

Fluvoxamine - The backstory

The inside story behind how fluvoxamine became a COVID therapy

By Steve Kirsch

Last updated: June 3, 2021

This document describes the background on how fluvoxamine came to be a treatment for COVID. See [Fluvoxamine FAQ](#) for information on using fluvoxamine for COVID.

Why did you write this document?

Two reasons:

- 1) To give people a sense for what it takes to make a significant difference in our world. In a nutshell, never giving up, 16 hour days, 7 days a week for more than a year. Well over 10,000 emails. It was like running an obstacle course full time where each challenge appeared to be insurmountable and you are a “nobody” in the industry. This document only captures a small portion of the challenges.
- 2) To bring to the table what is very wrong with the medical system today and suggest ways we can improve it. What happened to fluvoxamine is not an isolated incident. The systems need to be fixed.

We have today what is perhaps one of the greatest unnecessary losses of life in human history and it's important to understand why this happened and how to fix it. Had the medical system acted promptly on the compelling evidence on the table, hundreds of thousand could have been saved.

In a nutshell, the fundamental problem is the medical community is set up to be very careful in approving new treatments. The criteria used, test in a sufficient number of patients to ensure the treatment is both safe and effective, is fine for normal times. But for a pandemic which has killed 500,000 people and for a repurposed drug with a 37 year safety record, the rules should be more accomodating. There are two problems:

1. The medical community hasn't really considered how the rules should change in such a situation, so the old rules still apply.
2. The medical community has not seriously looked at all the evidence on the table for fluvoxamine. They think there are at most two randomized studies. I don't know of anyone who has looked at all the evidence listed in the [FAQ](#).

This evidence was available to everyone on December 1, but nobody other than one reporter (Esther Landhuis) was interested in hearing the evidence (in this case, learning what happened

at Golden Gate Fields): not the press, not the mainstream medical community. Even after both papers were published in peer reviewed journals as “Editor’s Choice”, there was no change in behavior; it was ignored. A few academic institutions did look at the data, found no issues, but concluded that it wasn’t worth the reputational risk to even change the practice guidelines to allow “shared decision making.” Most academic institutions refused to even look at the evidence because there wasn’t a phase 3 trial.

[Two doctors wrote a very compelling opinion article on using fluvoxamine now that will be published in a medical journal \(CMJ\)](#) soon. “Fluvoxamine is among the very few drugs that have demonstrated therapeutic potential and safety profile in a double-blind, randomized clinical trial in humans.”

I doubt that either FDA or the NIH Guidelines Committee will make a determination that the evidence merits widespread adoption until the Phase 3 trial completes sometime in June, despite the very compelling evidence that fluvoxamine will save many lives and cost none.

The Lenze RCT result was made publicly available on Oct 6, 2020 and confirmed by the Seftel study which had readouts as early as December 1. We’ve been sitting on that evidence since then.

It’s a major fault of our medical system that we cannot engage a respected panel to opine on all the evidence on the table and make a recommendation. Such panels require Phase 3 data before they will consider the evidence. This results in a tragic waste of human lives while we wait months to accrue patients (with no help from public health officials) because if they did look at all the data, I’m sure they would be convinced. For example, a [key opinion leader panel \(composed of experts from NIH, CDC, and leading academic institutions\) met on Jan 22, 2021](#) and after just one hour of looking at just a subset of the evidence, voted by more than a 2:1 margin to recommend “shared decision making” for the use of fluvoxamine for COVID.

What is a timeline of key events?

2019

Feb 6: University Virginia Sepsis paper calls out fluvoxamine as inhibitor of inflammation (Alban Gaultier’s Laboratory)

2020

March 25: Reiersen emails Lenze with idea to “repurpose SSRIs for COVID...especially fluvoxamine” [based on the Gaultier paper](#)

April 10: Lenze starts trial and recruits first participant

May 6: [Paris psych hospital observation](#) published showing 3.5X lower rate for patients vs staff

May 23: Lenze applies to CETF for funding (and gets call 1 hour later - on a Saturday)

June 20: CETF funds Lenze for \$67K

Aug 7: Nicolas Hoertel first publishes [paper on SSRIs being protective](#) (France)

August 24: Lenze reports Phase 2 results in private email to Kirsch

Oct 6: Reiersen first publicly tells the world it worked 100% at ISIRV-avg virtual conference. Nobody cares. [No press coverage even with CETF press release](#).
Nov 9: CETF funds Lenze phase 3 trial for \$500K
Nov 12: [JAMA publishes Lenze Phase 2](#)
Nov 12: [Mass COVID outbreak is known at GGF](#)
Nov 12: Steve Kirsch gives talk on CETF to Harvard Business School hosted by Dr. Seftel
Nov 13: [Mass COVID outbreak at GGF is now publicly known](#)
Nov 16: Seftel, the track physician at GGF, starts FLV @ track for the workers
Dec 22: [Emory Dean Vikas Sukhatme calls publicly for doctors to talk with their patients about fluvoxamine](#) (video on the Doctor's Channel)
Dec 22: Lenze opens phase 3 trial for enrollment

2021

Jan 21: Lenze Phase 3 enrolls 130 patients
Jan 22: [KOL meeting votes over 2:1 in support](#) of shared decision making
Jan 29: CETF (using [Proxima CRO](#)) files [initial EUA paperwork with the FDA](#)
Feb 1: Seftel results [published in OFID as "Editor's Choice" confirming 100% in Lenze trial](#)
Feb 4: EUA is assigned to Division of Pulmonology, Allergy, and Critical Care
Feb 15: Phase 3 trial enrollment at 258 patients
Feb 17: [WashU revises their guidance on fluvoxamine](#) to be more neutral; now describes how doctors should prescribe it.
Feb 22: 281 patients enrolled
Feb 24: [CityHealthUC](#) starts offering fluvoxamine to COVID patients
Feb 27: 300 patients enrolled in the trial, but only 240 can be used. At this point, only 9 people met the hospitalization endpoint criteria. If those people were all from the no treatment group, that's a 7.5% hospitalization rate which means the cohort in the Phase 3 trial was much healthier than in the Phase 2 trial, making it more difficult to see a difference.
March 4: 336 enrolled
March 5: 346
March 8: 354 (the Monday after 60 Minutes aired story)
March 9: 364 enrolled.
March 9: Facebook agreed to stop blocking our ads that advertised the Phase 3 trial
March 17: 412 enrolled
March 18: FDA rejects our EUA proposal citing insufficient data.
March 24: 449

When the fluvoxamine grant proposal came to CETF for funding what do you think?

The [CETF scientific advisory board](#) thought it was a novel idea, with solid scientific rationale based on the work of Alban Gaultier at the University of Virginia. The biggest complaint was that the study was underpowered.


The researchers at WashU only needed \$67,000 to complete the trial, it was already on-going, so we decided to fund it.





CETF also funded the Phase 3 trial with help from Fast Grants, Cures Within Reach, the Skoll Foundation, and the Flu Lab. The NIH turned them down for funding the Phase 2 and Phase 3 trials.


When did you find out fluvoxamine worked?

August 24, 2020 at 2:33pm when Eric Lenze sent me an email saying he had some exciting news. I replied 18 minutes after getting the email saying I wanted to know ASAP.

STOP COVID trial completed, first look at results today

 Lenze, Eric <lensee@wustl.edu>
To Steve Kirsch 8/24/2020

 You replied to this message on 8/24/2020 2:51 PM.

