When wading through the river of health advice, where you can find people saying one thing is good and other people saying the exact opposite is good, it's helpful to have a couple strategies for logically vetting information. Some lines of logic are better than others:

Lisa, I want to buy your rock

So I want to share with you four things to consider when analyzing health related information. There's many other strategies, and even when these four things check out it of course doesn't make something automatically true. But, they're quick, effective and get you in a better position to further your investigation.

So the four things are :

The History
The Context
The Mechanisms
The Short term vs. the Long Term

As we go through each of these four, we'll look at examples of how this can apply to evaluating diets or medications, but throughout the video, I'll look in particular at antidepressants. I should say at this point that this of course isn't intended to be medical advice, and if you happen to be on an antidepressant, whatever you do, don't abruptly stop taking it without consulting a professional.

Let's start with history. For diet, this usually means looking at the diet from an evolutionary perspective. For example, if I were looking at the fruitarian diet, I would be critical of the fact that it's very unlikely that we were eating primarily fruit in prehistoric times considering our guts shrank as our brain got bigger.[R] But, even if we were, the fruit we would have gotten back then wouldn't have been much at all like the modern day fruit that through cultivation has come to be much bigger and sweeter. As Daniel Lieberman points out in his book "The Story of the Human Body," "almost all the fruits

our ancestors ate were about as sweet as carrots." That means a prehistoric fruitarian diet would be more like a modern day vegetable diet.

Moving on, when looking at medicines or prescription drugs, we'd want to know the history - what was the logic that led to the development and application of the drug?
Let's compare the history of insulin to the history of antidepressants.

The history behind insulin [*Slate Video*], very briefly, goes like this: A disease called type 1 diabetes was discovered that was causing children to waste a way and die within months. German scientists suspected the pancreas was at fault for diabetes in 1889, and Eugene Opie in 1901 very accurately suspected that a lack of an internal secretion specifically from the islets of Langerhans in the pancreas was the major problem. Scientists made several attempts at turning the pancreas into a medicine, feeding patients raw pancreas, giving them ground up extracts of the pancreas - with not so great results. Finally, in January 1922, after many discouraging failed experiments, David Banting and Charles Best with the vital help of James B. Collip, successfully treated a boy's diabetes with a pancreatic extract. This marked the discovery of insulin and was a historical moment for medicine.

So, the cause of the disease was first well theorized, and then a medicine was created based on the assumed pathology.

What about antidepressants?

[*This section below comes from Robert Whitaker's "Anatomy of an Epidemic"]*
The order of events is very different. In 1955, Bernard Brodie and Arvid Carlsson found that an herbal drug called reserpine seemed to make animals "lethargic," "apathetic," and "depressed." [*Further reading*, 2]
This mood depressing drug also reduced brain levels of norepinephrine, dopamine and serotonin. These three are all technically monoamines but norepinephrine and dopamine are classified as catecholamines. Then, it

was found that the drugs iproniazid and imipramine could prevent the lethargy and apathy if given before the depressing drug reserpine - that is, they seemed to have a anti-depressant effect. These two so called "antidepressants" blocked the usual depletion of the catecholamines: dopamine and norepinephrine and blocked the depletion of the monoamine serotonin.

You may be familiar with the famous chemical imbalance theory of depression and other mental disorders. Joseph Schildkraut deserves some credit for this, in 1965 he said that "*some, if not all depressions are associated with an absolute or relative deficiency of catecholamines, particularly norepinephrine.*"[R] After that, researchers quickly turned much of their attention to serotonin, guessing a deficiency in serotonin to be a root cause of depression.

So researchers first understood how a drug worked, then assumed the cause of depression based on that drug's action. What's the problem with this?

The American Psychiatric Association's own 1999 textbook explains that assuming depression is caused by low serotonin because a drug that seems to prevent depression *raises* serotonin *"is similar to concluding that because aspirin causes gastrointestinal bleeding, headaches are caused by too much blood loss and the therapeutic action of aspirin in headaches involves blood loss.*" So in 1999 the APA is making fun of the how the chemical balance idea came to be.

Yet, at least as of 2014, several organizations are still pushing this chemical imbalance theory.

The next point is about context. This is especially important to consider for food or medications. For example, in the context of a low carbohydrate diet, plenty of good quality butter could be perfectly healthy and not make you gain weight, but if you're consuming lots of butter in the context of a *high* carbohydrate diet, the insulin effect of the carbohydrate is going to have

you store more of the butter you eat as body fat. And, eating a lot of carbs by themselves is very different from eating a lot of carbs when they're wrapped in fiber- in the form of vegetables.

There are many other contexts to look at, an obvious one is genes - certain populations can be more susceptible to certain diseases[R], and certain gene polymorphisms can affect your levels of certain vitamins like folate, Vitamin B6 and B12, beta-carotene and vitamin D.

It would be very interesting to see the differences in genetics or maybe microbiome status of Rich Roll and Mikhaila Peterson.

