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Yale epidemiologist Harvey Risch defends hydroxychloroquine in Newsweek—badly

Yale epidemiology professor Harvey Risch published an embarrassingly bad op-ed in Newsweek defending hydroxychloroquine to treat COVID-19. It reminded me how much acupuncture and hydroxychloroquine believers have in common.

 By [Orac < https://respectfulinsolence.com/author/respectfulinsolence_ip5frq/>](https://respectfulinsolence.com/author/respectfulinsolence_ip5frq/)



[July 24, 2020 < https://respectfulinsolence.com/2020/07/24/harvey-risch-defends-hydroxychloroquine/>](https://respectfulinsolence.com/2020/07/24/harvey-risch-defends-hydroxychloroquine/)



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I'm generally a big fan of epidemiology and epidemiologists. After all, epidemiology is how we know that tobacco smoking causes cancer and that vaccines do not cause autism, sudden infant death syndrome, autoimmune diseases, diabetes, or the other conditions and diseases attributed to vaccines by antivaxxers. Epidemiology is also how we will ultimately figure out who is at most risk for serious disease, complications, and death from COVID-19 and then use that information to fine tune the public health response to the pandemic and to develop additional interventions. So I scratched my head mightily yesterday when I saw an op-ed in Newsweek by Harvey Risch, MD, PhD, a professor of epidemiology at the Yale School of Public Health entitled [The Key to Defeating COVID-19 Already Exists. We Need to Start Using It < https://www.newsweek.com/key-defeating-covid-19-already-exists-we-need-start-using-it-opinion-1519535>](https://www.newsweek.com/key-defeating-covid-19-already-exists-we-need-start-using-it-opinion-1519535). What is this “key” that Risch is talking about? [Hydroxychloroquine < https://respectfulinsolence.com/tag/hydroxychloroquine/>](https://respectfulinsolence.com/tag/hydroxychloroquine/). No, seriously, I kid you not. He's talking about what I've started calling the “acupuncture of the COVID-19 pandemic”:

As professor of epidemiology at Yale School of Public Health, I have authored over 300 peer-reviewed publications and currently hold senior positions on the editorial boards of several leading journals. I am usually accustomed to advocating for positions within the mainstream of medicine, so have been flummoxed to find that, in the midst of a crisis, I am fighting for a treatment that the data fully support but which, for reasons having nothing to do with a correct understanding of the science, has been pushed to the sidelines. As a result, tens of thousands of patients with COVID-19 are dying unnecessarily. Fortunately, the situation can be reversed easily and quickly.

I am referring, of course, to the medication hydroxychloroquine. When this inexpensive oral medication is given very early in the course of illness, before the virus has had time to multiply beyond control, it has shown to be highly effective, especially when given in combination with the antibiotics azithromycin or doxycycline and the nutritional supplement zinc.

This far into the pandemic, with double-blind, randomized, controlled clinical trials starting to be published and showing, each and every one of them so far, that hydroxychloroquine shows no benefit versus [COVID-19 < https://respectfulinsolence.com/tag/covid-19/>](https://respectfulinsolence.com/tag/covid-19/) (I'll discuss them shortly), let's just say that I am flummoxed to find, in the midst of a crisis, that a seemingly respected epidemiologist is fighting for a drug that almost certainly doesn't work based on low quality and anecdotal evidence when far higher quality evidence is becoming available and even the bulk of the observational evidence has been negative, with [one notable outlier < https://respectfulinsolence.com/2020/07/09/henry-ford-hospital-hydroxychloroquine-trial-covid-19/>](https://respectfulinsolence.com/2020/07/09/henry-ford-hospital-hydroxychloroquine-trial-covid-19/). I am even more flummoxed to find that *Newsweek* provided this epidemiologist a platform to promote this argument, particularly given how he based it primarily on a commentary and review that he wrote in May, which is basically ancient history as far as the evidence base for hydroxychloroquine goes.

