**Harlan Krumholz:** Welcome to *Health & Veritas*. I’m Harlan Krumholz.

**Howard Forman:** And I’m Howie Forman. We’re physicians and professors at Yale University. We’re trying to get closer to the truth about health and healthcare. This week we’ll be speaking with Dr. David Fiellin, but first we’d like to check in on current hot topics in health and healthcare, and Harlan, what got your attention this week?

**Harlan Krumholz:** Yeah, Howie, I wanted to talk about [a study](https://www.sciencedirect.com/science/article/pii/S0002916523489046?dgcid=author) that came out that took a look at multivitamins and its effect on memory.

**Howard Forman:** Oh, I love that one.

**Harlan Krumholz:** Big one.

**Howard Forman:** Yep, yep.

**Harlan Krumholz:** You got to know that I’m a skeptic about all this stuff I’ve been telling everyone for years, all it does is enrich your urine, but—

**Howard Forman:** And by the way, I have vitamins at home and I rarely take them until this paper came out, but I haven’t even read the actual paper, so I want you to tell me what I should know.

**Harlan Krumholz:** Well, look, I’m not against placebo, by the way. I think placebo can have powerful effects, but I’ve been down on the ways in which vitamins, these supplements that you see all over the place, that they’re promoted very heavily. Well, the effect that they can have on people’s health, because in general the studies haven’t been very positive. But recently a study came out that showed up in *The American Journal of Clinical Nutrition*. Now we don’t usually see our landmark trials showing up in a journal like *The American Journal of Clinical Nutrition*. And yet, this study that came out of Harvard and other institutions, Columbia, Chan School of Public Health, and others, took a look at whether or not, and I’m just going to name it, Centrum Silver.

**Howard Forman:** They did too.

**Harlan Krumholz:** But it’s not meant to be about Centrum Silver as much as these—a multivitamin, whether the use of it every day could in fact help people’s cognitive performance. And they used this thing called [the Montreal Test](https://www.mdcalc.com/calc/10044/montreal-cognitive-assessment-moca), which was that this was the primary thing they were leveraging on, which is about showing people a bunch of figures and then having them draw them themselves and having to recall them. And it produces a bunch of scores that are reflective of executive function and recall, and so they had people take these pills and after about a year of the intervention, they took a look at this what’s called episodic memory. Really it’s this immediate recall of these things. And lo and behold, it was better in the people who got the multivitamin. Now, this was a placebo-controlled, randomized trial. The thing that’s surprised me about it showing up in this journal is that there are a lot of observational studies of foodstuffs that end up in highfalutin journals, that are probably suggesting a strength of evidence that they really don’t have.

And it’s because food behaviors are so confounded with so many other things that people do. People who eat certain ways also tend to have physical activity or do a lot of other things, use seat belts. I mean, people who are eating a lot of vegetables, for example, and fruits and watching their diets and not eating a lot of fatty foods are probably doing a lot of other things. So, these observational studies are hard to do in ways that will help us give us confidence about what the right thing to do is. But this was actually a randomized trial, and it was building on a prior randomized trial in which people were called up and they went through these tests and also found a benefit of multivitamins. This one was an internet test, so it was really actually being done as a large-scale, decentralized study, in which it was really easy for people to participate just online. And they had more than 3,000 people. And what they suggested was that the effects of the improved performance was the equivalent of three years of age-related memory change.

**Howard Forman:** That’s incredible.

**Harlan Krumholz:** So let’s just say maybe this is an exaggeration. I mean, I don’t know, it needs to be further validated, we need to understand it better. But other studies have demonstrated that these multivitamins are safe. And so, I will tell you, for someone who never took vitamins before, I’m starting to take some vitamins.

**Howard Forman:** Me too. Every day since I first heard the story. Every day. I was just going to say the other thing that was a little surprising, but maybe I just don’t know enough neurosciences that despite that pretty significant improvement and as you say, executive function, short-term retention, they saw no improvement in long-term retention of an information or any other sort of neurologic functions.