Suggested Meetings + Get more add-ins

Hi Steve. We got a chance to look at primary endpoint results today from the STOP COVID (fluvoxamine) trial. They look exciting! Can I give you a call this week to discuss?

thanks
Eric Lenze

Why didn't you tell anyone starting in August about the results?

I tried, but nobody would publish the story. Either they were too busy reporting on how the vaccine would save lives or they said I should come back when the phase 3 trial was done. It took months before the WashU study was published in JAMA.

JAMA allowed the researchers to talk about the results Oct 6, 2020 when Angela Reiersen first publicly tells the world it worked 100% at ISIRV-avg virtual conference. Nobody cared. There was no press coverage even [with CETF press release](#). My tweet on the results was viewed a total of 2,300 times with only 13 hearts and 7 retweets.

← **Tweet**



Steve Kirsch @stkirsch · Oct 6, 2020

This is huge: #fluvoxamine will save lives. Announced today at isirv Virtual Conference:

CETF Press release: bit.ly/30AGfVJ

Rationale for the trial: bit.ly/3njy4Hn

Talk abstract: bit.ly/3nxdLX9

French observational study: bit.ly/34AjZws

WashU double-blind RCT trial (n=151) shows **more than an 85% reduction in hospitalization** for participants who took **Fluvoxamine** within 7 days of first symptoms from COVID-19.

THIS IS GAME CHANGING NEWS

Had this been known this earlier, we could have

saved over 900,000 lives.

We've known for 3 months from observational studies in France that people taking SSRIs had a lower intubation and death rate. But this trial now confirms that because that fluvoxamine is a potent sigma-1 inhibitor, it's the key to stopping the inflammatory cascade that leads to hospitalization and death.



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Everyone was waiting for the paper to be published in JAMA before they would report on it or act on it.

Even after the paper was finally published in JAMA (with over 160,000 views), only a few people in the media paid attention. The *NY Times* and other major media ignored it despite our attempts to interest them.

I tried updating information in the fluvoxamine page on wikipedia, but all of my edits were reversed because of the *WP:MEDRS* rule that says you cannot cite papers published in peer reviewed medical journals as evidence since that is a primary source of medical information. So results like this and any papers that have results confirming those results are not permitted.

JAMA wrote an Editor's Note telling doctors not use fluvoxamine until the phase 3 trial is done. I tried to get them to change their position.

I posted the results on Medium, but shortly thereafter, without any notice whatsoever, I got a notice that they banned me for life for posting dangerous medical information.

I posted on LinkedIn, Facebook, and Twitter, but my follower base is too small to move the needle. Friends who reposted on Facebook had their posts censored.

Quora welcomes people with different opinions so I started writing about it there in order to get the word out. My answer on Quora on [how to treat the coronavirus](#) is the top rated answer for that question. Of the over 40,000 viewers to date (February 17), 3 people said that my information was wrong because if I was right, everyone would be using fluvoxamine, it would be all over the news media, etc.

I also created [skirsch.io](#) to make information relating to fluvoxamine and COVID available.

I tried to enlist the aid of any way to reach either doctors or the public directly, but was shut down nearly every time with the lone exception of the [Doctor's Channel which published a video interview on December 22, 2020](#). The doctor channels didn't want to let the doctors who ran the trials talk about the trials until it passed Phase 3.

Going directly to large groups failed because they would tell me I should educate the doctors, not the public.

I tried writing op-eds for newspapers but was rejected everywhere, even in my local newspaper, the San Jose Mercury News. It would be too dangerous to talk about such unproven treatments. Even after we changed the byline to Dr. Seftel, they still wouldn't publish [the op-ed we had written that called public attention to the publication of the Seftel paper in OFID the next day](#).

It's now February 26, 2021 when I am writing this and the largest forum of infectious disease docs to date where we were allowed to discuss the fluvoxamine data was the KOL meeting on January 22. Total number of attendees: only 30. Total number of events: 1.

When outbreaks happened at Kaiser, nursing homes, etc., I tried to reach the doctor in charge but never got a call back. I was able to contact Irene Chavez, the person in charge of the outbreak at Kaiser, and she told her secretary to set up a meeting, but her secretary said it would be a month before she would have time to talk to me, so I said "don't bother."

I talked to several public health officials in Santa Clara, Sacramento, etc. but they basically haven't done anything to help. They wouldn't even let the public or their doctors in their county know about the clinical trial, even though it could be life saving for people (since the Phase 2 data showed it prevented hospitalization from COVID by 100%). Basically, their job is to follow whatever the CDC tells them, not make judgement calls on promoting information about drugs with compelling evidence.

Celebrities and others with large Twitter followings won't help you because they don't want to tarnish their reputation on unproved medical claims.

There are so many things I tried but nobody would listen.

I even tried to notify my neighbors using Nextdoor, but all my fluvoxamine-related posts were removed in about 24 hours after being posted. I was later able to get them restored. Kudos to Nextdoor management for doing this.

My good friend Emerald Yeh, a nine-time Emmy winner, tried to get her peers in the news media to pay attention to the “Miracle at the Racetrack” where doctor Seftel cut the hospitalization rate to 0% of every employee who took the meds. I thought it was a great human interest story... a doctor who saved lives with a drug he read about in the top medical journal. No dice. Nobody would touch the story. They didn’t want to risk spread false hopes.

I put together a slide presentation on [How to Fix the Problem](#) that details my frustration in trying to get the word out. **See Slide 24 for how I was blocked from spreading the information.**

I also talk about the problems of getting the word out in [Steve Kirsch's answer to What is the current treatment for Covid-19? - Quora](#).

The bottom line is you can’t really get the word out until one or more of the following happens:

1. The [Phase 3 fluvoxamine trial](#) completes (or there is an interim DSMB look)
2. The drug gets listed on the [NIH COVID Treatment Guidelines](#)
3. The FDA issues an EUA.
4. Howard Bauchner, editor of JAMA, writes an op-ed on how he was wrong about fluvoxamine (he said do not use it until the phase 3 trial is done)
5. Tony Fauci starts talking about fluvoxamine
6. Major media does a story to bring this drug to the public’s attention, e.g., front page story in *The New York Times*, etc. (which is highly unlikely to happen without one of the above events happening)
7. CETF launches a massive \$20M advertising campaign to get the word out (which mainstream media may refuse to run). We don’t have sufficient funds to do this.

It’s tragic that no credible body will evaluate the compelling evidence already on the table even when there is at least a 99% probability that the Phase 3 trial will be successful (see [Fluvoxamine FAQ](#) for more on this; see the answer to “Shouldn’t we wait for more evidence like the Phase 3 study results before doctors start prescribing this drug?”).

What happened at Medium?

To support my claim that this evidence has been in plain sight for over 7 months and that it was clear that the data supported action by the medical community, I offer a simple example that I am intimately familiar with: my own personal efforts to get the world’s attention to both of these drugs. For example, on October 17, 2020, I [wrote about both fluvoxamine and ivermectin in a very long article on Medium -- a 23-minute read](#). I enumerated 21 points in support of using fluvoxamine in that article. I’d like to think I made a compelling case.

