The Truth About Food Toxins

WEBINAR SUMMARY

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INTRODUCTION

We all have fallen, hook, line and sinker for at least some of the misinformation seeping out of the confusing morass of dietary guidelines, weight loss programs, fad diets, and the food phobic messaging from influencers and diet guru's peddling in healthism and miracle cures. While it would be impossible to address every food-related myth in a single go, I want to tackle some of the most common ones to alleviate your concerns about what you eat. If you've fallen for these myths before, don't feel bad because I did, too! It's taken me a great deal of research over the past few years, and a very open mind, to fully unpack and deprogram these misconceptions, which come from cherry-picked studies and seemingly logical explanations that crumble under rigorous scrutiny and don't represent the scientific consensus.

How and why has my approach changed?

In the past, my research was focused on understanding ideas prevalent in the wellness community that aligned with my lived experience. I learned this way of thinking from prominent scientists and doctors who preceded me. Their work taught me to believe that if a food contains a compound that is harmful to one biological system, then the whole food must be bad for the whole us. I put a lot of stock into mechanistic studies (rodent and cell culture studies) that explained how a food compound is harmful, and I was buoyed in that approach by conformation bias.

There was no Eureka! moment, no singular event that made me see the logical fallacy in this way of thinking. Instead, my research first into the gut microbiome and then into nutrient profiling, coinciding in time with my growing dismay over ever more restrictive diets gaining popularity, made me gradually realize that I had been thinking about food all wrong. So, I actively disengaged with the wellness community.

Avoiding confirmation bias requires a conscious effort to seek a balanced and objective view of information. To begin, one should actively seek out diverse sources of information, considering various viewpoints and perspectives. It's essential to be open to the possibility that one's existing beliefs may not always be accurate and to question assumptions. Critical thinking, fact-checking, and seeking out credible sources can help in separating facts from opinions. Additionally, engaging in respectful discussions and debates with people who hold different viewpoints can provide valuable insights and challenge preconceived notions. Ultimately, the key to avoiding confirmation bias is maintaining intellectual humility, staying curious, and being willing to adapt one's beliefs based on evidence and reasoned arguments. For me, this included a return to my roots as a medical researcher, and taking a broader view of the scientific literature, independent of my beliefs and lived experiences. Instead of searching for an explanation for what I already believe, I dive much deeper into the research to understand the scientific consensus, or when that doesn't yet exist, where the preponderance of evidence lies.

All foods contain a huge variety of molecular compounds. When isolated in a lab, some food compounds are legitimately detrimental to our health, but that's not what we're eating. We're eating a food that contains hundreds if not thousands of different molecules, and even if some are harmful, we are most often compensated by a wealth of nutritive compounds that benefit our health. While we must acknowledge that single compounds in foods can drive allergic reactions and food intolerances, and certainly not every food works for every person, when we're looking at whether or not a food is a healthy choice *in general*, we need to consider the complexity and synergy of the complete food matrix and how that impacts all of our biological systems. That's why it's so important to look at prospective studies and randomized, controlled clinical trials that evaluate how the whole food, rather than the isolated compound, impacts whole-body health.

I now put the most stock in systematic reviews and meta-analyses—which are studies that pool together data from the entire research field, and which include assessing individual study quality and risk of bias prior to inclusion of its data in the analysis—that determine the magnitude of impact of a food or dietary pattern on a comprehensive collection of health outcomes. And, I highly value all-cause mortality data, which measures the overall impact of a food or behavior on general health and longevity as a broad indicator of benefit or harm. While these epidemiological studies require mechanistic or intervention studies to establish causality, which is where rodent and cell culture studies still come into play, they measure the big picture, i.e., how the whole food affects the whole us.

While our bodies and our gut microbiomes have extensive detoxification pathways, there can be a threshold of intake of certain food compounds or additives above our body's ability to detoxify—above that threshold of intake, it is known to cause issues. Many food toxin myths disregard the impact of dose. The adage "the dose makes the poison" underlies the field of toxicology, i.e., the study of how chemicals adversely impact health—everything is a poison in a large enough quantity. As an extreme example, you need water to live and dehydration can cause a variety of health problems such as bladder infections and kidney stones, yet it is possible to die from drinking too much water in a short period of time—in one report, drinking 6 liters of water over three hours was deadly.[1] Most food additives and pollutants have Acceptable Daily Intake (ADI) levels established, or alternatively a chronic reference dose or tolerable daily intake, both of which are an estimate of the amount of a substance in food or drinking water that can be consumed daily over a lifetime without presenting an appreciable risk to health. The ADI is typically 100 to 1000 times lower than the threshold known to cause harm (called the No Observable Adverse Effect Level [NOAEL], and this is an important part of the conversation when it comes to busting food-phobic myths. Just because something is harmful in large quantity, that does not mean it is harmful in any quantity—we must compare to the amounts we normally consume.

It's additionally important to stay up-to-date on scientific evidence, and recent studies have definitely changed the landscape of human knowledge of nutrition. Nutritional sciences is a very young field of research, and thanks to advances in methodology and

technology, new studies are adding to our understanding all the time. The issue isn't that nutritional science is still evolving, but rather how frequently diet dogma has preceded the necessary scientific foundation to underpin it. Some of the myths I will bust below, I can do so simply thanks to new evidence and scientific studies that challenge the status quo, rather than my shift to a more rigorous metric and objective view of the science. It is the responsibility of all scientists to adjust our stance when new studies demand it.

Myths about food quality, toxins and antinutrients perpetuate healthism—the misnomers that a person's health is entirely their responsibility, and that good health has moral value—by creating unrealistic standards and fueling the belief that only specific, often expensive, foods are deemed healthy, or that a costly supplement regime is a health necessity. The cacophony of food fearmongering out there may have you feeling confused about what foods are safe to eat, and pressured to conform to rigid notions of what constitutes "good" or "clean" eating. With all this conflicting information, it's easy to become discouraged and find yourself in that vicious cycle of guilt, stress, and ultimately, unhealthy eating habits. It is my goal with this webinar to bust these food toxin myths that may be harming your relationship with food and contributing to disordered eating patterns.

Moving forward requires taking a step back and letting go of value judgments about food that lack scientific support. Yet it's crucial to emphasize that this isn't about laying blame or feeling guilt, but rather about making room in our minds for a wealth of new, invaluable information focused on the positives that we can gain from a nutrient-focused approach like Nutrivore and where no food is off the table: Nourishment, not judgment.

So, with that preamble out of the way, let's summarize the current state of evidence on a dozen common food toxin myths.