Next up, Risch uses an appeal to authority—his, and that of an epidemiology journal:

On May 27, I published an article in the *American Journal of Epidemiology* (AJE) entitled, “Early Outpatient Treatment of Symptomatic, High-Risk COVID-19 Patients that Should be Ramped-Up Immediately as Key to the Pandemic Crisis.” That article, published in the world’s leading epidemiology journal, analyzed five studies, demonstrating clear-cut and significant benefits to treated patients, plus other very large studies that showed the medication safety.

This sort of appeal to the respectability of a scientific journal just makes me laugh these days. Journals far more prestigious than AJE have published utter rubbish before, for example *The Lancet*’s publication of [Andrew Wakefield](https://respectfulinsolence.com/tag/andrew-wakefield/) < <https://respectfulinsolence.com/tag/andrew-wakefield/>>’s case series and that [awful Surgisphere study](https://respectfulinsolence.com/2020/06/05/surgisphere-debacle/) < <https://respectfulinsolence.com/2020/06/05/surgisphere-debacle/>> on hydroxychloroquine in May. I could go on and name many other bad or even fraudulent papers in many other journals, but instead I’ll just refer to [Retraction Watch](https://retractionwatch.com/) < https://retractionwatch.com> for a sampling. The point is simple. Being published in a respected journal is not a guarantee of quality or that the study is even right. Indeed, I often point out that the highest profile journals, the ones that publish the most bleeding edge research, probably have a higher rate of studies that turn out to be wrong, because that’s what happens on the bleeding edge of science. Surely the eminent Prof. Risch knows this, but he makes the appeal anyway.

Since Prof. Risch referenced his own opinion article in AJE, I figured that I had to go and take a look at it. At this point, *Newsweek* annoyed the crap out of me because there was no direct link to the article, forcing me to go to the extra step of Googling its title and finding the article. Come on, *Newsweek*! It’s 2020! There’s no excuse for not including a direct link to the source and hasn’t been for at least a decade! Here, by the way, is the [direct link](https://academic.oup.com/aje/article/doi/10.1093/aje/kwaa093/5847586) < <https://academic.oup.com/aje/article/doi/10.1093/aje/kwaa093/5847586>>. At this point, I would also like to point out that Prof. Risch is on the [editorial board of AJE](https://academic.oup.com/aje/pages/Editorial_Board) < [https://academic.oup.com/aje/pages/Editorial Board](https://academic.oup.com/aje/pages/Editorial_Board)>, a fact conveniently not mentioned in his *Newsweek* op-ed that is highly relevant, given that editorial board members can exercise a lot of influence on what gets published in a journal.

Reading the article, I was struck at how weak the arguments were. Prof. Risch basically tries to compare hydroxychloroquine to remdesivir, which I discussed nearly three months ago, when the results of the first randomized clinical trial (RCT) was announced, in essence, by press release. And, guess what? I'm **not that impressed with the evidence** <
<https://respectfulinsolence.com/2020/05/01/remdesivir-gilead-wins/>> for remdesivir's efficacy against COVID-19, either! Prof. Risch argues:

More specific for consideration here, remdesivir has not been studied in outpatient use. The Scientists to Stop Covid-19 “secret” Report (12, p. 7) recommends widespread use of remdesivir, and “as early in infection as possible,” but no actual evidence as yet shows in humans that it would be helpful for routine outpatient circumstances and disease. The FDA recently approved use of remdesivir in the current public-health emergency circumstances (13), but only for patients with “severe disease defined as SpO₂≤94% on room air, requiring supplemental oxygen, mechanical ventilation, or extracorporeal membrane oxygenation (ECMO)” and “administered in an in-patient hospital setting via intravenous (IV) infusion by a healthcare provider.” This approval seems specifically not to allow outpatient use. Symptomatic outpatient infection is a pathologically and clinically different disease than the life-threatening inpatient acute respiratory distress syndrome caused by SARS-CoV-2, thus there is little reason to think that the same treatment would be useful for both (14).