A week later, when it was clear my article wasn't getting enough viewership, I wrote an email to Elemental (a Medium sister publication focused on "nearly everything under the health and wellness umbrella, so long as it's backed by science") entitled "Two drugs that can dramatically reduce the hospitalization and death rate from COVID-19... perhaps to zero" and included a link to my article. *Elemental* acknowledged my email on November 21, almost a month later in an auto-responder saying they get a lot of submissions.

Then on December 9, in response to my efforts to bring this lifesaving advice to the world's attention, Medium suspended my account, removed all the content I had written over the past 7 years, and banned me for life. In my appeal, I asked if they had any factual information supporting their contention that I was incorrect. They responded only that they believed my comments constituted elevated risk because I was making "*health claims or advice which, if acted on, are likely to have detrimental health effects on persons or public safety.*" Personal appeals made on my behalf to the CEO of Medium were denied. There was no data back then disputing my arguments and there still isn't today. To this day, I am not aware of a single shred of strong evidence showing that these drugs do not work as I claimed.

Why haven't the NIH, FDA, etc. taken action? Why haven't the docs educated the docs?

There is censorship on social media as documented above for me personally.

But it's not just me. I get emails every day from doctors who have had their content censored on YouTube and other platforms including Dr. Drew, Dr. Christy Risinger, Dr. Tess Lawrie, Dr. Pierre Kory, Dr. Mobeen Syed, Dr. Jennifer Hibberd, Dr. Andrew Hill, etc. I now have a high level contact at YouTube who was able to restore this content. Most platforms want to do their right thing, but it is difficult to do it all accurately at scale.

Larger entities don't like to take action based on limited numbers of datapoints. For fluvoxamine, we have randomized data on 277 patients. Despite a p-value of .0001, and 75% minimum effect size, scientists like to see around 1,000 patients treated before stating opinions that would be widely relied upon. I think this is a huge mistake when talking about repurposed drugs and a pandemic where 500,000 people have died. Unfortunately, there is no consensus on how the rules should be modified so we stick to the pre-pandemic set of rules.

IDSA will not review the fluvoxamine data without a Phase 3 trial.

NIH Guidelines committee will likely do nothing without Phase 3 data.

The FDA will take months to review the EUA submission and will likely wait for Phase 3 data (so they don't make a mistake).

The CDC defers to the judgment of the FDA and NIH.

You can't get it reviewed for incorporation into practice guidelines at Stanford, UCSF, etc. without Phase 3 data.

County health officials will do nothing to let docs inform the docs.

The press won't write about it until the NIH puts it on the Guidelines.

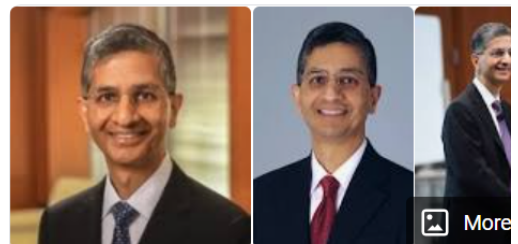
The Biden COVID task force defers to the judgement of the NIH, CDC, or FDA. All of my attempts to get them to meet with me were ignored. They did have meetings with the doctors on ivermectin which has mixed data and was given neutral reviews by the NIH and IDSA at the time. Meanwhile fluvoxamine had a 100% perfect track record of evidence and the most potential to save lives, but they would not take a meeting and they would not talk to Dr. Seftel or Lenze. There is often important information that is not always included in the published studies. For example, Dr. Seftel said [publicly on video that this is the most amazing therapeutic effect he's seen in his 25 years in medicine](#), but he can't put that in a paper. He also observed that most patients turned around in 3 days (back to normal), but they didn't do the formal analysis so it wasn't in the paper.

Frankly, it is very disappointing that the Biden task force wouldn't talk to him or any of the other researchers on the most promising drug that can dramatically reduce hospitalization and death. I find it astonishing that even today (Feb 17, 2021) with all the evidence on the table that this drug can be so game-changing for COVID that the Biden administration has done absolutely nothing to promote the Phase 3 trial of fluvoxamine. Everyone says "we have to wait for the phase 3 data", but nobody is lifting a finger to help publicize that very trial that they are so desperately waiting for. What is the public benefit to keeping this trial out of the public view? If the coronavirus is so important, why isn't President Biden uttering a word about the clinical trial of the most promising drug on the table to save people's lives?

Why is Dr. Fauci not telling anyone about the Phase 3 trial? Likely due to the limited amount of data (same reason IDSA and NIH won't talk about it).

Dean Sukhatme is a world expert on repurposed drugs and the Dean of a top medical school. And he's extremely respected with an h-score of 104 which puts him among the scientific elite (I don't know of any Med school Dean with a higher h-score, for example).

While you can ignore my calls for this drug because I lack the credentials, you have to pay



Vikas P. Sukhatme

h-index: 104

Affiliation: Emory University

Citations: 45,040

Research interests: Cancer, Immunology

attention to the only drug where a top medical school dean has called for off-label use. And where a key opinion leader panel drawn from CDC, NIH, and top academic institutions votes overwhelmingly to support off-label use (via shared decision making). Even the researchers on the drug who are very conservative and initially advised against using the drug for off-label have now [revised their guidance](#). The new guidance explains to providers who are interested in using the drug for COVID how to use it.

So the system is all set up so when you have a successful phase 2 and phase 3, people pay attention, but not before that because it is too risky of being wrong. So even if you have lots of data, all consistent, with the trials both showing a huge effect, and 99.9% or more chance of success in Phase 3 (based on quantity and quality of evidence so far), if you don't have the magical Phase 3 data, none of that matters. You could have 100 doctors, each giving out the drug with a 100% success rate for 100 patients each, and it wouldn't matter. That evidence would be considered "anecdotal" and ignored.

This is a huge mistake. The criteria for review should be based on a combination of p-value and effect size and safety, not in a phase 3 trial success, especially if it is a repurposed FDA-approved drug, and it's a pandemic! Why wait for a phase 3 study if it's more likely a failed phase 3 is due to an error rather than the drug truly being ineffective. The [Fluvoxamine FAQ](#) shows the evidence is too compelling to ignore.

Shouldn't we wait for more evidence like the Phase 3 study results before doctors start prescribing this drug? Or wait for this to be on the NIH guidelines?

It will take months for the Phase 3 trial to complete (or a DSMB review to happen). Should we wait?

The Jan 22 KOL meeting suggests not. They overwhelmingly (by more than 2:1 margin) "shared decision making" for the drug based on the evidence on the table.

We have sufficient evidence on the table today to make a determination because the benefits >> risk.

In addition, since **we can't find a comparable case with this much evidence going into the phase 3 where the phase 3 trial failed** (I have asked a lot of smart people to name one and they all failed to come up with even a single comparable example), I'd guess that the chance of the phase 3 trial failing is less than 1/10,000 meaning it doesn't make much sense to wait. At this point, if the Phase 3 trial failed, it would be more likely that the trial itself is at fault than the drug didn't work because there are simply too many "coincidences" that would have to be explained. Therefore, waiting for phase 3 is useless from a probability standpoint.