LECTINS

Lectins are a vast collection of carbohydrate-binding proteins and glycoproteins that are ubiquitous in nature and found in a wide variety of commonly consumed foods.[2] But just because a few lectins can have a negative health impact in some circumstances—for example, gluten triggering gastrointestinal symptoms in people with celiac disease and non-celiac gluten sensitivity;[3] or phytohemagglutinin being responsible for food poisoning from eating undercooked kidney beans[4]—that doesn't mean the entire class of molecules is bad for all of us.

A growing collection of studies are identifying *beneficial* effects of some lectins, such as inhibiting cancer metastasis and tumor growth, improving serum lipids and blood sugar regulation in diabetes, and antimicrobial effects that could be leveraged in the development of new antiviral medications—so we just can't paint this entire class of

molecules with the same brush.[5] Plus, proper food preparation inactivates many lectins—for example, soaking, sprouting, fermenting and/or boiling pulse legumes can reduce the lectin content to near zero.[6]

Lectin-rich foods like pulse legumes, whole grains, nuts and seeds offer consistent and impressive health benefits, which would just not be the case if their lectins were harmful.

In a 2021 study, eating 2½ or more servings of legumes per week reduced all-cause mortality by 17%, and cardiovascular disease by 14%, compared to eating only two servings per month, also lowering cardiovascular disease mortality, cancer incidence and cancer mortality.[7] A 2001 study showed that eating legumes four times per week reduced coronary heart disease risk by 22% and cardiovascular disease risk by 11% compared to eating them less than once per week.[8] And a 2014 meta-analysis likewise showed that four servings per week of legumes reduces coronary heart disease risk by 14%.[9]

A 2016 meta-analysis showed that eating three servings of whole grains daily (3 ounces, or about 90 grams) reduces risk of coronary heart disease by 19%, cardiovascular disease by 22%, cancer mortality by 15%, respiratory disease mortality by 22%, diabetes mortality by 51%, infectious disease mortality by 26% and all-cause mortality by 17%.[10] And a 2018 meta-analysis calculated that for each 1-ounce serving of whole grains daily, all-cause mortality decreases by 9%.[11]

A 2016 meta-analysis showed that eating one ounce (28 grams) of nuts, seeds and/or peanuts per day reduces risk of all-cause mortality by 18%, coronary heart disease by 27%, stroke by 11%, cardiovascular disease by 25%, cancer by 20%, respiratory disease mortality by 21%, neurodegenerative disease mortality by 19%, infectious disease mortality by 36%, and kidney disease morality by 34%.[12] And a 2015 meta-analysis calculated that 28 grams of nuts, seeds and/or peanuts per day was associated with a 27% reduced risk of all-cause mortality and a 39% reduced risk of cardiovascular disease mortality, and the highest nut and seed consumers saw a 14% reduced risk of cancer mortality.[13] Peanuts themselves are associated with diverse health benefits, including reducing cardiovascular disease risk, reducing risk of developing type 2 diabetes, reducing risk of age-related cognitive decline and Alzheimer's disease, and lowering inflammation .[14]

PHYTATES

Compounds like phytates and oxalates are considered antinutrients because they are naturally found in food as salts—i.e., complexes with minerals like calcium, copper, iron and zinc—which hinders the minerals they're bound to from being absorbed in our gastrointestinal tract. For example, vegetarians and vegans may need to consume more dietary zinc because the zinc in their diets comes predominantly from higher-phytate foods, which reduces its absorption.[15] But blocking nutrient absorption is a far cry from

depleting our bodies stores, which just isn't the case.[16] In addition, our gut bacteria do metabolize phytates and oxalates for us, making a large proportion of the minerals bound to them bioavailable.[17][18]

Although phytates are viewed in a negative light due to their antinutrient properties, they appear to have some impressive health benefits, potentially thanks to their molecular similarity to a vitaminlike compound called myo-inositol, which is known to improve insulin sensitivity and reduce anxiety. Phytate and myo-inositol are carbocyclic sugars, which are important structural components of cell membranes and which mediate cell signal transduction in response to a variety of hormones (including insulin), neurotransmitters, and growth factors and participates in osmoregulation. Myo-inositol is IP5 and phytate is IP6; phytate just has an extra phosphate group, and there's evidence for some similar biological effects to myo-inositol. And phytate has powerful antioxidant and anti-inflammatory properties![19]

For example, a 2013 study showed that high phytate levels lowered the risk of osteoporosis in menopausal females[20], and a similar 2022 study showed that phytate supplements reduced bone resorption in patients with urinary stones.[21] A 2018 study showed that higher consumption of phytates reduced glycated hemoglobin A1c in type 2 diabetics.[22] A 2019 study in people with hyperuricemia (high uric acid levels in the blood, which can cause gout and kidney disease) showed that supplementing with phytates reduced fasting serum uric acid levels.[23] A 2015 study in elderly people showed that higher phytate consumption, and higher urinary phytate levels, reduced vascular calcification which is protective in cardiovascular disease.[24] And a 2021 study showed that higher phytate consumption decreased cognitive decline in aging.[25]

Phytic acid-rich foods—including whole grains, legumes, nuts and seeds, and root vegetables—are associated with broad health benefits. This would not be the case if phytic acid was as harmful as the myths suggest.

OXALATES

Oxalates are often blamed for kidney stones (and other health problems for which there is no established connection in the scientific literature) with rumors online that eating too much spinach can cause calcium oxalate kidney stones in as little as two weeks.

Although there are different types of kidney stones, calcium-oxalate kidney stones are the most common, accounting for about 80% of cases. Certain dietary factors increase risk—high meat intake, high salt intake, low calcium intake, and low intake of fruits and vegetables—but the biggest risk factor is inadequate hydration.[26] When we have too-high concentrations of oxalates in the urine, a condition called *hyperoxaluria*, calcium oxalate crystals can form in the kidneys and develop into stones. Generally, the symptoms of

hyperoxaluria are that of kidney stones, including sharp pain in the back, side, lower stomach area or groin; urine that looks pink, red or brown due to blood; frequent urge to pee; pain when peeing; not being able to urinate or peeing only a small amount; chills, fever, upset stomach or vomiting. In rare cases, primary hyperoxaluria can present as calcium oxalate microcrystalline-associated arthritis in which case, joint pain would be a symptom before a kidney stone.[27] Calcium oxalate microcrystalline-associated arthritis is also seen in late-stage renal failure.[28] Dietary oxalates don't cause joint issues or gut issues more broadly, however.

Increasing fluid intake (hydrating ourselves better!) reduces the risk of kidney stones by increasing urine volume and diluting oxalate levels, in turn helping prevent stones from forming. In fact, ingesting enough fluids (whether through drinking beverages or eating high-water-volume foods like vegetables and fruit) to keep urine flow greater than 1 milliliter per kilogram bodyweight per hour nearly eliminates the risk of oxalate oversaturation in the urine, and can dramatically reduce kidney stone formation!

