have a decreased risk of in-hospital mortality when compared to those who received neither hydroxychloroquine nor azithromycin.

Conversely, a large retrospective cohort study reported a survival benefit among hospitalized patients who received either hydroxychloroquine alone or hydroxychloroquine plus azithromycin, compared to those who received neither drug.[10] However, patients who did not receive hydroxychloroquine had a lower rate of admission to the intensive care unit, which suggests that patients in this group may have received less-aggressive care. Furthermore, a substantially higher percentage of patients in the hydroxychloroquine arms also received corticosteroids (77.1% of patients in the hydroxychloroquine arms vs. 36.5% of patients in the control arm). Given that the Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial showed that corticosteroids improve the survival rate of patients with COVID-19 (see Corticosteroids), it is possible that the findings in this study were confounded by this imbalance in corticosteroid use.[11] These and other observational and single-arm studies are summarized in Chloroquine or Hydroxychloroquine With or Without Azithromycin: Selected Clinical Data.

Many of the observational studies that have evaluated the use of chloroquine or hydroxychloroquine in patients with COVID-19 have attempted to control for confounding variables. However, study arms may be unbalanced in some of these studies, and some studies may not account for all potential confounding factors. These factors limit the ability to interpret and generalize the results from observational studies; therefore, results from these studies are not as definitive as those from large randomized trials. Given the lack of a benefit seen in the randomized clinical trials and the potential for toxicity, the Panel **recommends against** using hydroxychloroquine or chloroquine with or without azithromycin to treat COVID-19 in hospitalized patients **(AI)**.

The Panel also **recommends against** using high-dose chloroquine to treat COVID-19 **(AI)**. High-dose chloroquine (600 mg twice daily for 10 days) has been associated with more severe toxicities than lower-dose chloroquine (450 mg twice daily for 1 day, followed by 450 mg once daily for 4 days). A randomized clinical trial compared the use of high-dose chloroquine and low-dose chloroquine in hospitalized patients with severe COVID-19. In addition, all participants received azithromycin, and 89% of the participants received oseltamivir. The study was discontinued early when preliminary results showed higher rates of mortality and QTc prolongation in the high-dose chloroquine group.[12]

Several randomized trials have not shown a clinical benefit for hydroxychloroquine in nonhospitalized patients with COVID-19. However, other clinical trials are still ongoing.[13,14] In nonhospitalized patients, the Panel **recommends against** the use of chloroquine or hydroxychloroquine with or without azithromycin for the treatment of COVID-19, except in a clinical trial **(AI)**.

The combination of hydroxychloroquine and azithromycin is associated with QTc prolongation in patients with COVID-19. Given the long half-lives of both azithromycin (up to 72 hours) and hydroxychloroquine (up to 40 days), caution is warranted even when the two drugs are used sequentially instead of concomitantly.[15]

Please see Chloroquine or Hydroxychloroquine With or Without Azithromycin: Selected Clinical Data for additional details.

Adverse Effects

Chloroquine and hydroxychloroquine have a similar toxicity profile, although hydroxychloroquine is better tolerated and has a lower incidence of toxicity than chloroquine.

Cardiac Adverse Effects

- QTc prolongation, Torsade de Pointes, ventricular arrythmia, and cardiac deaths.[16] If chloroquine or hydroxychloroquine is used, clinicians should monitor the patient for adverse events, especially prolonged QTc interval **(AIII)**.
- The risk of QTc prolongation is greater for chloroquine than for hydroxychloroquine.
- Concomitant medications that pose a moderate to high risk for QTc prolongation (e.g., antiarrhythmics, antipsychotics, antifungals, macrolides [including azithromycin],[16] fluoroquinolone antibiotics)[17] should be used only if necessary. Consider using doxycycline rather than azithromycin as empiric therapy for atypical pneumonia.
- Multiple studies have demonstrated that concomitant use of hydroxychloroquine and azithromycin can prolong the QTc interval;[18-20] in an observational study, the use of hydroxychloroquine plus azithromycin was associated with increased odds of cardiac arrest.[9] The use of this combination warrants careful monitoring.
- Baseline and follow-up electrocardiograms are recommended when there are potential drug interactions with concomitant medications (e.g., azithromycin) or underlying cardiac diseases.[21]
- The risk-benefit ratio should be assessed for patients with cardiac disease, a history of ventricular arrhythmia, bradycardia (<50 bpm), or uncorrected hypokalemia and/or hypomagnesemia.

Other Adverse Effects

- Hypoglycemia, rash, and nausea. Divided doses may reduce nausea.
- Retinopathy. Bone marrow suppression may occur with long-term use, but this is not likely with short-term use.

Drug-Drug Interactions

Chloroquine and hydroxychloroquine are moderate inhibitors of cytochrome P450 (CYP) 2D6, and these drugs are also P-glycoprotein (P-gp) inhibitors. Use caution when administering these drugs with medications that are metabolized by CYP2D6 (e.g., certain antipsychotics, beta-blockers, selective serotonin reuptake inhibitors, methadone) or transported by P-gp (e.g., certain direct-acting oral anticoagulants, digoxin).[22] Chloroquine and hydroxychloroquine may decrease the antiviral activity of remdesivir; coadministration of these drugs **is not recommended**.[23]

Considerations in Pregnancy

- Antirheumatic doses of chloroquine and hydroxychloroquine have been used safely in pregnant women with SLE.
- Hydroxychloroquine exposure has not been associated with adverse pregnancy outcomes in ≥300 human pregnancies.
- A lower dose of chloroquine (500 mg once a week) is used for malaria prophylaxis during pregnancy.
- No dose changes are necessary for chloroquine or hydroxychloroquine during pregnancy.

Considerations in Children

- Chloroquine and hydroxychloroquine have been routinely used in pediatric populations for the treatment and prevention of malaria and for rheumatologic conditions.

Drug Availability

- Hydroxychloroquine, chloroquine, and azithromycin **are not approved** by the Food and Drug Administration (FDA) for the treatment of COVID-19.
- Hydroxychloroquine is approved by the FDA for the treatment of malaria, lupus erythematosus, and rheumatoid arthritis. Chloroquine is approved for the treatment of malaria and extraintestinal amebiasis. Azithromycin is commonly used for the treatment and/or prevention of nontuberculous mycobacterial infection, various sexually transmitted infections, and various bacterial infections.

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echo that its prescribing meds is

1.) misperception that /\ not allowed

2.) doctors electing not to treat? really?

3.) threatened and intimidated? really?

4.) common cold?

5.) nobody recommending we wait until deathbed

6.) I'm one of the doctors

7.) override the health authority

8.) every pharmacy takes scrips from a medical doctor