**Harlan Krumholz:** So this was the weird thing, not everything improved, and I think this perplexed people about why did that happen. So, what’s the pro? Randomized, it’s a second study that’s looked at this, they both came to similar conclusions, good group of people doing it. On the other hand, why wasn’t there more consistency? Some people think this benefit is small. Like I said, they believe it’s equivalent to three years. I think that’s big.

**Howard Forman:** It’s big.

**Harlan Krumholz:** Anyway, there’s going to be a lot of discussion about this. But those of us who care about evidence might start changing our behaviors with regard to vitamins based on this study.

**Howard Forman:** And as you said, there’s no evidence that I’m aware of that vitamins in the doses of these particular vitamins we’re talking about, not these mega-doses that are sold separately, that in these doses that there’s any meaningful adverse effects, so the weight of decision-making for someone like me is just go ahead and take it.

**Harlan Krumholz:** So Howie, let’s get to David Fiellin.

**Howard Forman:** Dr. David Fiellin is the inaugural director of the [Yale Program in Addiction Medicine](https://medicine.yale.edu/intmed/genmed/addictionmedicine/), which is internationally recognized for its innovative treatment models. Dr. Fiellin is a professor of general and emergency medicine at Yale School of Medicine and a professor in the [Health Policy and Management Department](https://ysph.yale.edu/public-health-research-and-practice/department-research/health-policy-and-management/) at the Yale School of Public Health and an authority and scholar studying the intersection of primary care and addiction with a focus on opioid use disorder and alcohol use disorder.

He’s the editor-in-chief of the [*Journal of Addiction Medicine*](https://journals.lww.com/journaladdictionmedicine/pages/default.aspx) and the co-editor of various other addiction-focused publications. He holds a bachelor’s degree from Earlham College in Indiana and an MD from Emory University. He completed his internship and residency at Yale New Haven Hospital and was a Robert Wood Johnson Clinical Scholar at Yale School of Medicine prior to joining our faculty. So first of all, I want to welcome you, and when we were preparing for this, it’s the first time I ever heard of Earlham College. No offense to the many great alums, it’s a very...

**Harlan Krumholz:** This is Howie’s New York–centricity. As someone from Dayton, Ohio, of course, I knew Earlham [in Richmond, Indiana] very well.

**Howard Forman:** I told him that. I told him.

**Harlan Krumholz:** Every time I drove to Indianapolis, I drove right by.

**Howard Forman:** So, it is—but it is a small college, it’s 700 people. But what I was intrigued by...

**Harlan Krumholz:** An outstanding college, an outstanding small college.

**Howard Forman:** Yeah. What I was intrigued by is...

**David Fiellin:** Seven hundred on a good day.

**Howard Forman:** On a good day. I was intrigued by the fact that there’s this commitment to social justice, to community involvement, to fairness, to peace, and that almost defines the lens in which your whole career has gone. And I was just curious to hear from you, how that informed you, how you made a choice to go there coming from the northeast and what it has done for you.

**David Fiellin:** Well, thank you, Howie and Harlan. I appreciate the opportunity to be here and to highlight the wonderful experience that folks can have at [a school like Earlham](https://earlham.edu/about/mission-principles-and-practices/). Earlham is a Quaker college, and so, not surprisingly, it has the commitments and attracts students and faculty who address the areas that you described. My father was from Illinois, my mother was from Greenwich Village, and so I was curious growing up what it would be like to live in the Midwest. And they had had a wonderful experience going to a small liberal arts college, and so I opted to pursue that experience rather than going to a school in the northeast, primarily because I found schools in the northeast were populated by folks from the northeast. And I was curious in getting a wider view of the world.

I think the other thing about Earlham is, it’s a liberal arts education, and I’ve found that in the work that I do, which involves policy, education, clinical work and research, having exposure to a wide variety of undergraduate disciplines has allowed me to effectively work in this area. I opted to go into medicine after a period of time, graduating college, and was not necessarily destined to go into addiction medicine. I pursued internal medicine, general internal medicine, had a wonderful training experience. What one of my mentors, Alvan Feinstein, liked to refer as a two-year sabbatical, learning clinical epidemiology and research methods.

