Hey everyone welcome to the Optispan podcast.
On today's episode I'm going to do what I guess is a pretty harsh takeown of an essay that I find particularly poorly written and inaccurate by a guy named Chris Masterjohn.
This is something that was brought to my attention by one of our podcast subscribers who sent this to me.
Apparently Dr Masterjohn sent out an email including this essay and then also posted it on his Substack about rapamycin.
The title of the essay is the worst longevity idea ever conceived.
That's certainly his opinion and he's entitled to it.
Unfortunately the essay is filled with all sorts of misinformation outright falsehoods misleading claims.
So even though believe it or not I really do not enjoy doing this kind of thing I thought that it was important for me given my visibility and my expertise to set the record straight here.
First of all I don't know Dr Masterjohn I really don't know anything about him.
He has a website that talks about unlocking your greatest advances in health performance and longevity.
He's got what seems to be a fairly popular YouTube channel.
I have never heard of him before I don't think I've ever read any of his work.
So I don't really know anything about him.
Other than I'd be surprised if he's really an expert in longevity and I don't know him but I guess anything's possible.
I did attempt to look up his research track record on PubMed I'm assuming this is the same person 10 publications.
Including things on green tea extract and trans fats nothing that I could find related to longevity or mTor.
So as far as I can tell no research expertise on the topic.
But of course that doesn't mean somebody can't become an expert I'm absolutely a believer that curious smart people who want to do the work can in fact become experts on all sorts of topics.
Especially with the tools we have available today so that doesn't mean to say he's

not an expert.
But I think from my reading of this essay it's pretty tough for me to feel confident that Dr Masterjohn has taken the time and effort to really understand the topic unfortunately.
So what I want to do is I'm going to kind of read you the essay the email that went out and then I'll periodically stop and comment on it.
Pointing out the places where I think there are either mistakes false statements or misleading statements.
The essay starts rapamycin is a darling of the longevity community.
I don't know about that I guess it maybe it has become one.
Goes on I find it very hard to read the literature on this molecule without shuddering at the idea of taking it to lengthen lifespan okay opinion.
And yet it can benefit your mitochondria but only if you use it very carefully.
I have heard it said that rapamycin is the leading longevity molecule because of the robustness of the literature in mice.
That's an accurate statement.
But what the literature in mice robustly shows is that it causes cataracts testicular atrophy and impaired glucose metabolism at doses beneath those that lengthen lifespan.
Okay so first of all that last statement is completely false and I'll tell you why it's false.
I believe the study that he is primarily referring to here is a study titled rapamycin slows aging in mice from Rich Miller and colleagues.
They tested three doses of rapamycin 4.7 parts per million 14 parts per million and 42 parts per million in food beginning at age 9 months of age.
Turns out those are exactly the doses shown to increase lifespan in mice along with other doses.
And there's another study entitled rapamycin mediated lifespan increase in mice is dose and sex dependent and metabolically distinct from dietary restriction.
And as you can see from the survival curves all three doses of rapamycin increased lifespan in females two of the doses increased lifespan in males.
So first of all that statement that at doses below or beneath those that lengthen

lifespan is in fact a false statement.
But what about what the literature in mice robustly shows is that it causes cataracts testicular atrophy and impaired glucose metabolism.
Well let's see what the authors of the study said and a good place to start is the abstract.
Where they say we report here that many forms of age dependent change including alterations in heart liver adrenal glands endometrium and tendon as well as age dependent decline in spontaneous activity occur more slowly in rapamycin treated mice.
Suggesting strongly that rapamycin retards multiple aspects of aging in mice in addition to any beneficial effects it may have on neoplastic disease that's cancer.
So basically what the authors are saying is that rapamycin has a whole bunch of beneficial effects on health span across many different tissues and organs.
And also prevents cancer and also slows many aspects of aging.
Which of course Masterjohn chose not to talk about.
Instead he talked about some of the potential negative side effects ignoring all of the evidence for beneficial effects of rapamycin.
The authors did however say we also note however that mice treated with rapamycin starting at 9 months of age have significantly higher incidence of testicular degeneration and cataracts.
So two of the side effects that Masterjohn talks about here.
I don't know if this guy is actually in the field at all or pays any attention to the literature or other data that comes out at conferences.
But people in the field know that this report of cataracts generally has not been reproduced in future studies.
I don't want to say this is the only study to have seen this but I'm not aware of other studies that saw an increased risk of cataracts in mice.
And there have been studies that failed to see that.
So I think most people are of the opinion this was either it's a small effect or it may not be a real effect of rapamycin.
And even in mice I'm not aware of data in people.
The testicular degeneration part really means defects in spermatogenesis that is a