It might be useful to wait if phase 3 trials were always definitive, but they aren't. The most important example I know of is the Marik Vitamin C sepsis protocol. It was "proven" not to work because multiple phase 3 trials showed it was ineffective. However, in every case, it took longer than 24 hours to enroll patients in the trial but the protocol required that the patient be treated within 6 hours or all hope is lost. All the Phase 3 trials proved is that Marik was right about the value of early treatment in the ICU. This was an important trial to get right because 11M people die from sepsis each year and if Marik is right, we'd save 10M lives a year. But just as we put the placebo on a pedestal, we put phase 3 trials on a pedestal: they always trump less controlled data sets. Marik treated over 150 sepsis cases without reporting a single death. Nobody has been able to explain how he got so lucky when nobody else comes close.

If you were drowning and someone threw you a life preserver, would you ask "How many times has this been tested?" Probably not. You ask, "Hey can you throw me the life preserver that you think is the most reliable?" That's what fluvoxamine is. Not perfect, but the life preserver with the best evidence to date (and with a 37 year safety profile).

If our objective is to minimize the number of deaths (like our own), we should prescribe the drug(s) with the best evidence now.

If our objective is to minimize the chance that the NIH is wrong, we wait. This is of course the choice of the NIH and the medical community.

Which is more important to you personally? Saving your life? Or preserving their right:wrong ratio?

I would argue waiting is not in the public interest. It will not save lives in the interim period until a phase 3 trial is complete.

Therefore, it would be reasonable for the NIH Guidelines committee to make a temporary emergency recommendation which is later re-evaluated when the Phase 3 trial reports out. That will maximize the number of lives saved in the interim.

Have you applied for an EUA?

Yes, we filed our [initial EUA paperwork with the FDA](#) on January 29, 2021.

We hired [Proxima CRO](#) to do the filing. The entire team has been really awesome work with.

Our Pre-IND number is 154615.

On February 7, we heard that our application was assigned to the Division of Pulmonology, Allergy, and Critical Care and that it would be four weeks for the FDA to respond to our 9 questions (2 regulatory, 1 nonclinical, 5 clinical, and 1 administrative, specifically).

In the months ahead, we hope to be able to interact with the FDA via email, phone, or Zoom call, but for now, it is just a single email saying they have received our application and it was assigned.

When the FDA issued an EUA for convalescent plasma (CCP), it was done based on two randomized controlled trials that failed to show a benefit!

“At the time of the issuance of the original EUA for CCP, results from two RCTs had been published or made publicly available[1, 2]. **Both studies failed to demonstrate a significant benefit with CCP transfusion**”

<https://www.fda.gov/media/141480/download>

I think it is preposterous that a KOL panel (of experts from NIH, CDC, ...) can overwhelmingly recommend use of the drug after just a 1 hour review of just the two published studies plus a talk about the mechanisms of action (i.e., this is an obvious decision based on a very limited subset of all the data), yet it takes the FDA >4 weeks to essentially do the same thing (with no interaction allowed like in the KOL panel where they get to ask questions interactively). This is extremely inefficient and it is resulting in the unnecessary loss of human life.

My argument to the FDA is simple. The combined p-value of the two studies is <.0001 and the average effect size is 100%. Two randomized trials. Completely independently done. Both done by ULTRA high quality researchers. The drug is FDA approved for 26 years with a great safety profile. There were NO reported side effects when drug was dosed as we ask in the EUA: 50mg BID. Seftel was quasi-randomized, but the randomization was actually “better than random” (ie, he got the short end of the stick). PLUS, there is no anecdotal evidence that I’m aware of of anyone EVER getting “worse” after taking the drug. We claim sigma1 mechanism of action, which is a pathway that Francis Collins has blogged about as being super important in COVID. There are so many observational studies in support too. Stanford and UCSF just did CERNER database study and every single comparison lit up green except one (and that was close to zero effect and not statistically significant). Effect size on reduction of mortality: as high as 30%.

In short, this is about as “no brainer” as it gets.

The drug should be at the top of the priority list for an EUA due to # of lives potentially saved.

Yet it takes a week to figure out which department handles it?? Look, I realize that this is “fast” for the FDA relative to historical response times, but this is still absolutely ridiculous.

As an aside, Janet Woodcock, the interim head of the FDA is not at fault here. She's a real gem and she is helping to fix things and having success doing that. If anything, she should be given more power and ability to make changes. I really can't think of anyone in the medical area of government I have more respect for.

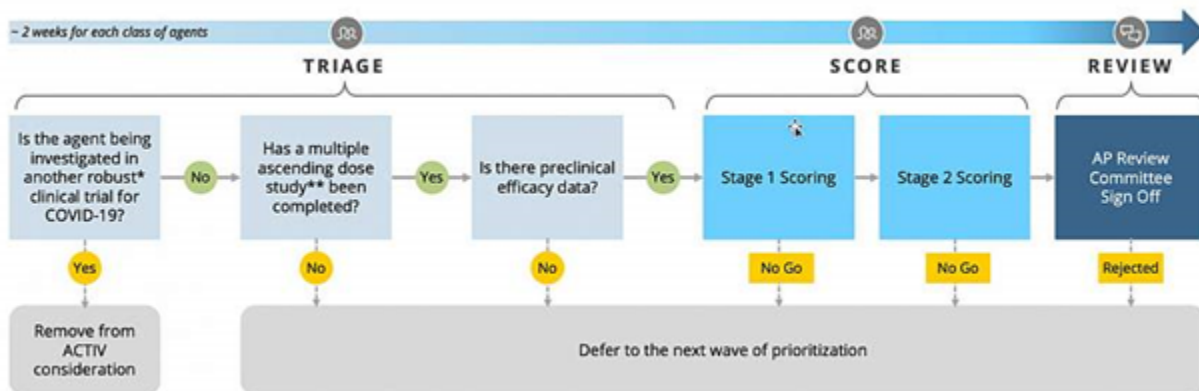
Are these problems unique to fluvoxamine?

No, ivermectin suffers from similar problems:

1. Videos are censored including the video produced the Andrew Hill, the consultant hired by the WHO to look at ivermectin
2. Academic community, NIH Guidelines panel discount the evidence and issue a "no opinion" recommendation despite overwhelming evidence of a positive benefit. It appears nothing less than a US-based Phase 3 trial is considered as evidence, yet they happily cite an observational study showing ivermectin led to premature deaths as acceptable evidence that it doesn't work. You really can't have it both ways. You are either relying on imperfect evidence or you aren't
3. Andrew Hill's paper summarizing the ivermectin data had the conclusions altered so the conclusions don't match the evidence in the paper. Hill refuses to disclose who wrote the conclusion but admits he didn't and admits it doesn't match the evidence

If the drug is so good, why isn't it in the ACTIV trial?

It doesn't qualify because the agent is already being investigated in a robust RCT.



What is the WHO doing about fluvoxamine?

Nothing.

Nobody from the WHO has contacted any of the researchers. They know about the drug because I told Jennifer Fromme, one of the project members of the project manager within the

Pandemic Influenza Preparedness Framework Secretariat at the WHO about the drug and that it was the most promising drug in the pipeline.

She expressed no interest in learning more. I have no idea what they are thinking. The original study was published in JAMA on November 12, 2020 and over 160,000 people read the paper.

Why should anyone believe you? You have no medical credentials.

True, but everything I write about can be verified. My writing is based on published studies, facts, and logical conclusions from those facts.

I am good at solving hard problems. I look for solutions from the vantage point of an MIT engineer. Given two options, drug or no drug, which choice saves the most lives? I excelled in probability and statistics, math, and science in high school and college.