Funny, though, until recently, hydroxychloroquine cultists were claiming that the drug would be effective against COVID-19 in seriously ill hospitalized patients and then, as evidence accumulated that it isn't, pivoted to the argument that it has to be given as early as possible in order to work. Clearly, there is a double standard at work here that Prof. Risch is not acknowledging. (We wouldn't want to suggest that goalposts are being moved, would we?) Moreover, his argument is bullshit, plain and simple. If a drug strongly inhibits coronavirus replication, there's no reason that it **couldn't** be effective both in advanced disease and in early disease—or even as a prophylactic treatment to prevent infection. It's true that it might not work as well (or at all) in **all** those situations, and it's even true that one treatment is unlikely to work as well (or at all) in all those clinical situations, but there's no *a priori* scientific reason to make the blanket declaration that one treatment can't possibly be useful in both situations.

Think of it this way. The life-threatening inpatient acute respiratory distress syndrome caused by SARS-CoV-2 is on a continuum of disease, not a completely different disease, from symptomatic outpatient infection. In any event, I also agree that, because remdesivir hasn't been studied in outpatient use, its use in outpatients is currently not that well supported, but, then, it is an intravenous medication only at present, making this argument rather a straw man, a red herring.

The rest of Prof. Risch's AJE article is a veritable Gish gallop of cherry-picked studies. hilariously, he relies heavily on uncontrolled "studies" and case series from two grifters, Didier Raoult and Vladimir Zelenko. I've written about Didier Raoult, a "brave maverick" [true believer in his combination of hydroxychloroquine and azithromycin and a bully](https://respectfulinsolence.com/2020/04/14/didier-raoult-bad-science-bully/) <https://respectfulinsolence.com/2020/04/14/didier-raoult-bad-science-bully/>, on several occasions, starting with his [truly execrable study](https://sciencebasedmedicine.org/are-hydroxychloroquine-and-azithromycin-an-effective-treatment-for-covid-19/) <https://sciencebasedmedicine.org/are-hydroxychloroquine-and-azithromycin-an-effective-treatment-for-covid-19/> claiming that his combination of hydroxychloroquine and azithromycin cleared coronavirus in all patients. None of these studies were controlled or randomized. Unbelievably, Prof. Risch cites Raoult's case series of 1,061 COVID-19 patients as though it were anything but [singularly uninformative](https://sciencebasedmedicine.org/hydroxychloroquine-and-azithromycin-versus-covid-19/) <https://sciencebasedmedicine.org/hydroxychloroquine-and-azithromycin-versus-covid-19/> and [useless](https://scienceintegritydigest.com/2020/03/30/an-observational-study-without-a-control-group/) <https://scienceintegritydigest.com/2020/03/30/an-observational-study-without-a-control-group/> for evaluating whether his drug combination is effective against COVID-19.

That's not the most embarrassing thing in Prof. Risch's article, though. This is:

The first study of HCQ+AZ (24) was controlled but not randomized or blinded, and involved 42 patients in Marseilles, France. This study showed a 50-fold benefit of HCQ+AZ vs standard-of-care, with P -value=.0007. In the study, six patients progressed, stopped medication use and left the trial before the day-6 planned outcome measure of swabsampled nasopharyngeal viral clearance. Reanalysis of the raw study data elsewhere (25) and by myself shows that including these six patients does not much change the 50-fold benefit. What does change the magnitude of benefit is presentation with asymptomatic or upper respiratory tract infection, vs lower respiratory-tract infection, the latter cutting the efficacy in half, 25-fold vs standard-of-care. This shows that the sooner these medications are used, the better their effectiveness, as would be expected for viral early respiratory disease. The average start date of medication use in this study was day-4 of symptoms. This study has been criticized on various grounds that are not germane to the science, but the most salient criticism is the lack of randomization into the control and treatment groups. This is a valid general scientific criticism, but does not represent epidemiologic experience in this instance. If the study had shown a 2-fold or perhaps 3-fold benefit, that magnitude of result could be postulated to have occurred because of subject-group differences from lack of randomization. However, the 25-fold or 50-fold benefit found in this study is not amenable to lack of randomization as the sole reason for such a huge magnitude of benefit. Further, the study showed a significant, 7-fold benefit of taking HCQ+AZ over HCQ alone, P -value=.035, which cannot be explained by differential characteristics of the controls, since it compares one treatment group to the other, and the treated subjects who received AZ had more progressed pneumonia than the treated subjects receiving HCQ alone, which should otherwise have led to worse outcomes. The study has also been described as “small,” but that criticism only applies to studies not finding statistical significance. Once a result has exceeded plausible chance finding, greater statistical significance does not contribute to evidence for causation (26).