Rich Roll is an ultra endurance athlete. In 2010, he completed 5 ironman-distance triathlons in under a week. Part of his fame comes from the fact that he manages these impressive feats of endurance while maintaining a vegan diet - a diet that, for him, was a key component to his athletic success. At age forty, Rich found himself winded just from climbing a flight of stairs. This was the trigger to get him to switch to a plant only diet. Two years later and fifty pounds lighter, he became the first vegan to complete the 320-mile super-endurance Ultraman event, finishing in the top 10 males.

On the other hand, we have Mikhaila Peterson, who, since at least as early as the age of 7 had severe rheumatoid arthritis, began taking antidepressants for severe anxiety and depression from around age 11, had many joints replaced by age 17 thanks to the arthritis, and had severe skin problems from age 19. At one point she was sleeping 17 hours a day and relied on Adderall just to keep herself awake, not to mention taking 2 different antidepressants and 6 other medications for her other health problems.

Then, thanks to a very strict elimination diet which allowed basically only meat and select greens, virtually all her problems cleared up: Her arthritis and skin conditions cleared up in 3 weeks, her depression disappeared in 3 months. A month after that, the extreme fatigue went away.

Grains, dairy, sugar and soy are what she's particularly wary of, but things as seemingly harmless as almonds, rice, white cabbage, bananas, citrus, onions and zucchini have all given her major issues when she's tried to reintroduce them into her diet. For the past six months she's now been on a diet that is just meat, salt and water - this was the last step in diet improvement for her. She says on her blog that on the all meat diet, she just feels better and better, her brain is the fastest it's ever been and she's happy and energized all day. And now, she takes no medications at all.

Rich Roll and Mikhaila Peterson's diets do have some similarities - they've both cut dairy, sugar, gluten and processed food, but the two diets are clearly **very** different. And while both of these people would surely say that these diets changed their lives, they probably couldn't imagine themselves on each other's diet. Different diets, but different contexts.

Going back to antidepressants, we'd want to know the context in which you introduce this medication. A genetic test [R] for example would be helpful, but before you introduce a drug that increases serotonin signalling, we would at least want to verify that the person actually has low serotonin levels. Especially because antidepressants are known to have a very high risk for complications including the potentially life threatening serotonin syndrome and a black box warning for "suicidal thoughts and behaviors."

But… As researchers at McMaster University explain, "*It is currently impossible to measure exactly how the [living] brain is releasing and using serotonin...*"[R]

However there is a kind of workaround for this. After serotonin is pumped into the synapse, it is either taken up into the pre-synaptic neuron for later use or it is metabolized by an enzyme into 5-hydroxyindole acetic acid (5-HIAA). Researchers can comb the cerebrospinal fluid for this metabolite for an indirect measurement of serotonin. So, we should expect that people with depression would have low levels of 5-HIAA meaning they have low serotonin.

But, how well does this pan out? In 1971, investigators at McGill University failed to find a “statistically significant” difference between the 5-HIAA levels of depressed patients and normal controls and there was no correlation whatsoever between depression severity and levels of 5-HIAA.[R] Then in 1974, two researchers at the University of Pennsylvania found that a serotonin depleting drug didn’t reliably induce depression at all.[R]

Then, in 1975, investigators at the Karolinska Institute in Stockholm found that thirty percent of the depressed patients they tested indeed suffered from low levels of the serotonin metabolite 5-HIAA. But, they also found that 25 percent of the “normal” group also had low cerebrospinal levels of these metabolites. In fact, more than *half* of the depressed patients had relatively *high* levels of the serotonin metabolite.[R] Finally in 1984, NIMH investigators wanted to see whether those depressed patients with low serotonin would be the best responders to an antidepressant. Unfortunately for the chemical imbalance theory, lead investigator James Maas wrote, “*contrary to expectations, no relationships between cerebrospinal 5-HIAA and response to [the antidepressant] amitriptyline were found.*”[R]

Simply put, researchers assumed that antidepressants were working their magic in a certain context based on what the antidepressant does, not based on proper evidence for that context.

The next thing you’ll want to investigate is the ***mechanisms*** behind whatever food, diet or medicine is in question. This can be a difficult step depending on your understanding of biochemistry and pharmacology, but that doesn’t mean the concepts are out of your reach.

For example, let’s say you hear that margarine is bad for heart health whereas good quality butter is actually good for heart health. For some, this may sound dubious as it’s the opposite of what we’ve been told in the past - You can even find the mayo clinic website saying “*Margarine usually tops butter when it comes to heart health.*” as recent as last month. But then you

learn that the vitamin K2 in butter promotes the decalcification of soft tissues like the heart because decalcification is a vitamin K2 dependent process. And, the hydrogenated vegetable oil in margarine *inhibits* these vitamin K2 processes making it easier for soft tissues, like the heart, to calcify.[R, *further reading*: *"Fat and Cholesterol Don't Cause Heart Attacks and Statins are Not The Solution"*]

"*Industrial hydrogenation of canola and soybean oils produces not only trans fat but also the dihydro form of vitamin K1 (dihydro-VK1), the side chain of vitamin K1 with one double bond being hydrogenated (Fig. 8). The dihydro-VK1 is not converted to vitamin K2, and inhibits the vitamin K2 dependent processes in human, e.g., bone homeostasis (Booth SL, 2001; Shea MK, 2009).*" -Kendrick, Malcolm. Fat and Cholesterol Don't Cause Heart Attacks and Statins Are Not The Solution (Kindle Locations 1307-1310). Columbus Publishing Ltd. Kindle Edition.