real effect in mice getting rapamycin at least mice getting rapamycin for a long period of time.
These mice started at 9 months of age.
Doesn't truly cause testicular atrophy per se as far as I know.
And of course there are things in people that do cause testicular atrophy like testosterone.
So I'm not aware of any evidence that rapamycin causes testicular degeneration in people.
Nor am I aware of evidence that people using rapamycin off label become sterile.
It's an interesting question certainly worthy of additional research.
But this really seems more designed to scare people than to present an unbiased view of the literature.
So I would say certainly the stuff about cataracts is kind of misleading given that that hasn't been robustly replicated in the literature.
Testicular atrophy sure we'll accept that the defects in spermatogenesis are a thing certainly in mice.
Impaired glucose metabolism I think is a really interesting question and this is often misunderstood again by people who are not really experts in the field or in the topic.
It is correct that rapamycin in mice at doses that increase lifespan causes at least in several studies not every study but several studies impaired performance on what's known as an oral glucose tolerance test.
And this is an experiment where you inject the mice with glucose and then you measure both blood glucose and insulin response over a period of time after that injection of glucose.
It's important to appreciate this is a non-physiological amount of sugar that you are injecting directly into the mice.
And it's there that indeed you do see at least in several studies impaired ability of the system to clear the glucose.
So that's really what we're talking about when people say that rapamycin has effects on glucose homeostasis or glucose metabolism.
It's also true that a subset of organ transplant patients taking high doses of

rapamycin experience a similar sort of defect in insulin sensitivity or glucose response.
So again this is what Dr Masterjohn is referring to and in that context that's true.
And I'll keep coming back to this it's really important not to extrapolate from what we see in organ transplant patients who are taking daily doses of rapamycin higher doses of rapamycin and strong immunosuppressants.
And oh by the way had an organ transplant not to extrapolate from those people to people using rapamycin off label.
Some of the effects may be the same many of the effects will be different.
But you can't assume that just because something is seen in organ transplant patients it's going to be seen in people of normal health status using rapamycin off label.
That should be obvious and yet many people including Dr Masterjohn continue to make this mistake.
Okay so in the context though of an oral glucose tolerance test I think it's fair to say there's evidence that rapamycin impairs the glucose response.
But what about in the absence of a non-physiological bolus of glucose in the context of normal aging or eating a normal diet.
So in this context I'm not aware of any evidence that people using rapamycin off label have impaired glucose tolerance or impaired insulin sensitivity.
Not saying it makes it better but I don't think there's any reason to think it makes it worse.
Except I do think if there was a big effect either way we'd probably know it by now.
So probably not much of a concern in people using rapamycin off label is my intuition.
Admittedly we don't have clinical trial data yet on either side.
But what Dr Masterjohn chose not to tell you and again maybe it's because he didn't know maybe he just simply chose not to share this.
But in long-lived mice receiving rapamycin they show no signs of impaired glucose metabolism when eating a normal diet at least in many studies.
It's really only in the context of the glucose tolerance test that you see what

appears to be a reduction in insulin sensitivity.
In fact some studies even show that mice receiving rapamycin who again are long-lived and have improved metrics of multiple health span measures have better insulin sensitivity from long-term administration of rapamycin.
In fact there's a study from Andre Barky who is I think everybody would agree one of the leading pioneers in the field of metabolism and specifically the intersection of metabolism and longevity.
Published a paper called duration of rapamycin treatment has differential effects on metabolism in mice.
And in that study quoting from the abstract as the treatment continued for 20 weeks these effects were reversed or diminished.
The mice had better metabolic profiles increased oxygen consumption and ketogenesis and markedly enhanced insulin sensitivity.
Those are the mice getting rapamycin okay so better metabolic profiles increased oxygen consumption and ketogenesis and markedly enhanced insulin sensitivity.
This runs exactly counter to Dr Masterjohn's claim.
Again I don't know why he chose not to share this data but you might want to take that into consideration.
So I would say that whole section is pretty misleading.
So we're about 100 words in and we've already got one outright false statement and two that again under a charitable interpretation we can characterize as misleading.
All right let's continue.
So he goes on in other words rapamycin lengthens lifespan at profound expense to health span.
Okay well I guess if you leave out all of the good things rapamycin has been shown to do for health span you might come to that conclusion.
This is only a partial list but here you go in rodents positive effects from rapamycin in the context of normative aging include lower incidence of cancers.
Protection against cognitive dysfunction improved heart function restoration of immune function improved kidney function.
Preservation of tendon reversal of periodontal disease improved intestinal