You don't need an MIT degree to figure out that the evidence supporting fluvoxamine is so overwhelming that it should have been approved months ago by the NIH and FDA. This is going to be very embarrassing for those agencies and it will erode the public trust in their ability to act promptly and make good decisions that are in the public interest. The longer they take to act, the greater the more they compound the problem.

I care about saving lives. I don't care about tarnishing my reputation in the very small chance that I'm wrong. That's an important difference compared with government agencies and academic institutions where avoiding reputational risk is, by far, the most important decision-making criteria.

Organizations such as the NIH have to keep the public trust so that their advice must necessarily be conservative based on a very high level of evidence (Phase 3 trials). I don't have that constraint. I make the calculations based on the evidence we have on the table today to see which path minimizes the death rate.

Prominent academic med schools won't touch fluvoxamine (at least as of this writing on Feb 17). Not a single one has come out in support of the drug despite overwhelming positive evidence and no negative data. Why not? It's all about reputational risk. Nobody wants to be the first one.

As of February 17, 2021, there is only one medical school dean, [Dean Vikas Sukhatme of Emory](#), who is willing to speak out that doctors should talk to their patients about fluvoxamine, but he's only allowed to make that statement if he is sure to state that these are his personal views.

My sole interest is to save lives. I look at this as a straightforward math problem: “Do you save more lives if you take Drug A or Drug B?” Patrick Collison, CEO of Stripe, thinks the same way as I do. He’s been a tremendous ally in the work to fund the scientists working on the studies.

Instead of putting the placebo on a pedestal where it is the preferred treatment (even when it kills 2% of infected patients) like the medical community does today, I treat the placebo as simply a drug option. I look at the evidence for both options and I calculate which option will save more lives. It’s a math problem based on statistics that are based on studies published in peer-reviewed medical journals.

The solution was obvious: the NIH has been doing the public a huge disservice by not recommending the use of fluvoxamine. Nobody has shown me a calculation that shows otherwise.

I have been funding medical research for more than 20 years including the early research of Elizabeth Blackburn who later went on to win the Nobel Prize in Medicine.

What are others saying about this?

Scientists in the US don’t want to speak out (with rare exceptions like Vikas Sukhatme who called for docs to consult with their patients on the drug).

From a researcher in Croatia who wrote an [op-ed published in a medical journal in Croatia](#) on using fluvoxamine:

You have compiled an excellent collection of studies on the safety and efficacy of fluvoxamine in covid-19 patients. I was aware of some, but certainly not of all the papers you summarized in the FAQ.

I actually discussed the JAMA paper (a pilot RCT) with my colleague, a professor of basic pharmacology in Zagreb, who was not convinced of fluvoxamine's efficacy since the numbers of patients enrolled were too low in his opinion. We were playing with statistics (he in SPSS and I used R), and actually if you move just one hospitalized patient from the placebo group into the fluvoxamine group, you will get (disappointingly) completely different results.

He was convinced eventually when I divulged to him the results of Dr Seftel's trial (unpublished at that point, but available online in his video interview), and then we combined the patient groups from both studies (purists would say we mixed apples with oranges due to different study designs), and the result was highly statistically significant in favor of fluvoxamine (that would be your point number 3 in the FAQ).

I think that a chance that a mistake was made in the JAMA trial (misallocation of patients) together with a high bias in favor of fluvoxamine in an open label study published in OFID is very small, particularly in view of all the compiled observational data.

Considering the safety profile of fluvoxamine (as long as the prescribers are mindful of drug-drug interactions), there is certainly a strong case for off label use of fluvoxamine in covid-19 patients even before the phase III trial is finished. I recommend it regularly to my patients asking about medicines available to them in case they test covid-19 positive.

Having said all that, the medical community tends to be conservative (even slow in adopting new treatment strategies), sometimes due to inertia, often due to fear of litigation and because of institutional and/or national guidelines. Perhaps the most important reason of all is that fluvoxamine is a generic drug, thus everyone can make a copy and hence there is no large profit to be made here for a pharmaceutical company, so it is left to the (underfunded?!) academia to push this compound forward for the common good of all..

So, yes, I agree with you, the risk benefit ratio is largely in favor of use of fluvoxamine in covid-19 patients even before the phase III trial results are known. If you can pull off an early interim data analysis of the phase III collected data, and if it is in favor of fluvoxamine, publishing it quickly may be helpful.

Best wishes

Robert Likic

My linkedin page: <https://www.linkedin.com/in/robert-likic-37308447/>

Why did you start CETF?

Because I saw an important path to a solution wasn't being adequately pursued.

When the pandemic hit, I reached out to the researchers I had funded and asked for their advice for whether, as an outsider, I could make a difference. The answer was ABSOLUTELY.

Three points were clear:

1. Early treatment is key. All viruses are best treated ASAP. Therefore, waiting until people were hospitalized before treating them is a big mistake because the collateral damage can be difficult or impossible to reverse. A virus is like a fire. The sooner you put it out, the easier it is and the less permanent damage is done.
2. Repurposed drugs are the fastest and least expensive way to end the pandemic. No guarantees repurposing works for any given virus, but had the government made a one time \$20M investment in the key drugs and researchers in March of 2020, I think the pandemic would have been over in 2020 since we'd have multiple effective solutions that would make COVID no more dangerous than a common cold. There is absolutely no doubt in my mind at this point (Feb 2021) that repurposed drugs being used today for COVID were more widely deployed, we could cut the death rate by a factor of 20 or more.
3. Top researchers working on the most promising repurposed drugs were not being funded. The canary in the coal mine was camostat. The world's top experts would take camostat if they got COVID, but nobody was funding a trial for it (we were the first). The world's most cited scientist of all time (in any field) Bert Vogelstein, couldn't raise the

\$1M he needed for his trial on doxazosin, a safe drug with a clear mechanism of action, shown in observational studies to reduce the hospitalization rate from COVID by 75%.

So it was immediately clear that others were ignoring the potential for repurposed drugs to end the pandemic. I started the [COVID-19 Early Treatment Fund](#) with \$1M of my own money to address that shortcoming, recruited a [12-member scientific advisory board](#) and [volunteer staff](#), and raised another \$4M, from the Skoll Foundation, the Flu Lab, and friends. CETF funded the fluvoxamine research at WashU.

Did you really have to intervene? Wouldn't this have happened without help from an outsider?

If left to the status quo medical establishment, fluvoxamine would be dead today. The NIH turned down funding the trial and WashU researchers were out of funds before we authorized the grant that allowed them to complete the trial. Even after a successful phase 2, NIH again turned down their Phase 3 trial. We would be dead in the water if we relied on NIH.

Leaving this to the experts has resulted in hundreds of thousands of deaths today. Where was the funding for repurposed drugs? The "experts" didn't fund the camostat trials. Why not?

Camostat was known early to be a top candidate as a repurposed drug. I spoke to 6 of the top coronavirus experts at the time... camostat tied for first place for the drug they would take.

Who funded the first camostat trial in Denmark? I did. Who funded the first camostat trial in the US? CETF did.

And now we have some evidence that blocking TMPRSS2 is part of the solution [as noted here](#).

So that's why I'm not leaving this to the experts. I think the experts have done an inadequate job.