We now even have mechanisms for how the cholesterol-lowering so called "heart-saving" drugs statins actually worsen calcification of the heart. As is illustrated in this 2015 paper, Similar to hydrogenated oils, statins block a step in this decalcification process. Now that you have a mechanism in mind, you can investigate further. If you look up "statin-induced arterial calcification," you'll find papers showing that yes, high dose or long term statin therapy advances arterial calcification.[R, R2, R3]

"*Statins inhibit the supply of geranylgeranyl residue and warfarin inhibits the reactivation of oxidized vitamin K1.*" -Kendrick, Malcolm. Fat and Cholesterol Don't Cause Heart Attacks and Statins Are Not The Solution (Kindle Locations 1303-1304). Columbus Publishing Ltd. Kindle Edition.

Going back to the antidepressants, this one of the problems - the mechanism for how they work is not known. For example with the common selective serotonin reuptake inhibitor, SSRI-type antidepressants - we of course know they inhibit reuptake of serotonin, but it's not known *why* that would have a therapeutic effect.

Listen to Psychiatrist Daniel Carlat's comment on this:
"*We don't really know how the medications actually work in the brain. So whereas it's not uncommon--and I still do this, actually, when patients ask me about these medications, I'll often say something like, well, the way Zoloft works is it increases the levels of serotonin in your brain, in your*

synapses, the neurons, and presumably the reason you're depressed or anxious is that you have some sort of deficiency. And I say that not because I really believe it ... I say that because patients want to know something, and they want to know that we as physicians have some basic understanding of what we're doing when we're prescribing medications. And they certainly don't want to hear that a psychiatrist essentially has no idea how these medications work."

So we don't actually know why they *would* work, and there's doubt about whether they actually *do* work. [Clip "No better than a placebo"][R,R2,R3] However, some people have experienced antidepressants as being truly helpful and life saving, making the topic of their efficacy complex and out of the scope of this video.

The last point is the Long Term vs. Short Term. This is a very tricky to consider when it comes to nutrition for many reasons, one being that the body is constantly adapting and responding to what you put into it. For example, many people have had weight loss success on caloric restriction diets, but some will find later on that it's difficult to maintain the lost weight thanks to an adaptation called "metabolic adaptation" where the body drastically reduces its resting metabolic rate and makes you hungrier from hormonal adaptations in response to the calorie cutting.[R]

Another complication is the fact that we often need to use biomarkers as predictors for guessing whether someone will develop a disease in the future - but we need to be sure these biomarkers are really an accurate way for predicting the disease. Cholesterol is the easy example of this - people who increased their vegetable oil consumption with the aim of keeping cholesterol down may be displeased to learn that inflammation is turning out to be a far better predictor of heart disease, and omega-6 rich vegetable oil is pro-inflammatory.[R]

This leads us to maybe the most concerning point about anti-depressants. Most of the more recent data on depression today turns out to be data on *medicated* depression. It's widely thought that depression is a chronic

disease, and patients are often informed that they'll have to take antidepressants for life to keep their chemical imbalance corrected - sort of like a diabetic who needs to take insulin long term. Then, it's very common for people to have a depressive relapse when going off the drugs, which is thought to be evidence for the necessity of drugs. But what happens in people who just don't take medication?

In Robert Whitaker's book "Anatomy of an Epidemic," he explains that before the age of antidepressants, people's depression would usually resolve *by itself*. A 1931 long term study of *2,700* depressed patients reported that more than half of those admitted for depression only had one depressive episode.[R] A Swedish physician, Gunnar Lundquist, followed 216 depressed patients for eighteen years and found that 49% never experienced a second depressive episode, and 76% became socially healthy and could resume their usual work.

Bulgarian psychiatrist Nikola Schipkowensky said that tricyclic antidepressants were inducing the disease to "change to a more chronic course."

Then, a 1995 NIMH study looked at people diagnosed with major depression who received antidepressant treatment and those who did not. At the end of 6 years, the people who received the medication were more than 3 times as likely to have stopped functioning in their usual societal roles.[R]

Finally, in 2006, ~~Robert~~ Michael Posternak led a study that looked at people who had a depressive episode who, after recovering from the first bout of depression with medication went on to relapse but did not use medication thereafter. It was found that 23% of these unmedicated people recovered in one month, 67% of them recovered in six months and 85% recovered within a year. So while antidepressants might be speeding up the recovery for some depressed people in the short term, thanks to the medication, the depression becomes a long term disease.[R]

History, Context, Mechanisms and the Short term vs. the Long term - four points for investigation that by themselves won't necessarily allow you to say "case closed," but it will help you more efficiently process incoming health or diet information and make better conclusions.

While the ability to gather heaps of knowledge was a valuable skill in the past, what is valuable nowadays is the ability to rapidly assess the merit of incoming information and ignore what is not useful.