Harlan came on actually as the director of that program as I was graduating and opted at the time to take the methods and the skills that I had learned in clinical epidemiology and apply them to an area that was under research, which was the specter of substance use and addiction. I really found in reviewing the literature at the time that it could benefit from many of the skills that had been applied to other areas of medicine, and that’s really been the focus. I think the other thing you highlighted is that the focus of our program is bringing addiction services, screening prevention, treatment to general medical settings, hospitals, primary care clinics, HIV clinics, emergency departments, OB-GYN settings.

Most patients who are experiencing substance abuse are hesitant to seek treatment. And so if we can bring the services to where those patients already are seeking care and receiving care, it allows us to be much more efficient and effective.

**Harlan Krumholz:** So many questions I want to ask you, but I want to get to this one first. So what about this Ozempic thing? Is this going to cure addiction? You’re one of the world’s experts in addiction. People are talking about these weight-loss drugs as being able to blunt the urges that people have who are facing substance use disorder. Is this just hype? You think there’s anything to it? What’s going on with this?

**David Fiellin:** Yeah, no, and thank you for bringing this up, Harlan. There is good preclinical data primarily in rat models that indicate that there is decrease appetitive behavior, decrease alcohol consumption in particular, there is some emerging human data like other medications and other strategies. We need to do more rigorous trials to really look at dose and frequency and duration to determine and compare it to effective treatments or other treatments to see whether or not it will form one of the mechanisms in our armamentarium of treatment.

**Howard Forman:** Two of the most common drugs that the public hears about now if they’re reading about this in lay press are [buprenorphine](https://www.samhsa.gov/medications-substance-use-disorders/medications-counseling-related-conditions/buprenorphine) and [naloxone](https://nida.nih.gov/publications/drugfacts/naloxone#:~:text=Points%20to%20remember-,Naloxone%20is%20a%20medicine%20that%20rapidly%20reverses%20an%20opioid%20overdose,with%20opioids%20in%20their%20systems). And I was wondering if you could just help people understand, in terms of opioid use disorder—and maybe first, define opioid use disorder for our listeners—but what roles do they play and why are they so critical to reducing mortality and maybe even morbidity from this?

**David Fiellin:** So opioid use disorder, like all substance use disorders, implies not just physical tolerance but also adverse consequences and essentially loss of control. We tend to use, and most folks have standardized on the diagnostic statistical manual, the fifth version or the DSM-5, which outlines nine criteria for substance use disorder. They include, physical dependence as manifested by intolerance and withdrawal but also the signs and symptoms that indicate that an individual has lost control. So, continued use despite adverse consequences, use and hazardous situations or performing role functions, repeated attempts to control or cut down.

So that loss of control. Then we say you have a substance use disorder, as opposed to an individual who may occasionally use cannabinoids, tobacco, even alcohol where they’re not manifesting adverse impact on their lives, and so that’s when somebody is transitioned to what we call a substance use disorder, opioid use disorder in the news of late these days. The two medications that you described function very differently. If you think about the analogy to diabetes, using a medication like naloxone is like treating DKA without addressing the underlying biology.

**Howard Forman:** And DKA, just for our listeners.

**David Fiellin:** …to naloxone. Yeah, I’m sorry: diabetic ketoacidosis. So the most severe manifestation of somebody’s blood sugar being out of control. And so, naloxone is a very effective medication. What it does is, it goes to the opioid receptor, it binds to the opioid receptor and it basically displaces other opioids that are in the system. And so this is highly effective in a situation where an opioid that a person has ingested—be it fentanyl, be it heroin, be it a prescription opioid—is causing overdose, respiratory depression, and basically a person no longer breathing.