So, what about avoiding high oxalate foods, like spinach, nuts, beets, rhubarb, tea, chocolate, strawberries, and wheat bran? Studies show inconsistent effects of dietary oxalates on urinary oxalates—most of the oxalates in our urine are ones our bodies produce. Oxalate precursors include the amino acid glycine (rich in collagen) and vitamin C.[29] A 2008 study concluded that "The impact of dietary oxalate on urinary oxalate appears to be small. For many stone formers, restricting dietary oxalate may be a relatively ineffective intervention to reduce urinary oxalate excretion."[30] And in a 2002 study, healthy females consumed 150 grams—about five cups—of spinach daily for three weeks.[31] Not only did the study participants *not* develop kidney stones, but they also had lower levels of oxidative stress.

There's also a link with the gut microbiome. Research shows that people with oxalate-degrading bacteria in their guts have significantly lower risk of developing kidney stones, even on high-oxalate diets. For example, people with *Oxalobacter formigenes* in their guts have a 70% lower risk of being recurrent kidney stone formers.[32]

Citric acid, found in citrus fruits, can also reduce kidney stone risk by binding with calcium oxalate crystals (which prevents the crystals from growing in size and becoming stones).[33] But, it's a myth that large doses of lemon juice will break up kidney stones once formed. Getting enough calcium is also important since dietary calcium reduces how much oxalate we absorb, leading to lower oxalate levels in the urine.

So, if you are prone to kidney stones, drinking enough water on a consistent basis is your best strategy to reduce your risk, along with getting enough dietary calcium and adding in some citrus fruits. There's some indication that drinking up to 50% more than the standard recommendations of 3 liters for men and 2.2 liters for women is important for people with recurring kidney stones. Also, go ahead and skip the alkaline water—not only are the various claims unfounded, but too-high pH water can negatively impact the gut microbiome.[34]

It's important to note that some people (about one in three million) have genetic disorders that cause too much oxalate to be produced within the body, and other people have absorption disorders that cause too much oxalate to get absorbed from the gut (including Crohn's disease, celiac disease, chronic pancreatitis, and side-effects from bariatric surgery). If this applies to you, talk to your doctor about whether or not it's appropriate for you to reduce your intake of high-oxalate foods.

VEGETABLE OILS

There's nothing wrong with vegetable oils. The reason why you might have heard that they're inflammatory is because they're rich in linoleic acid, the essential omega-6 polyunsaturated fatty acid. Omega-6 fats contribute to pro-inflammatory pathways, so in theory, we regulate inflammation when we balance our intake with anti-inflammatory omega-3s. But, while this is plausible from a mechanistic angle, a wealth of recent research in humans has not borne this out.

Most studies have shown a neutral or even protective effect of linoleic acid (and the vegetable oils rich in it) on inflammation, cardiovascular health, and all-cause mortality. For example, a 2014 meta-analysis found that over time, participants with highest intake of linoleic acid (up to a whopping 10% of total calories) had a 15% lower risk of experiencing a heart disease event, and a 21% lower risk of dying from heart disease compared to the lowest intake (more like 1% of total calories).[35] A 2020 meta-analysis looking at tissue levels of linoleic acid (a potentially more reliable indicator of intake than dietary recalls) found a strong, linear relationship between higher linoleic acid concentrations and *reduced* cardiovascular disease, cancer, and all-cause mortality.[36] The people with the highest levels had a 13% lower risk of all-cause mortality, 13% lower risk of cardiovascular disease mortality, and 11% lower risk of cancer mortality than the people with the lowest levels. And, a 2012 meta-analysis found no association between linoleic acid intake and any inflammatory markers, contradicting the theory that linoleic acid contributes to cardiovascular disease by increasing inflammation.[37]

Olive oil does have the edge over vegetable oils when it comes to supporting health. A huge 2021 prospective study showed that substituting butter or margarine for corn oil, canola oil and olive oil all lowered all-cause mortality and cause-specific mortality, including from cardiovascular disease, type 2 diabetes, cancer, respiratory disease, and Alzheimer's disease.[38] Olive oil had the highest magnitude of benefit (4% reduction in cardiometabolic mortality for every tablespoon daily), followed by canola oil (2% reduction) and corn oil (1% reduction). So, yes, from a health perspective, olive oil still wins. But, if you can't afford, don't have access to, or just don't like it, you're still going to enjoy overall benefit from other vegetable oils.

Another common myth about vegetable oils is that the industrial processing to make them causes them to be heavily oxidized, rancid, and full of solvent chemicals like hexane.

To make vegetable oil from plants, first the plant parts that are used to make the oil are harvested, deshelled, hulled, and cleaned.[39] If the seed is used to make the oil, it is crushed or broken up into smaller pieces. Sometimes a first-press oil is made by mechanical extraction, basically squeezing these tiny pieces until oils comes out (a.k.a. cold pressing), and then a second-press oil is made from solvent extraction. During solvent extraction, hexane is added to the crushed plant parts and then briefly heated, which causes a chemical reaction to allow the oil from the plant to separate out. The heat also causes hexane to evaporate—most vegetable oils have no detectable hexane residues.[40] In one study, the highest concentration of hexane detected was 0.4 milligrams per kilogram (1.1 liters) of oil.[41] The provisional chronic reference dose of hexane is 0.06 milligrams per kilogram bodyweight per day—so, a 70-kg person (154 pounds) would have to consume over 11 liters of vegetable oil every day to ingest enough hexane to worry.

Once the oil is extracted, it's then bleached using bleaching clay—not the bleach you use to clean—to remove any coloring pigments like carotenoids or chlorophyll which can make the oil more susceptible to oxidation in response to light. It's then deodorized to remove any odor and off-flavors, and contaminants (pesticides, polycyclic aromatic hydrocarbons, etc.). Finally, it is filtered to remove any residual solvents, leaving the oil in its final state, which is packaged and sold. The refining process gives vegetable oil its light color, makes it flavorless and odorless, and makes it *more* stable with a longer shelf life. The claim that refining vegetable oil makes it more likely to go rancid is untrue. In fact, refining vegetable oil reduces the likelihood of rancidity.

SWEETENERS

The science is mixed on whether replacing sugars with sweeteners facilitates weight loss or improves insulin sensitivity, with some studies showing benefit, some showing no effect, and some actually showing, counterintuitively, that sweeteners also contribute to insulin resistance. Nonnutritive sweeteners are sugar substitutes that include artificial sweeteners like aspartame as well as natural sweeteners like stevia and monk fruit extract.