I had a hard time believing that an actual professor of epidemiology at a school as reputable as Yale could write such drivel. The study he is referring to is Gautret et al., a study [so awful < https://scienceintegritydigest.com/2020/03/24/thoughts-on-the-gautret-et-al-paper-about-hydroxychloroquine-and-azithromycin-treatment-of-covid-19-infections/](https://scienceintegritydigest.com/2020/03/24/thoughts-on-the-gautret-et-al-paper-about-hydroxychloroquine-and-azithromycin-treatment-of-covid-19-infections/), [so full of flaws < https://sciencebasedmedicine.org/are-hydroxychloroquine-and-azithromycin-](https://sciencebasedmedicine.org/are-hydroxychloroquine-and-azithromycin-)

Since publication of my May 27 article, seven more studies have demonstrated similar benefit. In a lengthy follow-up letter, also published by AJE, I discuss these seven studies and renew my call for the immediate early use of hydroxychloroquine in high-risk patients. These seven studies include: an additional 400 high-risk patients treated by Dr. Vladimir Zelenko, with zero deaths; four studies totaling almost 500 high-risk patients treated in nursing homes and clinics across the U.S., with no deaths; a controlled trial of more than 700 high-risk patients in Brazil, with significantly reduced risk of hospitalization and two deaths among 334 patients treated with hydroxychloroquine; and another study of 398 matched patients in France, also with significantly reduced hospitalization risk. Since my letter was published, even more doctors have reported to me their completely successful use.

This is painful to read. Seriously, this is an epidemiologist? Apparently so, but he's an epidemiologist who confuses correlation with causation:

Beyond these studies of individual patients, we have seen what happens in large populations when these drugs are used. These have been “natural experiments.” In the northern Brazil state of Pará, COVID-19 deaths were increasing exponentially. On April 6, the public hospital network purchased 75,000 doses of azithromycin and 90,000 doses of hydroxychloroquine. Over the next few weeks, authorities began distributing these medications to infected individuals. Even though new cases continued to occur, on May 22 the death rate started to plummet and is now about one-eighth what it was at the peak.

A reverse natural experiment happened in Switzerland. On May 27, the Swiss national government banned outpatient use of hydroxychloroquine for COVID-19. Around June 10, COVID-19 deaths increased four-fold and remained elevated. On June 11, the Swiss government revoked the ban, and on June 23 the death rate reverted to what it had been beforehand. People who die from COVID-19 live about three to five weeks from the start of symptoms, which makes the evidence of a causal relation in these experiments strong. Both episodes suggest that a combination of hydroxychloroquine and its companion medications reduces mortality and should be immediately adopted as the new standard of care in high-risk patients.

An Epidemiology 101 student should be able to dismantle the argument above. This is the sort of argument antivaxxers make, such as that the expansion of the vaccine schedule in the early 1990s was followed by a rise in the prevalence of autism, or claims that nations with more vaccines in their recommended schedule have higher infant mortality rates. The question to ask is: What else happened around the times that the magic drug hydroxychloroquine was disbursed to Pará or taken away from Switzerland? But, no. Whatever changes in COVID-19 mortality we're observed must be due to the magic drug. Also, which is it? I thought that the addition of azithromycin, zinc, or doxycycline to the hydroxychloroquine was important!