function and reduced gut dysbiosis.
Preservation of ovarian function and protection against hearing loss.
Although early there is initial evidence suggesting similar beneficial effects on aging heart in dogs and restoration of age-related declines in immune function in humans.
We'll put all the references in the show notes but again that's only a partial list.
The number of studies that have shown beneficial effects of rapamycin on a diversity of health span metrics in mice is certainly in the dozens if not more than a hundred.
And there's evidence in both dogs and people that at least some of these improvements in health span metrics are conserved outside of mice.
So the statement that rapamycin lengthens lifespan at profound expense to health span is just not true okay another false statement.
Moving on I have also heard it said that if you get canker sores from it you know it's working.
I've heard that said too I really don't think certainly that's not a scientific thing to say.
But the idea is that about 15% of people using rapamycin off label develop canker sores.
If you develop a canker sore you know you've taken a dose of rapamycin that's sufficient to cause canker sores I think that's about all we can say.
Okay next in the essay and this is I'll let you make your own decisions.
He says if it is drilling a hole in your mouth what do you think it's doing to your brain.
Rapamycin inhibits the synthesis of lipids and collagen and impairs the healing of wounds.
It blocks the synthesis of lipid rich myelin just the same okay.
So first of all comparing causing a canker sore to drilling a hole in your brain that's just silly.
And this whole sort of equivalency again Dr Masterjohn given that he's got a PhD I'm sure realizes this.
So I'm guessing this is an attempt to kind of try to make a point in a not very

logically consistent way.
It's sort of like saying well oxygen damages DNA and causes cancer so you should stop breathing oxygen.
I know he's smarter than that so again I have to sort of assume this is intentionally misleading people or some sort of effort to scare them.
Rapamycin does not drill a hole in your brain.
Of course this is about the dose right so if you completely shut off mTor sure that's going to cause defects in all sorts of stuff.
Including synthesis of lipids and collagen and wound healing and neuronal function and things like that.
Nobody is talking about taking rapamycin at a dose or consistently enough to have those effects.
In fact I don't even think it's possible to do that through oral delivery of rapamycin.
It turns out that at least one person has tried taking over 100 milligrams of rapamycin and all that person got was transiently higher lipids.
So I don't think it's really feasible to accomplish that if you tried.
And certainly the doses that people are using off label do not have that effect.
So this is just an attempt to scare you.
So then the essay goes on below I will argue that rapamycin can indeed help turn over damaged mitochondria when used in a temporary series of feeding fasting cycles.
But outside its possible use for genetic defects in breaking down old cellular components it should not be used in perpetuity.
Okay so that's an opinion no data to support it but everybody's entitled to their opinions.
I guess I would only say people who care about facts try to make their opinions match the facts.
The essay goes on the basic problem with rapamycin is this it inhibits mTor a signal of nutrient abundance.
I don't think that's a problem we are evolved to cycle through nutrient scarcity and abundance during ordinary fasting feeding cycles okay.

So meant that's not scientific we are evolved to cycle through nutrient scarcity and abundance.
Maybe you could make an argument for that.
But just because we have evolved to do something or our bodies have evolved to do something that doesn't mean that that's optimal for longevity.
That's an assumption and in fact in most cases it's probably an incorrect assumption.
Why because evolution doesn't act on longevity it acts on reproductive success.
And the optimal response for reproductive success is often not the optimal response for longevity.
In fact it's often the opposite it often causes accelerated aging.
So this idea that just because we evolved to do something that that's going to be best for your longevity.
There's no reason to believe that in fact that runs counter to how we currently understand the interaction between natural selection and aging works.
So I just don't think this is relevant and it's probably wrong in the context he was trying to make the argument anyways.
Okay the essay goes on when things are scarce we clean house when things are abundant we rebuild.
Think of it as selling off all the old clothes in your closet to raise money and make room for new ones.
Endlessly cleaning out your closet doesn't in and of itself get you nice things okay.
Again that's sort of misleading even in transplant patients taking high doses of rapamycin daily.
Autophagy that's what he's talking about when he's referring to the cleaning out of your closet here.
It cycles it's just that in that context when people are chronically taking rapamycin it's at a different baseline and it's probably a little bit less effective.
Again there's some literature on chronic high doses of rapamycin having impacts on both mTor complex one and mTor complex two which could lead to dysregulation of autophagy.
That hasn't really been shown in people.