Whether there is an association between sweeteners and cardiovascular disease has not been as extensively studied as other foods or food additives. But, a 2022 study out of France that included over 100,000 participants followed for about 10 years showed that total sweetener intake—including cyclamates, saccharin, thaumatin, neohesperidine dihydrochalcone, steviol glycosides (i.e., stevia), and salt of aspartame-acesulfame potassium—increased risk for cardiovascular disease, including heart disease and stroke.[42] High intake (mean was 77 milligrams of total sweeteners per day, the equivalent

of about 1.5 cans of diet soda) versus zero intake showed an overall 9% increased risk of cardiovascular disease. The statistical model accounted for age, sex, physical activity, smoking, educational, family history of cardiovascular disease, energy intake without alcohol, alcohol consumption, sodium, saturated fatty acids, polyunsaturated fatty acids, fiber, sugar, fruit and vegetables, red and processed meat. Interestingly, the same cohort was analyzed for associations between sweetener intake and cancer risk.[43] High intake of sweeteners increased total cancer risk by 13% compared to no intake, with highest association being with aspartame and acesulfame potassium, and breast cancer and obesity-associated cancers. Although not all studies have shown an association between sweeteners and cancer.[44]

A 2022 study analyzing data from the Women's Health Initiative showed an association between artificially sweetened beverage consumption and cardiovascular disease.[45] Consuming one or more such beverages daily increased risk of cardiovascular disease by 14% and stroke by 24%. A 2021 meta-analysis showed that consuming artificially sweetened beverages had no effect on all-cause mortality or cardiovascular disease mortality provided intake was 1.5 servings (a serving being 12 ounces) or less per day.[46] Consuming 2.5 servings per day, on the other hand, increased risk of all-cause mortality by 13% and cardiovascular disease mortality by 25%.

While this sounds pretty damning for sweeteners, it's worth comparing this effect to an equivalent amount of added sugars. If we're looking at 1.5 servings as an important threshold, that would be the equivalent of about 60 grams of sugar, or 12% of a 2,000-calorie diet. A huge 2014 study showed that consuming 10% to 24.9% of calories from added sugars increased cardiovascular disease risk by 30%, and consuming 25% or more of calories from added sugar increased cardiovascular disease risk by 2.75 times![47] But, note that staying below the 10% of calories from added sugars threshold doesn't have any clear detriment to our health. It's worth emphasizing that this 10% rule applies to *added* sugars, not carbohydrates in general or sugars that come from whole foods like fruit. When we consider all dietary sugars, including those inherent to whole foods like fruit, we see that limiting to 25% of calories is the way to go.[48]

If added sugar intake would otherwise exceed 10% of total calories, it seems like it would be a good trade to swap some added sugars out for sweeteners, even artificial ones. In the 2022 Women's Health Initiative study discussed above, drinking one or more sugar-sweetened beverages per day increased risk of cardiovascular disease by 19%, coronary heart disease by 35% and stroke by 30%. And in the 2021 meta-analysis discussed above, each 12-ounce serving of sugar-sweetened beverages daily increased risk of all-cause mortality and cardiovascular disease mortality each by 8%. A 2021 study calculated that, for each sugar-sweetened beverage daily that is replaced with the equivalent amount of artificially sweetened beverage, unsweetened coffee or tea, or plain water reduces all-cause mortality risk by 4% to 7%.[49] So, substituting sugar-sweetened beverages with artificially-sweetened beverages is a good trade in terms of our health, but it's best to consume sweeteners in moderation. There is currently insufficient data to state whether

natural sweeteners like stevia and monk fruit are any better or worse than artificial sweeteners like aspartame.[50][51]

FOOD DYES

Despite five decades of research, a causal link between artificial food dyes and hyperactivity in children still has not been established.[52] In the 1970s, concerns emerged regarding the potential relationship between food additives and behavioral issues in children. Artificial food colorings and additives—including sunset yellow, tartrazine, carmoisine, ponceau 4R, and sodium benzoate—were identified as potential culprits influencing hyperactivity in children. However, study findings were widely debated in the scientific community, and the US Food and Drug Administration Food Advisory Committee did not find causal evidence to support a link between food dyes and hyperactivity.

Challenge studies, where children are given a mix of artificial food dyes or a placebo and then their behavior is monitored, have yielded mixed results, with about half of the studies conducted (13 out of 25) showing a statistically significant association between artificial food dye consumption and adverse behavioral outcomes.[53] While there certainly is some evidence to support a relationship between food dye exposure and adverse behavioral outcomes in children, there is also a high degree of interindividual variability in the sensitivity to synthetic food dyes. Recent studies have highlighted potential genetic and neurological factors, suggesting a complex interplay that requires further investigation. So while some people can have legit intolerances to food dyes, these additives aren't bad for the rest of us in the quantities we normally consume.

The Acceptable Daily Intake (ADI) levels for food dyes are set based on carcinogenicity, meaning that as long as you're consuming that amount of food dyes or less, even if you do so every day for the rest of your life, you don't need to worry about increased cancer risk.[54] When it comes to food dyes, estimates of exposure show that, for most people, their food dye intake is a small fraction of the ADI.[55] For those that do exceed the ADI, the top contributors are juice drinks, soft drinks, icings and ice cream cones.

It is prudent not to exceed the ADI for food dyes (or anything else); an easy way to accomplish this is to limit ultra-processed food intake to 20% of total calories or less. Besides the dopamine-rush that drives hunger, cravings and food addiction, the more ultra-processed foods we eat, the higher our risks of obesity, cancer, type 2 diabetes, cardiovascular disease, depression, and dementia.[56] This is attributable both to exceeding the ADIs of food additives, as well as consuming too much added sugar and salt, in addition to lower nutrient intake. A 2021 meta-analysis showed that the more ultra-processed foods a person ate, the lower their intake of fiber, protein, potassium, zinc, magnesium, vitamin A, vitamin B3, vitamin B12, vitamin C, vitamin D, and vitamin E.[57] The

only nutrients considered that were not significantly decreased by ultra-processed food consumption were iron, calcium, phosphorus, vitamin B1, vitamin B2 and sodium. The people who ate the most ultra-processed foods were only getting about 60% of the daily value of fiber, magnesium, vitamin A and vitamin E while also falling quite short of potassium, calcium, zinc, and vitamin D. This is the direct result of consuming ultra-processed food instead of more nutrient-dense options.

A 2019 prospective study of nearly 20,000 Spanish university graduates (average age was 37 at the beginning of the study) followed for 15 years showed that, after accounting for confounding variables, people who consumed four or more servings of ultra-processed foods daily had a 62% increased risk of total mortality.[58] Plus, with every additional daily serving of ultra-processed foods above that amount, risk of total mortality went up another 18%. A similar 2022 study out of the U.K., which followed over 60,000 people over the age of 40 for ten years, showed that people who got 43% or more of their calories from ultra-processed foods had a 17% higher risk of cardiovascular disease and a 22% higher risk of total mortality, than people getting 20.8% or less of their calories from ultra-processed foods.[59] A 2021 meta-analysis calculated that, for every 10% of our daily calories that comes from ultra-processed foods, our risk of total morality goes up by 15%.[60] Yikes!