It amuses me that on the very same day that Prof. Risch published his Newsweek op-ed, the *New England Journal of Medicine* published a [clinical trial < https://www.nejm.org/doi/full/10.1056/NEJMoa2019014>](https://www.nejm.org/doi/full/10.1056/NEJMoa2019014) of 667 patients with mild-to-moderate COVID-19 randomized to receive placebo or hydroxychloroquine (with and without azithromycin, yet!), with the primary outcome being clinical status at 15 days. Can you guess what the result was? (Sure, I knew you could.) It was completely negative. But, wait! I can see Prof. Risch countering with the observation that this was a trial of hospitalized patients. We have that covered too! One week ago yet another randomized controlled trial of hydroxychloroquine was [published in *Clinical Infectious Diseases* < https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa1009/5872589>](https://academic.oup.com/cid/article/doi/10.1093/cid/ciaa1009/5872589). It was a Spanish trial of 293 non-hospitalized patients with mild COVID-19, exactly the sort of study that Prof. Risch wanted. Guess what? It was negative. No benefit was observed with HCQ beyond the usual care. It is true that both of these studies did have one significant weakness, namely that they were both open label, but an open-label randomized trials are still way better in terms of determining the efficacy of a drug than any of the crappy observational studies cited by Prof. Risch to argue that everyone should be getting hydroxychloroquine now. One could even argue that the trials were underpowered to detect smaller effects, but Prof. Risch is not claiming small effects on mortality. Here's claiming that hydroxychloroquine is a game changer that could save hundreds of thousands of lives!

This study was only the latest in the [drip-drip-drip of negative studies < https://sciencebasedmedicine.org/hydroxychloroquine-ebm-sbm/>](https://sciencebasedmedicine.org/hydroxychloroquine-ebm-sbm/) of hydroxychloroquine. Before that, there was the publication of a [randomized controlled clinical trial of the drug as post-exposure prophylaxis <](#)

<https://www.nejm.org/doi/full/10.1056/NEJMoa2016638>> that was entirely negative. This was followed by two more, first, a [Spanish post-exposure prophylaxis trial < https://www.sciencemag.org/news/2020/06/three-big-studies-dim-hopes-hydroxychloroquine-can-treat-or-prevent-covid-19](https://www.sciencemag.org/news/2020/06/three-big-studies-dim-hopes-hydroxychloroquine-can-treat-or-prevent-covid-19)> that was also negative. Then there was the [Recovery Trial < https://www.recoverytrial.net/files/hcq-recovery-statement-050620-final-002.pdf](https://www.recoverytrial.net/files/hcq-recovery-statement-050620-final-002.pdf)> from the UK, which failed to find a benefit from hydroxychloroquine in hospitalized patients treated with the drug, leading to the revocation of the EUA.

Prof. Risch notes:

First, as all know, the medication has become highly politicized. For many, it is viewed as a marker of political identity, on both sides of the political spectrum. Nobody needs me to remind them that this is not how medicine should proceed. We must judge this medication strictly on the science. When doctors graduate from medical school, they formally promise to make the health and life of the patient their first consideration, without biases of race, religion, nationality, social standing—or political affiliation. Lives must come first.

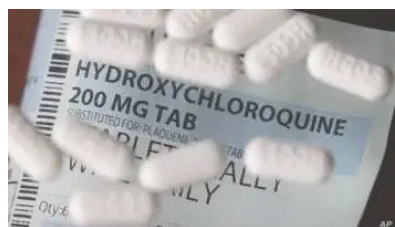
I agree that the issue has become politicized, but who caused the politicization? It was clearly the hydroxychloroquine cultists associated with Donald Trump and, indeed, Donald Trump himself. I also agree that we must judge this medication strictly on the science, which is why I conclude that there was no scientific or ethical reason for hydroxychloroquine to become a de facto standard of care for COVID-19 before proper randomized controlled trials were completed showing benefit.