Bert Vogelstein couldn't get funding for his doxazosin trial. He needed \$1M. 75% effect size. He's the smartest guy on the planet in my opinion in the medical field. Without a doubt, he's the most cited scientist of all time in any field. He came to me for funding because he couldn't get money from NIH. We didn't have funds to fund his trial at the time (since people didn't feel comfortable donating to CETF), but we should be able to get his trial started soon thanks to another high tech guru, Patrick Collison. It is the high tech people who are making some very important contributions here.

So I think it's a mistake to dismiss help from outside the field.

Failures with the current system I experienced

500,000 people died. What did we learn from it that we will do differently the next time? This was just the dress rehearsal for the real thing (“Contagion” gives you a clue). What are we doing to learn from the mistakes we made on this one and what are we doing to prepare for the next one? Is there an on-going pandemic task force that will produce a report and be empowered to make recommendations to congress to institute changes? If not, then aren’t we destined to repeat the mistakes?

1. The biggest failure is the failure to even realize this was a failure. Why isn’t there a special full time appointed commission to make a list of issues, prioritize them, and recommend solutions to congress. to learn from this (no full time special panel ... with no lawmaker since full time job)? There is nothing!!! There is a Jan 6 task force for when 5 people died but when 600,000 people die, there is NOTHING?!?!?!?
2. the total failure of evidence-based medicine since physicians sit back and wait for the data to come to them rather than carefully analyze studies on the table.
3. FACEBOOK and other social media companies need to be regulated. Facebook removed “Covid 18 Vaccine Side effects” with over 70K member just “disappeared” without a trace. Everyone had taken a vaccine or knew someone who did. Why was this group silenced?
4. Why was V-SAFE info not being made publicly available like VAERS?
5. Why weren’t the vaccine manufacturers voluntarily disclosing the cause of the 4,200 deaths in VAERS? (there are likely many more)
6. Were the vaccine makers required to track all deaths and adverse effects when under EUA? Where is the public disclosure of this?
7. If the vaccine was so safe, why not show the analysis of the 4,200 deaths reported in VAERS? Transparency would INCREASE confidence the vaccine was safe.
8. Why was PEG not removed from the vaccine formulation. We essentially delivered spike protein everywhere including heart, brain, ovaries. PEG is a two edge sword: causes anaphylaxis on its own AND it causes widespread distribution of spike protein that should have been localized to the shoulder.
9. Why didn’t anyone speak out that we have a defective virus?
10. There were lots of signs by late may that this vaccine was dangerous; vaers showed 120X higher rate of death than other vaccines; my friends were having severe side effects: heart attack, arms shaking, numbness, etc. many debilitating. NEVER heard that before with any virus. The range of reactions was OFF THE CHARTS. Why didn’t this trigger an alert?
11. The symptoms were so subtle, people didn’t associate it with the vaccine since everyone had different symptoms.
12. Bell’s Palsy incidence was high. This should be a tip off that the vaccine wasn’t safe.
13. Why were early treatments suppressed. I told Cliff Lane about the Phase 3 trial results on May 28. He didn’t bother to respond.
14. May 28: 14 teenagers with heart problems after getting vaccine. Come on. Where’s the red flag here?

15. NIH should have made recommendations based on precautionary principle where if treatment is safe and some evidence that it works, encourage its use. NIH could have approved based on expert opinion. Why didn't this happen? The evidence was a PERFECT fit for the drug working
16. Researchers were NOT allowed to immediately repurpose their existing NIH govt grants; were denied. Had to reapply.
17. NIH recommendations are not based on "how do we minimize lives lost"
18. NOBODY wanted to fund the FLV trial. Basically CETF and FastGrants. Everyone else turned us down including NIH. The NIH didn't review the Phase 3 trial until after the DSMB met which is more than half way through 6 months after trial started.
19. For drugs approved in other countries, can only try off label in a trial which means 1 year before we have any idea if it works which is very time inefficient. So for camostat we are 1 year into it and clueless as to whether it works for outpatients.
20. Even if you doc prescribes ivermectin and fluvoxamine, the pharmacy doesn't have them because Merck is cutting supplies. We'd have better luck getting these drugs in a third world country than in the US. \$166 for Ivermectin and \$60 for Fluvoxamine from CVS
21. No PPE supply availability
22. Google and facebook block our ads for clinical trial
23. India ad agency says to do a youtube video and promote on social media but YouTube will take down any such video as a violation of their policy, even though this is a public health emergency
24. Took too long to get PCR test approved: how speed up by certifying independent labs to certify tests
25. Test turnaround is way too long (PCR is <2 hrs)
26. Testing availability should be massive so known places where can get tested
27. Early detection via oura ring like device that is inexpensive
28. How can NIH say HCQ is bad when 100% of studies show positive benefit?
29. How can NIH say IVM is neutral when 51/52 studies positive?
30. Total failure of EBM... couldn't figure out a drug works for >1 year, yet racetrack workers could tell for certain instantly in < 2 weeks by observing their colleagues. The racetrack workers got it right, determined it 1 year earlier, and were confident in their decision. Nobody had to guess. The generalization is that if patients are allowed to choose from a wide range of safe options, they will all very rapidly all zero in on the best options about 1 year faster than our top scientists can figure it out.
31. Anyone should be able to access any drug in a clinical trial in a pandemic without the mfg having to agree to it, e.g., people should be able to get leronlimab, IFN lambda
32. Takes Year to do trial since no organized patient recruitment
33. Nobody wants to enroll since 50% chance of getting placebo; much better if open label and patient chooses the option.
34. Public health not telling people about trials
35. Testing companies NOT allowed to advertise for trials on test results without user permission. Seriously? All test results should tell people to talk to doctor about the choices available
36. \$ not available to fund studies, scientists

37. Who Decide on drugs
38. FDA IND negotiation unreasonable... can delay a trial 3 months
39. FDA takes 7 weeks to answer yes/no question. Any viable drug should be able to get a realtime meeting in a few days.
40. EUA requires drug company + IND evidence
41. No exceptions to EBM dogma
42. NIH is looking into funding FLV phase 3 after it is more than halfway done
43. Infrastructure should be put in place so can just submit a drug to be study and every doctor in US must offer you free choice of the available study drugs
44. Invest up front in developing multiple generic solutions like INF lambda, GS-44... Instead Victoria is on her own
45. Create supplies of generic solutions (like GS-44...) sitting on shelf. May not be perfect but will mitigate the next one.
46. Study this one for transmission and get accurate stats on how the virus is transmitted. Masking outdoors was never needed but we still don't have definitive research
47. Process for getting drug on the "approved for choice" list... how?
48. Fund orgs like CETF who are distributed and can make rapid funding decisions. Otherwise NIH is funding bottleneck.
49. Do not require IND to get an EUA
50. Allow any doc to offer drug option not on the official list so we can collect evidence on that drug for the official list. Doctor will not have liability as long as an IRB approves the drug for testing
51. Relax the criteria for safety to allow a researcher to self test the drug on test on volunteers without violating the law
52. Objective criteria for EUA... if no one can identify confounders or bias and $p < .01$, should qualify for the mass trial. Make it objective criteria vs. FDA just "not convinced".
53. Allow any telemedicine doc to prescribe in all states.
54. Censorship, demonetization, banned for life, revoke ability to post, delete account if you say ivermectin works on email or social media. YouTube has a guideline that specifically prohibits. How spread the word.
55. I am told by media people (who want my message on FLV to be heard) to never say HCQ works in early treatment because they said it would immediately trash my credibility and people will stop listening and write me off as a nut case. This helps perpetuate the misinformation. When you repeat the same lies over and over, the sheep will believe what they are told. This has been a very effective and dangerous trick done repeatedly in history and is happening today. Hitler got away with his madness for years using such a strategy. The allies fought and eventually ended the war after extreme casualties.
56. HCQ EUA was revoked based on looking 1) at irrelevant endpoints 2) using only late stage studies (vs. outpatient). This further cements the narrative.
57. We Dismiss studies done outside US no matter who did it. Never take time to look into the details. We are Content to sit back and wait for studies from reliable sources. You need to go through the raw dataset to get to the bottom of things. That's what we have done with the Boulware, Skipper, Rajasingham (HCQ) and Lopez (IVM) studies.