And so it’s among the most effective strategies, and one of the things that we’re really trying to promote today is wide availability of this medication given that people can experience overdoses when they’re using fentanyl, but also we’re seeing it as fentanyl and other high-potency synthetic opioids as contaminants in other drug supplies such as cocaine, and so the way you might start seeing more widely available naloxone, the way you see cardiac defibrillators and the like. As a public health response, we need to be able to have these medications available when these events occur. Now the other medication you asked about is buprenorphine, and this is a partial agonist or a partial receptor-binding medication at the opioid receptor.

And, this is a medication that is used for long-term treatment of opioid use disorder. The notion is that, once a patient is stabilized on a medication like buprenorphine, or the other highly effective medication is methadone. Once they’re stabilized on these medications, the patients no longer experience the withdrawal and the craving that they would’ve experienced before they were in treatment. One thing that folks probably don’t realize is people with established opioid use disorder typically are no longer getting high anymore. In order to obtain the amount of fentanyl or heroin that they used to use to experience euphoria, that ship has long sailed.

And so they’re primarily using these substances to prevent the experience of withdrawal. And so a medication like buprenorphine, which binds to the receptor, prevents them from feeling that withdrawal and it also blocks the effect that they might get if they’re to use heroin or fentanyl on top of those medications. So what it means is that a patient can work, they can take care of their children, they can function normally in society, and they’re not experiencing euphoria.

The medications are taken once a day, they’re not injected, they’re avoiding the infectious complications, and their cognitive abilities are intact. And so that’s a medication that we use to treat patients longer term. And, the amazing thing is, it can decrease mortality in individuals with opioid use disorder who have experienced an overdose by 50%. And so we need to be very aggressive in making sure that people have access to these medications.

**Harlan Krumholz:** One of the questions I have, though, is, just oncologists in the period where there were few options, the failure rates are so high. And particularly earlier in your career when there were fewer options to treat people. I just wonder how did you find it in yourself to be able to continue when despite best efforts, the failure rates were so high?

**David Fiellin:** It’s an interesting question. I’m a primary care physician, a general internist, and I’ve never cured the diabetes in my patients or hypertension in my patients. And I will say that one of the most rewarding things that I’ve ever done as a physician, and certainly in primary care, is to take somebody who’s been using opioids, injecting heroin or fentanyl every day for the past 5 or 10 years and have them come in, start a medication like buprenorphine, and they come back within three or four days and they say, “You’re the best doc in the world. I’ve never felt so normal, I’ve never felt like I can function again. I’m back. I’m taking care of my kids, my wife is talking to me, I’m saving a hundred dollars a day.” As you said earlier, we often see the failures, and we don’t highlight the successes that many of these individuals experience.

And yes, it was very gratifying to the physician in me to feel like I was making a profound change in people’s lives. My early work was with folks who were primarily exposed and using prescription opioids, and my experience in Connecticut was, most of these folks were like everybody I grew up with and for whatever reason, they became exposed to opioids and developed an opioid use disorder. And so I would have individuals who were working in our hospitals, being coaches on their kids’ soccer teams, folks who were providing service in fast food industry and other types of service industries, it was not as if this was only a destitute population, sort of the tip of the iceberg that we tend to see.

**Harlan Krumholz:** One quick follow-on, on this is, how complicit do you think the medical establishment was?

**David Fiellin:** To answer your question, I think we were complicit in, number one, failing to rigorously question the efficacy of opioids in chronic pain. I think they work for a subset of individuals with chronic pain, and number two, the medical field and the medical establishment was too aggressive in prescribing these beyond their indication.

**Howard Forman:** Just want to get one last question in while we still have you. You’re not entering care through an addiction medicine practice. The most likely place that you’re entering the system is through the emergency room right now. And so efforts are being made to train our emergency medicine providers to be better prepared for initiating treatment, not just the acute treatment of respiratory failure but hopefully beginning recovery in some way. Just wondering, I know you’ve done a considerable amount of work in this area. I’m wondering how promising that is and what it will take to get our emergency medicine workforce to be hand-in-glove partners with addiction medicine to be approaching this holistically and 360 degrees.