Despite those scary statistics, this doesn't actually mean that ultra-processed foods can't fit into a healthy diet. Just because something is harmful in large quantities, doesn't mean that it's harmful in any quantity. The Spanish study above shows us that there isn't much impact on health if we stay below about two or three servings of ultra-processed foods per day; the British study above measured that cusp of negative impact at about one fifth of our daily caloric intake. And, there's definitely enough data to say that a couple of servings of ultra-processed foods per day, especially in the context of an otherwise whole-foods diet, is not going to have a meaningful impact on our health.

A 2022 meta-analysis showed that not all ultra-processed foods are equally problematic.[61] While sugar-sweetened beverages, artificially-sweetened beverages, and processed meat all increased risk of total morality, breakfast cereals were associated with lower mortality—the people who consumed the most breakfast cereals (including everything from oatmeal and All-Bran to Fruity Pebbles and Lucky Charms) had a 15% lower mortality risk than the people who consumed the least breakfast cereal; and those who mainly consumed whole grain breakfast cereals has a 23% lower mortality risk. (Those who only consumed sugary cereals had no change in mortality risk.) This may reflect the fortification of breakfast cereals, meaning they have more to offer nutritionally than, for example, a can of cola, in addition to the fiber content of whole grain breakfast cereals. Certainly, more research is needed to fully understand which ultra-processed foods get an exemption from the list of foods that increase risk of health problems.

That's right, I'm saying that you don't need to completely give up ultra-processed foods. Aren't you glad you stuck with me? I think a fair interpretation of the current scientific evidence is that, if you're meeting your body's nutritional needs from the 80% of your diet that is whole and minimally-processed foods, the 20% of your calories that comes from

ultra-processed foods is unlikely to cause any harm. Some people refer to this as the 80/20 rule.

GLYCOALKALOIDS

The argument against consuming nightshade vegetables, like tomatoes, is based in part on the existence of glycoalkaloid poisoning, and in part on specific negative effects of isolated glycoalkaloids, such as solanine being inflammatory in animal and cell culture models of colitis.[62]

Symptoms of glycoalkaloid poisoning include nausea, diarrhea, vomiting, stomach cramps, burning of the throat, cardiac dysrhythmia, nightmares, headache, dizziness, itching, eczema, thyroid problems, and inflammation and pain in the joints.[63] A potentially lethal dose of glycoalkaloids is 3-6mg/kg bodyweight (for a 150-pound person, that's 204mg to 408mg) with toxicity observed at 1-3mg/kg bodyweight (for a 150-pound person, that's 68-204mg). While case reports of glycoalkaloid toxicity are most commonly in the context of green potatoes, it definitely does happen with other nightshade vegetables and plants.[64] Red, ripe tomatoes have 0.4 mg/kg (our 150-pound person would need to eat 374 pounds of tomatoes to get to 68mg, the lowest threshold for toxicity).[65] Green tomatoes have 48 mg/kg (3.1 pounds of green tomatoes to get to 68mg). And, tomato leaves have 975 mg/kg, which means a 150-pound person could experience toxicity at just 0.15 pounds (2.5 ounces) of leaves.

However, the dose makes the poison; and at the amounts we normally consume, glycoalkaloids are beneficial as summarized in a rigorous 2023 review.[66] Solanine and chaconine are anti-inflammatory and cardioprotective. Tomatine is neuroprotective. Tomatidine reduces risk of cardiovascular disease, osteoarthritis, osteoporosis, and asthma.

Tomato and tomato products overall reduce markers of inflammation.[67][68] A 2020 population-based cohort study evaluated the National Health and Nutrition Examination Surveys (NHANES) to assess the impact of long-term tomato and lycopene consumption with respect to total and cause-specific mortality.[69] A total of 23 935 participants were included. Researchers found tomato intake (1.8 cups per day) was associated with a 14% reduced risk of total mortality, a 24% reduced risk of coronary heart disease mortality, and a 30% reduced risk of cerebrovascular mortality.

HEAVY METALS

The presence of heavy metals such as arsenic, lead, mercury, and cadmium in food products and ingredients is certainly a concern.[70] These metals, which are naturally widespread in the environment, can accumulate in plants, animals, and water sources and ultimately find their way into the food supply. The ingestion of these heavy metals can lead to a range of adverse health effects, including organ damage, developmental abnormalities, and an increased risk of cancer.[71] This underscores the importance of monitoring and regulating heavy metal levels in our food to protect public health.

The chronic reference dose for methylmercury is 0.1 µg/kg/day. Some fish can contain more than this amount of methylmercury in a single serving—swordfish, one of the highest mercury fish, contains 0.55 µg/g, so if a 70-kilogram person consumed a 115-gram (4-ounce) serving, they would exceed the ADI by 9 times.[72] However, for the vast majority of fish, mercury is not a concern thanks to the selenium also found in seafood.[73]

Selenium is required for activity of twenty-five to thirty different enzymes (selenoenzymes) whose job is to protect the brain from oxidative damage. Methylmercury irreversibly binds to selenium—this is bad if we're exposed to methylmercury because it renders selenoenzymes inactive. In fact, this is the mechanism through which methylmercury is believed to damage the brain and nervous system: by inhibiting the ability of selenoenzymes to protect these tissues from oxidants.[74] Very importantly, most typically consumed varieties of fish contain much more selenium than methylmercury.[75] This is good for the fish (they don't die from mercury exposure) and even better for us. Selenium-bound methylmercury is not efficiently absorbed by our bodies. The methylmercury that is absorbed is already bound to selenium, so it can't interfere with our selenoenzymes. The only exceptions are those top-predator fish from contaminated waters in which the methylmercury bioaccumulation is higher than their selenium content, which is a fairly short list: king mackerel, marlin, pilot whale, shark, tarpin, tilefish, and swordfish, although data is mixed on swordfish and several studies show that swordfish is okay.

There have been a few European studies showing a U-shaped response curve to fish consumption, where moderate fish consumption reduces all-cause mortality and cardiovascular disease risk but higher fish consumption increases risk of all-cause mortality. The authors of these studies have postulated that this may be due to increased exposure to toxins like methylmercury. However, this isn't seen in studies of North American or Asian cohorts, where fish is equally as likely to contain these toxins but there's a linear relationship between health and fish intake—the more fish the better.[76][77] The authors of a rigorous 2017 meta-analysis proposed an alternate explanation for a U-shaped dose-response curve in Europe but a linear or curvilinear response curve elsewhere in the world: method of preparation.[78] Traditional preparations of fish in many parts of Europe include deep-frying, pickling or salting, and it may be this high-salt and/or trans fat intake to blame for the higher all-cause mortality seen with higher fish

consumption. These studies do highlight that, when upping your fish intake, it's best if you eat fish prepared in a variety of ways—baked, steamed, poached, grilled, stir-fried, pan-seared, and as sushi or sashimi—and not always reach for the battered fish and chips.