So autophagy is still going to happen though that cycling is still going to happen.
Is still going to go up and down as the organ transplant patients are eating and exercising and going about their daily lives.
It's not like autophagy is always cranked up in people taking rapamycin.
In fact if anything it's probably the opposite it's probably happening less effectively in people chronically taking rapamycin.
But of course nobody using rapamycin off label is doing that nobody's dosing daily almost everyone is weekly.
So this whole idea is irrelevant and I would argue in fact this entire section of the essay is irrelevant.
So so far everything we've got is either false misleading or sort of irrelevant to the premise of the essay which is that rapamycin bad.
And unfortunately this just continues.
So the essay goes on there is no master signal of nutrient abundance.
There are instead a complex web of nodes that all synergistically signal nutrient abundance.
These include among others mTor leptin insulin citrate ATP and NADH.
You can't take one molecule to mimic fasting and expect it to work the same as actually fasting.
And you certainly can't expect to take it in place of fasting while eating an abundant diet and expect nothing to go wrong okay.
Again in my view this really represents a fundamental lack of knowledge around the literature.
I don't think anybody who has studied rapamycin in the context of longevity or who has talked about rapamycin as a potential translational gerotherapeutic is arguing that it's any type of replacement for fasting.
Is it a partial caloric restriction mimetic yeah it's partially mimicking caloric restriction because one of the things caloric restriction does is it turns down mTor.
That's what rapamycin does but caloric restriction does a whole bunch of other stuff that rapamycin doesn't do as does fasting.
But nobody's arguing that it's a replacement for fasting.
And the idea that things have to go wrong if you only turn down mTor without

fasting that's not scientific and it's not based on data.
It's based on I guess a personal bias.
In data and the data shows that animals on rapamycin live longer and are healthier in fact.
And maybe Dr Masterjohn doesn't know this but rapamycin is actually much more effective at increasing lifespan in mice than fasting is.
Chronic caloric restriction is of course the gold standard that gives the biggest effect on lifespan if you go down to like 65% reduction in calories.
That's work from Rick Weinrich and Roy Walford from way back in the 1980s.
But more recent literature comparing the effects of rapamycin to those of fasting show that rapamycin is five six times more effective at increasing lifespan than fasting alone.
So the idea that somehow rapamycin because it's only hitting mTor and fasting is doing 15000 things including hitting mTor that rapamycin is the one that's going to have problems.
Doesn't actually match the data at least with respect to lifespan and health span in mice.
So again it's pretty irrelevant to the original thesis but the premise of this section is again just wrong I don't know how else to say it.
Okay so for those of you keeping score we're about 400 words in now and so far we have a couple of misleading statements three outright false statements and the rest is really irrelevant to the premise of the essay.
I wish I could say it gets better but it doesn't and by now I'm starting to get pretty bored with the whole process.
So rather than read you the entire thing going forward I'm just going to call out the stuff that I see is the most egregious.
The stuff that's incorrect or at least designed to be misleading.
Feel free to amuse yourself if you want to read the whole thing just please please don't take it seriously okay.
So the essay goes on the next sentence rapamycin lengthens lifespan in mice yay we have something that's true.
Oh but then it goes on however it also scars their hearts raises their glucose