**David Fiellin:** I’m very hopeful. I think there are a number of factors that are driving this. First of all is just a prevalence of the condition. Second of all is the fact that, as you say, we have effective treatments and the stories that I mentioned or alluded to earlier on, I think as our colleagues start to experience those types of successes, it becomes very rewarding and reinforcing for the behavior. And I think the third thing that’s important is that there are change leaders in the field who are really advocating, and some of it’s a bottom-up approach. I think the younger generation of medical students, residents, fellows, and attendings have trained in places in large academic medical centers that maybe have adopted these types of practices and seen the benefit and seen the role that emergency department can play in initiating effective treatments. I’ve been pleasantly surprised to see, traveling all around the country, meeting my ED colleagues, what a public health approach they take.

They see gun injury, they see motor vehicle accidents, and this is just another example of obviously the end stage disease that they see, but that they can intervene on early on. So, this is all now falling in the realm of what we call implementation science. And I’ve seen it repeatedly over and over. Twenty years ago, we were talking about getting primary care physicians on board to start medications and treat opioid use disorder. We haven’t gotten there far enough, but we’ve made great progress. Same thing with HIV physicians and then now in hospitals; quite frankly, it’s amazing that you can go into a major academic medical center and see a cardiologist, an oncologist, a subspecialist in surgery, but you’re likely to receive care from a social worker for an addiction.

Nothing against social workers, but number one, oftentimes they’re not adequately trained, and they will admit so, and they also don’t have the same type of understanding of the underlying biology of these processes. And I think that’s a paradigm shift that hospitals and health systems around the country will need to come to grips with, and we need to train a larger workforce. There are only four or five thousand addiction specialists in the country.

**Harlan Krumholz:** I can see the parallels with obesity very well. We tend to sequester these as behavioral, when in fact, like you said, they’re actually biological issues that need to be addressed in addition to social context and so forth. Okay, look, I’ve got one last question. You grew up in New York, but you’ve got a Rob Gronkowski jersey behind you in the room. People can’t see this, but I can see this. What the heck, man? Are you in New England or New York? What’s...

**David Fiellin:** Yankees, Giants, and Knicks. Listen, I’m in my kids’ bedroom. New Haven is actually the borderline between Boston and New York fans, and I am an island in this house in favor of the Yankees.

**Howard Forman:** Yes, it is. It is the dividing line.

**Harlan Krumholz:** You mean you lost your child to New England? Oh my goodness. Oh my goodness.

**David Fiellin:** Very observant, Harlan.

**Harlan Krumholz:** Look, want to want to just express deep gratitude for you being here for and even more, for all that you’ve done in this important area, you’ve advanced it so far, you’ve done it with teamwork with a great team, a lot of wonderful colleagues. You’re always generous and giving credit to others too. I’ve seen you and your work is just at the highest level. And I just want to both congratulate for what you’ve done, I’m looking forward to what you’re going to continue to do and appreciate you being on the podcast with us.

**Howard Forman:** Thanks, David.

**David Fiellin:** Thank you to you both, and I appreciate again, the opportunity.

**Harlan Krumholz:** Well, that was a terrific interview.

**Howard Forman:** It was great.

**Harlan Krumholz:** I really loved hearing from David, and I’m so proud of a RWJ Clinical Scholar alumnus that’s just done so well and not only advance the field but help so many others and continues to be so active and make such contributions. But let’s get to another favorite part of the show for me, which is hearing what’s on your mind? What are you thinking?

**Howard Forman:** So this is related to what you talked about in the intro a little bit. So, an article in *The New York Times* this week, mostly about the specific dietary supplement called berberine, which that the article itself was entitled “[The Truth About Nature’s Ozempic](https://www.nytimes.com/2023/06/07/well/eat/berberine-weight-loss-ozempic.html).” It caused me to revisit how we regulate dietary supplements in this country. And the article itself explains how berberine is an extract of certain plants. It might have, and in fact, there is evidence of a potential in treating insulin resistance, hyperlipidemia, hypertension, and even obesity and even high cholesterol.