It is recommended to stick to low mercury seafood options during pregnancy, such as shellfish (including oysters, clams, scallops, mussels, crab, shrimp, lobster), salmon, trout, herring, haddock, pollock (Boston bluefish), sole, flounder, Atlantic mackerel, and lake whitefish. A 2015 meta-analysis concluded that consuming moderate amounts of fish during pregnancy, the benefits outweighs potential risks in terms of fetal neurodevelopment.[79]

The chronic reference dose for inorganic arsenic, the more toxic form of arsenic, is 0.3 µg/kg/day. Rice accumulates more arsenic than other food crops; and in fact, it is the single biggest food source of inorganic arsenic. A 2016 investigation of rice sold in the USA showed that the average concentrations of inorganic arsenic are 92 µg/kg in white rice, 154 µg/kg in brown rice, 104 µg/kg in infants' dry white rice cereal, and 119 µg/kg in infants' dry-brown rice cereal.[80] Other studies have shown similar levels in infant rice cereal.[81][82] A serving of rice is 28 grams, measured raw (which translates to about ½ cup cooked), so a 70-kilogram adult would need to eat 8 servings per day of white rice or just shy of 5 servings per day of brown rice, every day, to hit the chronic reference dose level for inorganic arsenic. For infant cereal, a serving is 3.8 grams. For a 11.4-kiolgram 1-year old (the assumed size used to establish the chronic reference dose), they would have to eat over 8 servings of either white-rice or brown-rice cereal to hit the chronic reference dose. After these studies were published, regulatory agencies including FDA and EFSA announced new regulation to lower the levels of arsenic in infant cereal.

A 2008 study looking at rice purchased from retail stores in upstate New York showed that have shown that rice grown in California has the lowest arsenic levels of domestically-grown rice, whereas rice grown in Texas and Arkansas had higher levels than average.[83] This study also showed that rice grown in China had much lower levels of arsenic than rice grown in the USA or Europe.

The chronic reference dose for cadmium is 1 µg/kg/day. The chronic reference dose for lead is 0.26 µg/kg/day for young children and 0.16 µg/kg/day for older children and adults. Chocolate contains among the highest concentrations of cadmium and lead in our food supply, but you'd have to eat *a lot* of chocolate on a daily basis in order to worry about these heavy metals.

A comprehensive 2018 study measured the lead and cadmium levels in 144 samples of cocoa powder, dark chocolate, milk chocolate, and cocoa nibs purchased at retails stores in Maryland.[84] Both lead and cadmium levels correlated with the amount of cocoa solids, and so were highest in cocoa powder, followed by cocoa nibs, dark chocolate and then milk chocolate. The mean cadmium level detected in dark chocolate was 0.27 mg/kg, meaning a 70-kilogram adult would need to consume 9 ounces (250 grams) of dark chocolate per day (3 large chocolate bars) to hit the chronic reference dose for cadmium. Considering the

highest level of cadmium detected in the study, you'd still need to eat over 2 ounces every day to hit the chronic reference dose for cadmium. The mean lead level detected in dark chocolate was 0.03 mg/kg, meaning a 70-kilogram adult would need to consume over 13 ounces (370 grams) of dark chocolate per day to hit the chronic reference dose for lead. Considering the highest level of lead detected in the study, you'd still need to eat three and a half ounces (100 grams) daily to hit the chronic reference dose for lead.

There are so many health benefits of eating chocolate! A 2017 meta-analysis of prospective cohort studies found a 10% reduced risk of developing heart disease and a 16% reduced risk for stroke among people who ate the most chocolate vs. the least.[85] In addition, the people with the highest intake of chocolate had an 18% lower risk of developing type 2 diabetes compared to people with the lowest intake of chocolate, with the greatest risk reduction occurred at two one-ounce servings per week (25% lower risk) and no protective effects occurring above six servings per week. A Cochrane systematic review from 2017 found that flavonol-rich chocolate and cocoa products can cause a small but significant reduction (2 mmHg) in blood pressure among healthy adults, and a slightly greater reduction in systolic blood pressure (4 mmHg) among people with hypertension.[86] These protective effects of chocolate may be due to its phytonutrient content and its stearic acid (which has been shown to help reduce diastolic blood pressure)! Another 2017 meta-analysis of prospective studies found that people eating moderate amounts of chocolate (less than seven servings per week) had a 14% lower risk of developing heart failure, compared to people eating no chocolate.[87] However, eating 10 servings a week was associated with slightly higher risk (a 7% increase, compared to no chocolate), suggesting more isn't always better! And a 2015 randomized controlled trial of 60 adults with type 2 diabetes and high blood pressure found that eating 25 grams of dark chocolate (versus 25 grams of white chocolate) every day for eight weeks led to lower fasting blood sugar, hemoglobin A1c, and a marker of inflammation (high sensitive C-reactive protein) by the end of the study, whereas the white chocolate group saw no changes in those parameters.[88] Clinical trials have produced some promising findings on chocolate's ability to help us maintain a healthy body weight, too. A 2019 meta-analysis of randomized clinical trials—35 in total—found that studies that included at least 30 grams per day of chocolate, for a length of four to eight weeks, led to a significant reduction in body weight and BMI among participants.[89]

So, while we certainly don't want to eat chocolate in excess, an ounce or two per day is very beneficial!

PESTICIDES

It's a complete misnomer that organic foods are way better for you than conventional, from both a safety perspective and a nutrient density perspective.

While occupational exposure to pesticides definitely can cause health problems, the amount of pesticide residue in our foods—yes, even the Environmental Working Group's Dirty Dozen—is far, far, far below the level we need to worry about. In fact, a 2011 analysis showed the Environment Working Group's methodology to rank commodities with respect to pesticide risks lacks scientific credibility—all twelve of that year's fruits and vegetables had pesticide residues well below the established chronic reference doses.[90] And in fact, three quarters of the pesticide exposure estimates were more than one million times below the chronic No Observable Adverse Effect Levels (NOAEL) from toxicology studies.

A 2020 systematic review, the largest performed to date with its inclusion of 35 studies, evaluated the health impacts of organic versus conventional foods and concluded that no definitive statement could be made on whether organic foods improve health.[91] This review looked at studies that showed that organic food consumption reduced risk of infertility, birth defects, allergic sensitization, ear infections, pre-eclampsia, metabolic syndrome, overweight and obesity, and non-Hodgkin lymphoma, but was extremely critical of these results since the effects were well within the range easily explained by what's called *healthy user bias.*

People who regularly consume organic foods are much more likely to be health-conscious females who are physically active, eat a higher ratio of plant to animal foods, eat more whole foods, and eat few if any ultra-processed foods.[92] They're also more likely to be in a higher income bracket and have achieved a higher level of education, very important social determinants of health.[93] When so many health-related behaviors align, it's next to impossible to fully account for them in statistical analysis, which biases the results, hence the term healthy user bias. These people are not healthier because they eat more organic foods, they're healthier *and* they eat more organic foods.