Prof. Risch concludes by destroying yet another one of my irony meters:

In the future, I believe this misbegotten episode regarding hydroxychloroquine will be studied by sociologists of medicine as a classic example of how extra-scientific factors overrode clear-cut medical evidence. But for now, reality demands a clear, scientific eye on the evidence and where it points. For the sake of high-risk patients, for the sake of our parents and grandparents, for the sake of the unemployed, for our economy and for our polity, especially those disproportionally affected, we must start treating immediately.

The first two sentences could have been written by me. No, really, they could. I've been saying how politics and ideology have overridden the science when it comes to hydroxychloroquine. The difference is that I come to exactly the opposite conclusion, namely that it was the hydroxychloroquine cultists who were driving the use of this medication in the absence of any good evidence (or even a powerful scientific rationale) for its efficacy. (Indeed, one recent in vitro paper showed that chloroquine (a drug highly related to hydroxychloroquine) **can't inhibit infection of human lung cells** < <https://www.nature.com/articles/s41586-020-2575-3>> with SARS-CoV-2, and a recent primate study shows that hydroxychloroquine **doesn't protect against infection** < <https://www.nature.com/articles/s41586-020-2558-4>> with SARS-CoV-2.)

I'd be willing to bet that Prof. Risch has no idea how the idea that the antimalarial drugs chloroquine or hydroxychloroquine might have efficacy against COVID-19; so I'll repeat the story to show just how flimsy the evidence base was. Based on an observation of 80 patients full of confirmation bias, Chinese doctors in Wuhan noted that no patients with lupus erythematosus became ill with COVID-19 and hypothesized that the chloroquine or hydroxychloroquine that they were taking might be the reason. (These drugs are also mildly immunosuppressive, hence their use to treat autoimmune diseases.) Of course, during a pandemic, it is people who are immunosuppressed are the very people who most rigorously obey orders to practice social distancing and self-quarantine and thereby protect themselves from infection. Be that as it may, the Chinese doctors started using the antimalarial drugs, and anecdotal evidence of success was reported, leading to randomized clinical trials that were announced by the Chinese government to have been "promising." None of this stopped China from incorporating these drugs into its recommended regimen. The World Health Organization followed suit, as did several countries, and thus was **born a new de facto standard of care** < <https://respectfulinsolence.com/2020/04/03/zelenko-smith-abandoning-evidence-based-medicine-for-covid-19/>> for COVID-19 based on, in essence, no evidence other than some in vitro evidence that the drugs inhibit replication of SARS-CoV-2, the virus that causes COVID-19, anecdotes, and incredibly weak clinical trial evidence. Now the randomized clinical trial evidence is starting to accumulate, and it's basically in line with the very low prior probability that these antimalarial drugs could be effective against COVID-19



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<https://respectfulinsolence.com/2020/05/22/cult-of-hydroxychloroquine-versus-arrhythmias/>>

The cult of hydroxychloroquine versus dangerous arrhythmias <
<https://respectfulinsolence.com/2020/05/22/cult-of-hydroxychloroquine-versus-arrhythmias/>>

May 22, 2020

In "Bad science"



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<https://respectfulinsolence.com/2020/07/09/henry-ford-hospital-hydroxychloroquine-trial-covid-19/>>

Henry Ford Hospital hydroxychloroquine trial: Not good evidence that the drug works for COVID-19 <

<https://respectfulinsolence.com/2020/07/09/henry-ford-hospital-hydroxychloroquine-trial-covid-19/>>

July 9, 2020

In "Clinical trials"



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<https://respectfulinsolence.com/2020/04/03/zelenko-smith-abandoning-evidence-based-medicine-for-covid-19/>>

Drs. Vladimir Zelenko and Stephen Smith: Abandoning evidence-based medicine to promote unproven drugs for COVID-19 <

<https://respectfulinsolence.com/2020/04/03/zelenko-smith-abandoning-evidence-based-medicine-for-covid-19/>>