There is no evidence that it has anywhere near the effectiveness of semaglutide, which is better known as we go Wegovy or Ozempic, right? But it is also neither inactive or innocuous. Unlike our prescription drugs, dietary supplements do not require the FDA to assure safety and effectiveness, which I think a lot of people don’t know. The [Dietary Supplement Health and Education Act of 1994](https://ods.od.nih.gov/About/DSHEA_Wording.aspx) is a mere 11 pages long co-sponsored by the Republican senator from Utah, Orrin Hatch, very well respected, and the Iowan senator, Democratic senator from Iowa, Tom Harkin.

But in that very short bill, a lot of protections are in place for the supplement industry, which by the way is a more than $150 billion global industry. So dietary supplements are considered in the category of food. They have fairly strict labeling requirements but, unlike drugs, do not have a formal process by which they are tested for safety and effectiveness. They generally have a disclaimer on the packaging that explicitly says that the supplement has not been tested by the FDA for these purposes. The FDA does require a review, but not for approval per se. It’s basically just a review of the safety of the new supplement ingredients, though they actually don’t even review old ones prior to the act.

And this passive effort rarely results in limitations of sales. So the agency is permitted to restrict the substance if it poses a “significant and unreasonable risk under conditions of use on the label or is commonly consumed.” They don’t mention anything about effectiveness. So I went on TikTok and Twitter to see how often berberine is being talked about and marketed. And it’s astonishing. I mean, particularly on TikTok, tens of millions, probably hundreds of millions of views for dozens of active accounts promoting berberine, many with reasonable statements of concern, but others that are just flat-out full promotion mode.

So libertarians may be happy that the supplement market is so unfettered, but in an age that is often driven by poor information on social media, where the average viewer may not be discriminating beyond who has a lot of followers, dangers lurk, and our listeners should do their own due diligence before quickly adopting new supplements.

**Harlan Krumholz:** You know Howie, you’re bringing up a really good point, and I know actually the [FDA] commissioner, Dr. Robert Califf, when he first came in, said that he really wanted to address some of these issues. And it does drive me crazy to see some of these claims. I mean claims that you would never see on pills, on foods, and on supplements and on a wide range of things that just have, as you’re mentioning, such a different threshold. And I think it can be quite deceiving to people because they may have this belief that any of these claims go through the same kinds of screening and they don’t, they don’t, they simply don’t. So, yeah, I think this is a big problem. I think people spend a lot of money, they actually even put themselves at risk because they do this instead of using something that’s been shown to be even be effective, and this is an area that definitely needs improvement. I’m so glad you brought it up and talked about it.

**Howard Forman:** Thanks.

**Harlan Krumholz:** You’ve been listening to *Health & Veritas* with Harlan Krumholz and Howie Forman.

**Howard Forman:** So how did we do to give us your feedback or to keep the conversation going? You can find us on Twitter.

**Harlan Krumholz:** I’m [@hmkyale](https://twitter.com/hmkyale/), that’s H-M-K Yale.

**Howard Forman:** And I’m [@TheHowie](https://twitter.com/TheHowie/), that’s @-T-H-E-H-O-W-I-E. You can also email us at health.veritas@yale.edu. Aside from Twitter and our podcast, I’m fortunate to be the faculty director of the healthcare track and founder of the MBA for Executives program at the Yale School of Management. Feel free to reach out via email for more information on our innovative programs where you can check on our website at [som.yale.edu/emba](http://som.yale.edu/emba).

**Harlan Krumholz:** *Health & Veritas* is produced with the Yale School of Management and the Yale School of Public Health. Thanks to our researchers, Ines Gilles and Sophia Stumpf, and to our producer, Miranda Shafer, they are absolutely amazing. Talk to you soon, Howie.

**Howard Forman:** Thanks very much, Harlan. Talk to you soon.