fattens their liver and shrinks their testicles.
Wow these are all misleading statements or outright falsehoods okay so let's start with the heart.
This is really bad I actually don't know where he's getting the scar the heart stuff from.
Multiple labs have shown improvements in age related heart function in different mouse strains at the doses used to increase lifespan.
We've shown some evidence early for this in dogs a company called Trivia Vet just got FDA approval for heart disease in cats.
There are multiple case reports in humans for things like hypertrophic cardiomyopathy.
Rapamycin is also FDA approved for use in cardiac stents.
So I really don't think that rapamycin scars the heart if anything it makes heart function better in the context of aging.
I really tried hard to figure out where he was getting this from.
This is in a section where he talks about intermittent rapamycin use.
And he cites a study that looked at the effects of different doses of rapamycin dosed intermittently from Linda Partridge.
In that study the authors actually conclude rapamycin treatment reduced age-related changes in heart.
The text specifically says in summary these results suggest that both chronic and intermittent rapamycin feeding significantly and to a similar extent slowed the advancement of age-related cardiac outcomes such as heart rate and left ventricular hypertrophy.
So in the study the only study that I could see that he might be referring to the authors actually show that rapamycin makes things better in the heart in the context of aging.
I don't know it sort of feels like intentional deception but maybe he just never read the actual study or didn't understand it.
Okay so I already addressed the glucose comment so he said it raises their glucose that's in the context of an oral glucose tolerance test at the doses that increase lifespan.

Most studies again I don't want to say every because you can probably find a study to support whatever claim you want to make if you want to be biased.
I'm not aware of any studies that showed an increase in glucose or HBA1C in the context of normal aging.
Most studies show no change and at least some including the one by Andre Barkkey that I showed earlier show improvements in insulin sensitivity and glucose homeostasis.
So that's misleading.
Fattens their liver no idea where he's getting this liver comment from at the doses that increase lifespan.
I mentioned this earlier from one of the studies from Rich Miller they showed improved liver function a bunch of other studies have showed improved liver function.
That's been seen over and over again.
My lab and others have also shown that rapamycin can protect against obesity and fatty liver induced by a high-fat diet.
So the idea that rapamycin fattens their liver is certainly not a fair representation of the literature in the context of doses used for longevity and health span.
And what about shrinking their testicles that sounds bad.
So I already addressed this really I think saying it that way is more for shock and fear value than a true representation of the data.
It absolutely causes defects in spermatogenesis in mice I don't know of evidence for that in people using it off label but certainly that's possible.
I don't know of any evidence for testicular shrinkage in people using it off label for what it's worth I haven't noticed any testicular degeneration.
So again I think this is misleading at least designed to induce fear in people where that's really probably not necessary.
Okay so now Dr Masterjohn goes on to talk a lot about the doses of rapamycin used in mice and tries to compare that to the human dosing.
His argument is essentially that the doses used to increase lifespan in mice are higher than the doses people are taking off label.
And therefore because there are so many bad side effects at the doses that

increase lifespan in mice which as hopefully you now can appreciate is not true.
In fact there's a whole bunch of benefits and very few side effects but anyways because those doses are higher than what people are taking off label.
That means that people taking rapamycin off label I don't know aren't going to have the side effects something like that.
So first of all this is completely irrelevant right what we need to do is see what are the effects of rapamycin at doses people are using off label in people.
That's really the question we want to answer.
It's a little bit unfortunate that Dr Masterjohn kind of missed the whole allometric scaling thing.
So I mean it turns out that you can't just extrapolate dosing from animal to animal.
You have to use this scale that allows you to understand sort of the actual physiological effects of the drug when you go across animals.
And it has to do with body size and surface area.
So again I think it's sort of an irrelevant entire section of the essay but there's also this little math problem.
There's actually a pretty good paper that lays this out for anyone who's interested a simple practice guide for dose conversion between animals and humans.
It's got a nice table in there that tells you the scaling factors sort of estimate how drugs should be dosed if you're going across species.
So then we move on and Dr Masterjohn attempts to trash rapamycin based on studies in marmosets.
Marmosets are a non-human primate that is relatively rapidly aging for primates and I think has a lot of promise as a model for studies in aging.
Unfortunately it seems like he probably hasn't been keeping up with the data here.
So he cited a paper from 2014 and he claimed that rapamycin doesn't increase lifespan in marmosets.
First of all there's nothing in that paper about rapamycin and lifespan in marmosets at all so it's a false claim.
But the primary investigator on that project Dr Adam Salmon presented data at