April 3, 2020

In "Bad science"

By Orac

Orac is the nom de blog of a humble surgeon/scientist who has an ego just big enough to delude himself that someone, somewhere might actually give a rodent's posterior about his copious verbal meanderings, but just barely small enough to admit to himself that few probably will. That surgeon is otherwise known as [David Gorski](https://www.sciencebasedmedicine.org/editorial-staff/david-h-gorski-md-phd-managing-editor/) <
<https://www.sciencebasedmedicine.org/editorial-staff/david-h-gorski-md-phd-managing-editor/>>.

That this particular surgeon has chosen his nom de blog based on a rather cranky and arrogant computer shaped like a clear box of blinking lights that he originally encountered when he became a fan of a 35 year old British SF television show whose

special effects were renowned for their BBC/Doctor Who-style low budget look, but whose stories nonetheless resulted in some of the best, most innovative science fiction ever televised, should tell you nearly all that you need to know about Orac. (That, and the length of the preceding sentence.)

DISCLAIMER:: The various written meanderings here are the opinions of Orac and Orac alone, written on his own time. They should never be construed as representing the opinions of any other person or entity, especially Orac's cancer center, department of surgery, medical school, or university. Also note that Orac is nonpartisan; he is more than willing to criticize the statements of anyone, regardless of political leanings, if that anyone advocates pseudoscience or quackery. Finally, medical commentary is not to be construed in any way as medical advice.

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Up ↑

[an-effective-treatment-for-covid-19/>](#) (and [maybe even fraudulent < https://forbetterscience.com/2020/03/26/chloroquine-genius-didier-raoult-to-save-the-world-from-covid-19/>](#)), that it was quite properly dragged on science and medical Twitter for days and weeks afterward. That Prof. Risch would cite such an abomination of science tells you all you need to know about him.

Next, Prof. Risch cites Vladimir Zelenko. No, seriously, an epidemiologist is citing an unethical case series that hadn't even been published yet in May. The link he provides in the citation is a [link to a Google Documents page < https://docs.google.com/document/d/1pJgHlqIZuKOziN3txQsN5zz62v3K043pR3DdhEmcos/>](#) that no longer exists and was last accessed in April. I suspect that this was probably the same spreadsheet of patients that Zelenko had posted in early April that [looked like this < https://i.maga.host/b4wRjtt.jpeg>](#). I'm now leaning towards Prof. Risch's commentary having not been peer-reviewed, because if an AJE peer reviewer let an author cite a link to a Google Document and call it a "two-page report," its peer review sucks, and its editor should be ashamed of himself for publishing this. Zelenko's [evidence is so crappy < https://respectfulinsolence.com/2020/04/03/zelenko-smith-abandoning-evidence-based-medicine-for-covid-19/>](#) that anyone citing it seriously should be thoroughly mocked.


The fourth study cited by Prof. Risch is the Prevent Senior study carried out in Brazil. It, too, was an awful study, as [outlined by Elisabeth Bik < https://scienceintegritydigest.com/2020/04/18/thoughts-on-the-prevent-senior-study/>](#). There was no randomization and no good documentation if the patients actually had COVID-19 or not. The two groups compared were not equally sick, and the reasons for hospitalizations and deaths were not listed. Moreover, the study was performed by an insurance company in Brazil which was promoting its telemedicine app for COVID-19:



Dr Gaetan Burgio, MD, PhD. @GaetanBurgio · Apr 18, 2020


Replying to @GaetanBurgio

Now there are others issues with this study.
1/ Clinical trial was registered 2 days ago and they are not yet recruiting



Efficacy and Safety of Hydroxychloroquine an...
Efficacy and Safety of Hydroxychloroquine and


Efficacy and safety of Hydroxychloroquine and Azithromycin for the Treatment of Ambulatory...
clinicaltrials.gov

 **Dr Gaetan Burgio, MD, PhD.**
 @GaetanBurgio

2/ The study is performed from an insurance company in Brazil which has promoted its telemedicine application for [#COVID19](#) ! So they have an interest to show efficacy of telemedicine against COVID19. the fact they have declared no COI is a joke

preventseneior.com.br/detalhes_notic...