58. Drugs like camostat and bromhexine that are approved in other countries should be made available for doctors in the US for testing. Doctors should be able to try repurposed drugs on their own, convince their peers to try, and if there is a signal, they should be able to advance the drug for inclusion in the full trial.
59. To limit risk, newer drugs that come into rotation can be randomized to 1% of docs so if there is any downside, quickly realized, just like software has a phased rollout.
60. ANTICOV is testing HCQ and the HIV drugs. Why not testing the top contenders?
61. Yale camostat trial: 1 year, 50 patients, interim analysis and they don't tell us what happened. This is the top drug and we're one year into the trial.
62. BARDA funding was zeroed halfway in
63. NCATS is prohibited from funding phase 3 trials
64. Low NCATS budget insufficient
65. Prioritization of drugs test was poor; camostat should have been prioritized on day 1.
66. We should be proactively developing monoclonals for all virus types, e.g., why didn't we have a coronavirus monoclonal already sitting on the shelf? \$1B investment to get monoclonals for these viruses.
67. fastest is repurposed anti-viral + anti inflammatory, we have both, but 1 year into it: no trial on the obvious combos ; lambda + flv;
68. Seftel showed treating early with flv prevented long haul in 100% of patients.... That's like flipping a coin 100 times and getting heads. Nobody looks at long-haul in their trials so we don't know if just FLV. and nobody has replicated it, but people should have jumped to replicate as soon as known.
69. This was the fire drill. We are woefully unprepared for a real fire.
70. Complacency: no team to look for confounders, bias to explain 0 hospitalization 0 long haul, but if everyone died they'd be all over it. We sit back and wait 1 year for phase 3 RCT because that's easier than having to analyze the data.
71. NIH Guidelines problems. Is David Wiseman right about his feedback on the HCQ section? Have NIH Guidelines have a public review process? Or allow open debate?
72. Have Vikas or someone similar chair the group and pick the participants. Otherwise nothing will get done while everyone argues.
73. Politicization of covid. In India, all top down and super conservative. Brazil horrible where want to ban early treatment because President says it is good. Court orders the government not to advertise early treatment. Doctors get fined in holland or jailed in Zimbabwe.
74. Need expedited right to try. If get covid, need proxalutamide instantly but by the time you can get it, it's too late so right to try doesn't work.
75. Should be able to talk about promising treatments and state FACTS in ads, e.g., in a clinical trial, xyz happened, even if drug not approved, if the phase 2 or 3 trial was under IND.
76. Shorter lead times for IND approval during pandemic, e.g., allow IRBs to approve.
77. NIH doesn't fund phase 3 trials! They fund basic research. So BARDA is supposed to fund these trials but were given \$20M and they are out of funds. So NOBODY to fund Seftel trial... including philanthropists

78. ACTIV-6 started >1 year after the pandemic! Still not launched as of may 5. Don't even know what drugs they are testing!
79. CETF can't raise funds so could afford a CRO which would have accelerated enrollment. So had to take super slow road that takes 1 year. Are we proud the govt didn't fund that? Was that the right move?
80. In short, should be a special set of rules that apply in a pandemic.
81. US Pharmacy can't provide IVM + FLV on 5/5/21. Are we a third world country? Pharmacy refusing to fill prescriptions done off-label, manufacturer limiting supplies as well.
82. Cyproheptadine got rejected in the ACTIV trials. What's the criteria here and did it get fairly rejected? Is the committee truly making decisions that are in the public interest here? Half the anecdotes have lungs
83. It's a trillion dollar problem but ACTIV lacks funds to test all the drugs it should test so had to turn down cyproheptadine
84. NO \$\$\$ for long haul trials
85. Took year till tested ivermectin and fluvoxamine
86. Mfg and pharmacy refuse to supply the drugs docs prescribe en mass. HOw does that help save lives?
87. How can HCQ have 29/0 positive rating and not get an EUA + NIH recommendation? If you look at the ACTUAL skipper data, you find the error. Did the FDA ever ask for the Boulware data before revoking the EUA?
88. Give out \$\$ to orgs like CETF to distribute
89. **Law change:** A patient should have a right to request and be treated with an approved drug used off-label if and only if there the patient can produce a published study that supports its use where benefits>risks?
90. Incentives needed to trial repurposed drugs
91. Selection criteria for drugs to test
92. Centralized control vs. random studies
93. Existing network for outpatient clinical trial
94. Next pandemic: encourage docs to try things and report in so lots of experiments to find a "signal" + test combinations. Or simply have 1000 arm trial forget placebo at this point... race to best outcomes
95. Have 10 different groups independently making hypothesis for what to test

From vikas:

Couldn't agree with you all more. Lots of good points here.

The robotic/slavish adherence to EBM stifles creativity and innovation but it is the legally safe and peer approved way to practice medicine. My contribution to understanding the cause of preeclampsia came from

observations in a single patient later supported by data in more patients. I tell medical students to keep their eyes on outliers, interesting cases, etc. I also encourage them to read the key EBM studies many of which actually excluded patients in categories they are treating!

And, in a pandemic, you would have thought that as a society we would have encouraged “exploration” but for the most part not so in the US. And that has had implications the US does not realize. The first question the Indian authorities ask is : “Why are you suggesting these ideas to us and not adopting these guidelines in the US?”

Another related point – the UF group trying adenosine for COVID got compassionate use approval for 2 patients and now their pharmacy is balking. Do a trial they say. Then, the IRB says get FDA exemption or file full IND – if they do not get the latter, they are more or less stuck as few academic places have such ability and resources! Here again, we have a system failure. The FDA has just written to us not allowing an exemption on a small ivermectin trial I wrote and was willing to fund aimed at deeply interrogating with sophisticated assays the human response to the drug in COVID patients.

Worth writing up somewhere with all the points in this email thread and more?? Ladapo has covered many of these points perhaps already but is it worthwhile reiterating? Anyone take the lead and I am willing to sign.

What are the most important key messages you want people to know?