the most recent American Aging Association conference which I was at.
Where he reported that rapamycin does in fact increase lifespan in marmosets.
I think that's really a pretty big deal because it shows for the first time that rapamycin probably does slow aging in a nonhuman primate.
So not only is the claim false but the actual data are exactly the opposite.
One thing though that Masterjohn did get right here and I do think this is also worth paying attention to is there is some evidence from the marmoset studies that rapamycin could have a negative impact on osteoarthritis.
The data are not again in my view particularly compelling so far.
And even Dr Salmon at the conference kind of downplayed this effect.
But it is absolutely worth understanding better whether it's a real effect and whether it might be true in people.
Again so far I'm not aware of any data that rapamycin exacerbates accelerates has any negative impact on osteoarthritis.
And if anything the sort of anecdotal stuff I've heard is the opposite.
But it's something to watch out for absolutely something that clinical trials in people should pay attention to.
This is important should be paid attention to I personally don't think there's a lot of reason for fear at this point.
But again it is a potential warning signal that we want to watch.
Okay so then the last part of the essay goes on and talks about and it's titled humans get trash testosterone oral inflammation and impaired wound healing.
All of this is based on organ transplant patients completely irrelevant for people using rapamycin off label.
Again I've said it before organ transplant patients take higher doses they take it daily they have chronic inhibition of mTor complex one.
They're also taking a bunch of other true immunosuppressants and by the way they had an organ transplant okay.
So very different situation than pretty typically healthy people taking lower doses of rapamycin once a week.
There's a whole bunch of evidence to support that.
Unfortunately Masterjohn I think is just trying to win an argument and so he's

taking stuff from organ transplant patients.
And suggesting that this is what happens in people using rapamycin off label.
The truth is as far as I know there is no evidence yet that off label use of rapamycin does anything to testosterone one way or the other.
I'm not saying it makes it better I'm not saying it makes it worse I haven't seen any evidence one way or the other.
Perhaps not directly relevant but there's actually much stronger evidence that the drug metformin which uninformed people think is much safer than rapamycin reduces testosterone in men.
Some men certainly the evidence is stronger for metformin reducing testosterone than it is for rapamycin reducing testosterone.
At least at the doses that people are using these drugs off label for potential gerotherapeutic effects.
Wound healing again I'm not aware of any evidence at all that off label use of rapamycin impairs wound healing.
It might it might not if you are using rapamycin off label you might want to stop if you have a major surgery coming up.
But other than that again I haven't seen anything to make me think that if it has an effect on wound healing either way it's going to be a big effect.
And you could come up with plausible explanations for how rapamycin might actually improve wound healing.
So again I don't think we know the answer but to suggest that we do know the answer and that it has a negative effect is just intellectually dishonest in my view.
What about oral inflammation so this is pretty interesting.
The currently available data suggests that off label use of rapamycin probably reduces oral inflammation and might have a positive impact on periodontal disease.
So right now again as far as I know this is all anecdotal I've seen some analysis of data.
But it's again from self-reported rapamycin users.
But the interesting thing is that that fits with the data from mice where we have seen that rapamycin reverses periodontal disease in aged mice.

You take old mice that have developed periodontal disease you give them rapamycin and within about 8 weeks it regrows bone around the teeth.
It knocks down gingival inflammation so inflammation of the gums gingivitis.
And it remodels the oral microbiome back towards something that is more like a youthful composition.
So that's pretty exciting and Dr Jonathan Anne who actually led the original study in mice now a professor at the University of Washington.
Is carrying out a randomized double blind placebo control clinical trial in people to test whether or not rapamycin can improve outcomes in the context of periodontal disease in humans.
That's what we need we need these kinds of clinical trials to actually get real data that we can feel confident in.
Not essays by people who are not experts in the topic that they are influencing on.
So I'm excited to see how this clinical trial comes out I hope it will be informative.
It will also give us more data around safety so that will be important as well.
So again there's really a couple things writ large that bother me about this whole essay.
The first is that Dr Masterjohn presents himself as an expert in longevity but I would say it seems pretty clear to me that he's not particularly knowledgeable about the literature in this space.
I don't really care that he doesn't have any track record in the field.
But the lack of effort put into understanding the literature I find pretty problematic.
The second is that it seems and again I really try hard not to put intent on people.
But in some places it really seems like there's an intentional effort to scare people by making misleading statements.
It feels like trying to win an argument rather than trying to honestly evaluate the data.
Dr Masterjohn ignored all of the mouse data and there is a bunch of it showing robust and reproducible improvements in lifespan and multiple health span metrics.