Many of the individual studies examined by the systematic review did not account for different types of foods being eaten on an organic versus conventional arm of a study—sure when people are on an organic diet, they have higher antioxidant capacity, but this can be easily explained by the fact that they were also eating more fruits and vegetables. The benefits can be explained by higher diet quality, not the fact that the diet was organic.

And lest we think the authors of this systematic review just have an axe to grind against organic food, other research groups have concluded the same in their systematic reviews: organic foods are neither safer, nor healthier, than their conventional counterparts.[94][95] Organic and conventional foods—whether we're talking about produce, meat, dairy, legumes, eggs, grains, etc.—are equal in their health effects.

It's also a myth that organic fruits and vegetables are way more nutritious than conventional. Of course, there are no complete nutrition datasets for organic produce, but using the nutritional comparison studies that have been done (typically evaluating differences in 7 or 8 nutrients), I crunched some numbers for you.[96][97][98][99] (Briefly, to do this comparison, I replaced the nutrient values in the Nutrivore Score calculation,

amalgamating data from four studies, to differentiate any impact from organic growing practices.) The results are completely underwhelming! Some nutrients are enhanced in organic produce, increasing overall nutrient density, but sometimes the reverse is true, decreasing overall nutrient density. And, for all but tomatoes, the difference is within 10%. Insert sad trombone noise.

Nutrient Density of Organic vs. Conventional Fruits and Vegetables

Food	Nutrivore Score Conventional	Nutrivore Score Organic	% Difference
carrots	932	1026	+10%
tomatoes	1056	839	-20%
lettuce	1896	1968	+4%
spinach	4287	4410	+3%
potatoes	265	253	-5%
cabbage	2034	2184	+7%
strawberries	1070	1044	-2%

If you're surprised and wondering why organic fruits and veggies aren't more nutrient-dense, science can answer this question very easily. It turns out that the quality of the soil, what fertilizer is used if any, and other growing conditions have larger effects on crop nutrient-density than the chemicals they're treated with.[100] And, these factors vary farm to farm, region to region, and season to season. So, you're likely still getting more nutrient-dense versions of fruits and veggies when you shop for in-season produce from local farmers markets or farm stands since family farms tend to use regenerative farming practices that improve soil quality. But, if farm-fresh produce isn't accessible to you, it's not something to worry about.

All-in-all, whether you buy organic foods should be a personal choice motivated by preference and not by any expectations of increased nutrient density or better health.

GOITROGENS

The thyroid gland produces hormones that control metabolism as well as influence other essential systems in the human body, such as the cardiovascular system, the immune system, calcium homeostasis and so much more! You may have read that you shouldn't eat cruciferous vegetables because their glucosinolates (or, more specifically, glucosinolate metabolites called isothiocyanates) are goitrogens, i.e., compounds that interfere with

thyroid hormone synthesis, typically by blocking the activity of the enzyme thyroid peroxidase (TPO).

Despite a lack of human studies, early reports of goiters in iodine-deficient animals eating high amounts of cruciferous vegetables led to concern that this vegetable family should be off-limits for people with hypothyroidism. However, a variety of animal studies have shown that this concern is unfounded, even in the context of iodine deficiency.[101][102][103]

The thyroid health effects of cruciferous vegetables have also been evaluated in humans. In a 2019 study, participants were given a broccoli sprout extract rich in isothiocyanates, or placebo, daily for 12 weeks—there was absolutely no change to thyroid hormones (free T4, thyroid stimulating hormone and thyroglobulin) nor the percentage of participants who met the diagnostic criteria for autoimmune thyroid disease.[104] Similar results were found in a 2006 clinical trial in which participants consumed broccoli extract beverages three times per day for 7 days, and no changes to TSH, total T3 or free T4 were observed.[105]

Yes, cruciferous vegetables, even raw, are safe for people with thyroid problems. Furthermore, cruciferous vegetables are associated with diverse health benefits thanks to their glucosinolates and various glucosinolate metabolites.

A 2017 systematic review evaluating fruit and vegetable intake showed that eating 100 grams of cruciferous vegetables per day, on average, led to a 16% decrease in total cancer risk.[106] A variety of studies have found that overall cruciferous vegetable consumption is associated with lower risk of specific cancer, too, including:

- bladder cancer (up to a 20% lower risk),[107]
- breast cancer (up to a 15% lower risk),[108]
- colorectal cancer (up to an 18% lower risk),[109]
- endometrial cancer (up to a 21% lower risk),[110]
- gastric cancer (up to a 19% lower risk),[111]
- lung cancer (up to a 25% lower risk),[112]
- ovarian cancer (up to an 11% lower risk),[113]
- pancreatic cancer (up to a 21% lower risk),[114]
- prostate cancer (up to a 10% lower risk),[115] and
- thyroid cancer (up to a 13% lower risk).[116]

A 2017 systematic review showed eating 100 grams of cruciferous vegetables per day (about 1 serving), on average, led to an 18% decrease in ischemic stroke, a 17% decrease in hemorrhagic stroke, and a 12% decrease in all-cause mortality and cardiovascular disease.[117] A 2019 meta-analysis turned up similar results, showing that for every 100 grams of cruciferous vegetables consumed daily, risk of cardiovascular disease decreased by 11% and risk of all-cause mortality decreased by 10%.[118] And, a 2011 analysis found a 31% reduced risk for cardiovascular disease mortality and a 22% reduced risk for total

mortality among individuals with the highest intake of cruciferous vegetables, which was 1.5 to 2 servings daily compared to about 2 servings per week.[119]

The isoflavones in soy (which are discussed in more detail in the next section) have also been feared of having goitrogenic activity. However once again, human studies show this isn't something to worry about. In a 2011 study, menopausal females were given a supplement of soy isoflavones daily at two different doses for two years—there was no change in thyroid hormone levels.[120] In a similar 2012 study, there were no changes in thyroid hormone levels in menopausal females after three months of taking a soy isoflavone supplement, with the exception of a small increase in the free T3 to free T4, indicating improved thyroid function rather than suppressed thyroid function.[121]

PHYTOESTROGENS

Phytoestrogens are phytonutrients with a structure similar enough to estrogen that they can bind to estrogen receptors in our body, modulating estrogen activity.[122] There are four main classes: isoflavones, which are abundant in soy and many pulse legumes; coumestrol, which is found in soy; lignans, which are high in flaxseed, sesame seed, other seeds, and grains; and stilbenes, which are abundant in grapes, berries, and nuts. Of these phytoestrogen-rich foods, few have received as much bad press as soy, based on early research (especially in animal studies) that raised concerns around its isoflavone content, bringing fears that it could spur the growth of hormone-sensitive cancers, impact fertility, increase estrogen levels in men, harm thyroid health, and contribute to heart disease. Unfortunately, this left soy with a soured reputation that sometimes still haunts it today.