1. **There should be a committee of experts, appointed by President Biden, to make recommendations for changes that need to be made so we are much better prepared for a more malevolent virus (such as the fictional one in the movie Contagion).**
2. **We do not need to wait for more data; waiting for more data will cost far more lives than it will ever save.** Fluvoxamine is a safe and effective drug that can significantly reduce hospitalization and fatality rates, but we'll only see the numbers go down if doctors start prescribing it. If everyone used just fluvoxamine when they are diagnosed with COVID, we could likely cut the hospitalization and death rate by 75% or more which would be a huge saving of human life. But without either NIH or FDA approvals, doctors will be reluctant to go against the published guidelines.
3. **We should be testing these drugs that work on outpatients on inpatients now.** But no hospital seems interested in opening such a study, even if we will supply all the funding.
4. **The FDA needs a more efficient process to evaluate repurposed drugs submitted for an EUA.** Our application for fluvoxamine has languished at the FDA for more than 5 weeks without any communication other than "we are working on it." The FDA should evaluate these drugs based on the current evidence on the table at the time of application and quickly make a probabilistic assessment as to whether the drug is likely to save lives. That assessment should take less than a week for a repurposed drug.
5. **The FDA should have an EUA phased rollout in cases that are just shy of the normal EUA bar.** For fluvoxamine, it could be rolled out to 1,000 patients and see what happens, then exponentially increase on each release just like phased rollouts of new software in the tech industry.
6. **The NIH COVID Guidelines committee should broaden the inclusion criteria for the list of recommended drugs.** The fastest way to lower the death rate is to start using drugs with less than perfect evidence. This can be done, for example, by including drugs where the prima facie evidence shows that the drug is likely to reduce hospitalization and/or death rates by 25% or more.
7. **Create a national registry of outcomes.** The NIH should create a national registry of clinical outcomes, as suggested by Vikas and Vidula Sukhatme in their op-ed in *Health Affairs*. This is a superb approach to enabling us to capture data and rapidly learn from successes and failures of drugs newly added to the NIH Guidelines or given an EUA. This means that if either the NIH or FDA made a mistake, it can be very rapidly corrected. This makes mistakes less costly which in turn means the standards for approval can be lowered.
8. **We need to start trials of multi-drug combinations of the most effective drugs immediately.** Early treatment is key, but we don't have any individual drugs with 100% efficacy, so testing drug combinations ASAP is key.

9. **Key opinion leaders in the medical community have to start speaking out that we should not wait for more evidence.** The evidence on the table shows beyond any reasonable doubt that fluvoxamine will save lives. We need more people in the medical community to invest the time to look at the evidence and realize that all this evidence is very unlikely to happen by chance.
10. **Fund the organizations that have made the biggest impact so they can finish the job.** It's important to fund the best drugs and the best researchers. Take \$100M and divide it up among the top 2 or three charitable organizations that have done the most to rapidly fund the best research on repurposed drugs. There is so much left to do that people don't realize.
11. **Encourage academic institutions to change the rules for evaluating evidence to be less strict during a pandemic.** Today, we can't get a fair hearing anywhere because without a Phase 3 trial, we don't qualify. A repurposed drug in a pandemic should have a lower standard.
12. **The FDA should set public criteria for approving repurposed drugs in a pandemic.** Today, nobody, including the FDA, knows where the bar is. Having clear guidelines like p-value, # of randomized trials, total patient population tested, # of observational trials, having a clear mechanism, etc. could be a criteria. Then everyone would know. Also, we should be able to engage in an interactive discussion within 3 business days after an application is submitted, e.g., a 1 hour zoom call similar to the KOL meeting. This makes the entire process MUCH more efficient.
13. **Tell the NIH to make it clear what the criteria is for listing a repurposed drug with evidence on the NIH Guidelines.** This should be known, but today it is a secret.
14. **Encourage every public health official to talk about outpatient clinical trial availability in their area.** Require COVID test results pages to have links to enable people to enroll in clinical trials that apply to them.
15. **Issue an HHS directive that enables docs in a pandemic to prescribe across state lines** (or at least apply for and get a national telemedicine license); do we really need to regulate docs differently in different states?!?!

How should we reform the system so this doesn't happen again?

1. See the list above
2. No public health official has ever talked about any outpatient clinical trial that could benefit patients in their area. How can we incentivize this behavior?
3. Implement this [Establish A National Real-World Decentralized COVID-19 Program](#)
4. Docs don't like to take any risks and there is nothing to tip the scale to allow patients influence the doc, esp. When the patient is captive in the hospital or ICU. Patients should be able to absolve docs of liability if they request a drug to be used on them where they can show medical evidence that it has been beneficial and the doc is unable

to come up with any evidence showing it harm>benefit, i.e., the patient should be allowed to assume the risk. This can be done by requiring that the doctor warn the patient, the doctor verifies that there is evidence of benefit (to prevent patients from ingesting crazy things) and that the patient signed off on, “the doctor warned me about the risks.” Patients are allowed to do this in other countries so this is not like this is irresponsible. So a hospitalized patient should be able to get ivermectin, fluvoxamine, and cyproheptadine if they want. They cannot do that today without a court order which is ridiculous.

5. Why did it take so long to process the FLV EUA application? The FDA should triage each EUA when it comes in. Our EUA basically sat in an “to be looked at queue” for 3 weeks. It would have been even longer, but I wrote an email to Peter Stein asking why we haven’t heard anything. He didn’t know at the time. How could he not know of what should have been the #1 priority for an EUA?
6. Give NCATS a budget of \$400M per year and increase it to \$1B/yr during a pandemic
7. Remove the restriction that NCATS isn’t allowed to do Phase 3 trials. This restriction was added by drug companies and is not in the public interest. It’s a ridiculous restriction.
8. Make deliberations more public, e.g., in the NIH Guidelines group. Would be nice to at least know what they are working on and have a public review cycle before they publish.
9. Fund organizations such as CETF that can move quickly, fill gaps, and take risks
10. Change the rules so for a repurposed drug that shows evidence of at least a 20% effect size in 2 INDEPENDENT trials and the p value in both trials is statistically significant with the combined p value <.001 and the FDA is satisfied that the trials are either randomized or sufficiently quasi-randomized (e.g., by examining the comorbidities of the cohorts), then it should be an automatic EUA unless the FDA is aware of compelling evidence for this not to be the case.
11. Set a max time frame for FDA responding to EUA filing in a pandemic of 2 weeks. Right now, they can take forever. There is no time limit for them to respond.
12. Set up an outpatient clinical trial network that can test drugs that are cycled into the trial
13. Require that all public health officials inform the public of the clinical trials in their area
14. Provide public funding to support advertising of clinical trials of repurposed drugs
15. Create an expedited process for submitting drugs into the adaptive trial
16. Require people to enroll in clinical trials like they do in the UK
17. Implement Vikas Sukhatme solution for gathering data on off-label drug use by providing the funding for it and directing NCATS to implement it. See [this article in TrialSite News](#).
18. Have a fully publicly open database of health results.... Open to everyone just like they did with the CERNER COVID database. If they can do it here, why not fund these companies to do it for all diseases for the entire country, e.g., government pays CERNER and EPIC and the public has access to the data without restrictions in the same way researcher have access to the CERNER COVID database.
19. Create a Presidential committee tasked with reforming the system based on lessons learned here
20. Enable organizations such as CETF to get government funding
21. Stop the censorship of anything not on the NIH Guidelines, e.g., how can we stop social media platforms from censoring ivermectin videos done by legitimate doctors? There

should be an exception carved out here for medical info from licensed medical professionals. Those videos should NEVER be censored if they are licensed docs talking about medicine and if they are, the medical professionals should be able to sue the social media platforms.

22. Waiting for phase 3 trials is nuts when multiple studies show large effect sizes, there are multiple observational studies in support, all the anecdotal data is positive without exception, and the drug is known to be safe and the virus kills an average of 2% of infected people. How do we change the attitudes here?