And he cherrypicks a few potential negatives which in most cases turn out not to even be accurate.
Either they haven't been reproducible they're seen at doses that are not relevant for the doses that have been shown to increase lifespan in mice.
Or that are being used off label in people or they're seen in organ transplant patients which we've already discussed.
And there was no mention of the admittedly incomplete but growing body of data from people using rapamycin off label at once weekly dosing schedules.
That are so far I think painting a different picture.
So again the honest answer in my view is that right now we don't know if rapamycin will increase lifespan or health span in people or dogs.
It definitely does in mice.
I would also say the current data I think are starting to pretty strongly suggest that off label use is pretty safe in people.
Probably the largest data set on this comes from our 2023 study where we looked at 333 people using rapamycin off label.
And we compared them to more than 100 people who have never used rapamycin.
Again lots of weaknesses with this data set but it's kind of the best we have right now.
And we asked them about a whole bunch of side effects and there were seven things that were different between the two groups.
The only one that was higher in the rapamycin users group was canker sores.
The other six that were statistically significantly different between the two groups were lower in the rapamycin users.
So from this really doesn't seem like the side effects are very bad nobody likes canker sores that's a real side effect.
Nothing else reached the level of statistical significance and there may be some benefits that go along with rapamycin treatment okay.
So that's the data that we've got right now the Pearl trial and I think the paper was just recently published.
Showed again no significant side effects pretty low doses of rapamycin I think if we

go to the sort of bioequivalent doses it's probably I don't know one and a half to two migs a week once a week.
So no significant side effects and a trend toward improvements in body composition and quality of life in women.
Again I'm not trying to make the case that it proves anything the arrows pointing in the right direction.
Joan Manik published two pretty large clinical trials with Everlymus a derivative of rapamycin at five migs a week.
That again showed side effects comparable to the placebo group and evidence for improved vaccine response.
And there are a whole bunch of case reports in the literature and anecdotal reports from people using rapamycin off label showing various positive outcomes.
Again with few negative ones as far as I've seen.
So that doesn't prove anything could there be bias in the data that we've got where people who've had side effects tend not to document it or tend not to be believed.
It's certainly possible I don't want to suggest we know that rapamycin off label use has minimal side effects or no side effects we don't we don't know that yet.
But I think I'm feeling pretty confident from the number of people I've talked to in the data that I've collected that if there are significant side effects they're very rare.
And most people can tolerate rapamycin use off label very well and many people perceive quite significant benefits on quality of life in a variety of ways.
Most of them having to do likely with reduced inflammation okay.
So that's my take more broadly I think this should be a lesson if you got this email and you read it and you got freaked out.
It should be a lesson that you need to be really careful who you trust especially on the internet.
Again I don't know Dr Masterjohn he's probably a really nice guy he's probably knowledgeable in his domain.
But I can tell you he's not an expert in longevity and whether through intent or incompetence or just lack of effort he's spreading misinformation about

rapamycin.
But is easily proven false by the actual data.
Yes he's got a PhD he's amassed a following of people who think he knows what he's talking about to me that's a problem.
And he's not the only one in this space.
To Dr Masterjohn I look I get it I wouldn't like it if somebody put a video like this about something I wrote out there.
I'm guessing you won't be happy with this video I would love really honestly I would if you are genuine in your desire to want to accurately inform people.
I'd love to have you on the podcast I'd love to have a conversation with you about rapamycin or any other longevity related topic.
I genuinely want to get to new insights by having conversations with people not have to correct misinformation that people are putting out there.
But if you do take me up on this offer you better come prepared to deal in facts and data not opinion.
This is science and that's what matters in science okay.
So thank you for watching this episode of the Optispan podcast.
As I mentioned this happened because one of our viewers brought this to my attention.
If you have anything I know a lot of you like to have me comment on stuff like this.
I'm pretty busy but I do try to make time to give my opinion on things that I think are important.
Have the potential to help people have the potential to harm people as in the case of this.
So please continue to provide those comments you can always shoot us an email.
Please sign up for the newsletter on our website and you can send us an email through that.
And as always feel free to ask any questions or post your comments below thanks so much for watching and I hope to see you next time on the Optispan podcast.