5:16 AM · Apr 18, 2020 


 207  See the latest COVID-19 information on Twitter

Seriously, this is embarrassing. Prof. Risch's article should really be retracted. It's that bad. The [comments < https://academic.oup.com/aje/article/doi/10.1093/aje/kwaa155/5873637?searchresult=1> published about it < https://academic.oup.com/aje/article/doi/10.1093/aje/kwaa151/5873638>](#) were deservedly scathing, and Prof. Risch's [responses to the criticisms < https://academic.oup.com/aje/article/doi/10.1093/aje/kwaa152/5873640>](#) were downright embarrassing, basically doubling down and dismissing valid criticisms, while pulling the "delay can't be tolerated during a pandemic" gambit.

But back to the [Newsweek op-ed < https://www.newsweek.com/key-defeating-covid-19-already-exists-we-need-start-using-it-opinion-1519535>](#) :


Hydroxychloroquine to is the acupuncture of the COVID-19 pandemic. What do I mean by that? Like [acupuncture <https://respectfulinsolence.com/tag/acupuncture/>](https://respectfulinsolence.com/tag/acupuncture/), hydroxychloroquine is an intervention with a very low prior plausibility (although, in fairness, the prior plausibility of acupuncture is much lower than even that of hydroxychloroquine) whose cultists behave just like acupuncture cultists when it comes to evidence. They believe their magic treatment works; so, like acupuncturists, they tend to downplay accumulating evidence from double-blind, placebo-controlled trials and point to much poorer quality observational studies, while making excuses like these, described for a similar situation, the use of [vitamin C to treat cancer <https://respectfulinsolence.com/tag/vitamin-c/>](https://respectfulinsolence.com/tag/vitamin-c/):



Mark Hoofnagle @MarkHoofnagle · Apr 6, 2020
 

Replying to @MarkHoofnagle

But it does speak to an interesting phenomenon - that of physicians who seem willing to sacrifice credibility to get public attention for sloppy work. The behavior is quite cranky, and I'm sure the defense against negative studies will be claims of persecution and conspiracy.






Mark Hoofnagle
 @MarkHoofnagle


The usual, and inevitable progression will be (same as vit C bugs) that the “miraculous” therapy:


1. Only works if given early (the missed window excuse)
2. Only works in ‘x’ clinical subset
3. Only works with higher dose (when a little fails, give more!)

...

9:40 AM · Apr 6, 2020 

 40
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Mark Hoofnagle
@MarkHoofnagle

4. Is immune to study by academics because they're owned by pharma and there is no money to be made on generic
5. 6. Doesn't work to treat severe disease but merely progression of the disease (modified missed window)

...

9:40 AM · Apr 6, 2020



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...



Mark Hoofnagle
@MarkHoofnagle

6. Can't be studied further and pound the table, yell efficacy is established and it's a crime not to give it a try because it might save some lives we just don't know which ones.
7. You would want it to be used on *your* loved one if your choice at a chance to save their life.

9:40 AM · Apr 6, 2020



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Mark Hoofnagle
@MarkHoofnagle

Basically, endless excuses followed by yelling and then emotional blackmail.

You know, like how scientists do.

9:43 AM · Apr 6, 2020



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Because I'm dedicated to evidence and science when it comes to medical decision making, I always concede that it is still possible that hydroxychloroquine might still be found to have some anti-COVID-19 activity, although it's becoming increasingly clear that, if there is any activity it will likely be **very** modest and require large clinical trials to detect, to the point where it'll probably be clinically insignificant. That being said, it's amazing how much believers in acupuncture, vitamin C to treat cancer, and hydroxychloroquine to treat COVID-19 have in common.

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