Since the early days of soy research, an enormous number of studies have emerged looking at both the short-term and long-term health effects of soy, including in living humans. And now, the evidence is clear: not only are soy and its isoflavones safe; they're convincingly protective of many the diseases they were once feared to exacerbate!

There's just no truth to claims that phytoestrogens, especially the isoflavones in soy, will cause gynecomastia (a.k.a. "man boobs"), lower sperm counts, or cause any other "feminizing" effects in males.[123] A 2021 meta-analysis of clinical studies found no evidence that soy protein or isoflavone intake had any effect on male reproductive hormones, including testosterone or estrogen levels.[124] Nor does soy impact onset of puberty,[125] nor affect female fertility.[126]

A 2022 meta-analysis found that soy isoflavones had a clear *protective* effect for breast cancer in both pre- and post-menopausal women.[127] A 2019 review and meta-analysis determined that soy caused no significant changes in thyroid hormone levels.[128] A 2019 systematic review and meta-analysis even found a strong inverse correlation between soy

isoflavones and all-cause mortality, with those eating the highest levels of soy isoflavones having a 10% lower risk of death from all causes![129]

In fact, consuming phytoestrogens is associated with many health benefits, including cognitive improvements and reducing risks of osteoporosis, cardiovascular disease, type 2 diabetes, breast cancer, ovarian cancer, prostate cancer, and bowel cancer.[130][131] In fact, the health benefits of soybeans are largely *attributed* to the phytoestrogenic isoflavone content of the whole food.

In a 2008 prospective study following nearly 65,000 women for an average of 4.6 years, found that consuming 32 grams of soybeans per day was associated with a 47% lower risk of developing diabetes.[132] Interestingly, intake of soy protein and processed soy products didn't show a significant protective effect. In 2015 meta-analysis of cohort studies encompassing nearly 2 million participants, higher soybean intake was associated with a 15% lower risk of developing colorectal cancer.[133] A 2022 systematic review likewise found that higher soybean intake was associated with a 10% lower risk of cancer, with every additional 25 grams per day increase in soy intake correlating with a 4% drop in cancer risk.[134] (No risk-reducing effect was seen with soy protein.) A 2019 meta-analysis found that whole soybean intake was associated with a lower risk of risk of death from all causes, as well as specifically from ischemic cardiovascular disease—whereas soy protein intake alone showed no significant protective effect.[135] A 2013 randomized controlled trial found that 40 grams day of whole soybeans resulted in significant reductions in LDL cholesterol.[136] A double-blind, placebo-controlled trial from 2014 found that whole soy consumption (but not purified isoflavones) significantly lowered serum hs-CRP, a measure of inflammation.[137]

BPA

Yes, bisphenol A (BPA) has estrogenic activity, meaning that it can act like estrogen in our bodies. Toxicology studies show that high doses of BPA—on the order of 100,000 micrograms per kilogram bodyweight per day (µg/kg/day)—cause reduced gestational and postnatal body weight gain, negatively impact the ovary (increased cystic follicles, depleted corpora lutea, and antral follicles), and negatively affect hormone levels (increased serum estradiol and prolactin and decreased progesterone).[138] Based on toxicology studies, the U.S. Food and Drug Administration limit for BPA exposure is set to 50 µg/kg/day, and the European Food Safety Authority limit is set to 4 µg/kg/day. However, while controversial even among scientists and causality has yet to be established, there are newer studies indicating potential harm to our health at much lower exposure levels of BPA, implying a Lowest Observed Adverse Effect Level (LOAEL) in the range of 2.5 µg/kg/day—so the limits set by regulatory agencies are under review.[139]

The good news is that average human exposure is much less than these levels.

A large 2011 nationally-based urine biomonitoring study with broad demographics concluded that median aggregate human BPA exposures in the United States from all routes of exposure were 0.034 µg/kg/day—117 times lower than the current EFSA tolerable daily intake level and 1,470 times lower than the ADI established by the FDA.[140] What fraction of that exposure comes from canned foods? A 2015 study showed that, on average, we're exposed to 0.013 µg/kg/day of BPA from our diets (compared to other sources like thermal receipts), almost all of which comes from canned vegetables.[141]

But, what if you eat a lot of canned foods, like *a lot*? Even in that case, you probably still don't need to worry. A 2011 study had participants consume canned foods at each of three meals during a day, while blood and urine samples were collected approximately hourly all of that day until the next morning (a 24-hour period).[142] This study showed that BPA is efficiently eliminated from the body—the halflife of BPA in humans is three to six hours—and estimated the participants' BPA exposure averaged 0.27 µg/kg/day. This is nearly 15 times lower than the EFSA tolerable daily intake level and 185 times lower than the ADI established by the FDA.

Our exposure to BPA, from canned foods as well as other sources like water bottles and thermal receipts, is way lower than current ADI. However, if the suggested LOAEL of 2.5 µg/kg/day is adopted by regulatory agencies, whether our average exposure to BPA remains lower than the ADI will depend on the safety factor applied. If a modest safety factor of 10 is applied, our average exposure would remain below the ADI, but eating canned foods at every meal would exceed the ADI. While controversial, there are some scientists calling for the ADI to be lowered to 0.2 ng/kg/day, a level that would require a complete overhaul to food packaging.[143]

Manufacturers of canned foods are increasingly opting for BPA alternatives, such as bisphenol S (BPS) and bisphenol F (BPF). While not as thoroughly studied as BPA, there is evidence that these BPA substitutes are less toxic than BPA.[144][145] That being said, all bisphenols exert endocrine disrupting effects at high enough exposures, at which point they are harmful to a variety of biological systems.[146][147] More research is needed to establish ADIs for these BPA substitutes and their regulation in food packaging.

What about the nutritive value of canned foods? When we actually crunch the numbers, we see that canning has a minimal impact on nutrient density, compared to other cooking techniques, across food groups. For example, the Nutrivore Score of raw spinach is 4548, and canned spinach has a Nutrivore Score of 4117, still impressively high. Canned green beans have a Nutrivore Score of 588 (and an impressive 661 if you include the liquid), compared to 605 when fresh. And, canned pink salmon has a Nutrivore Score of 752 compared to 625 when fresh. The exception here is fruits canned in syrup, since the added sugar contributes calories and not much nutrition. For example, peaches canned in light syrup have a Nutrivore Score of 81 compared to 295 for fresh peaches and 319 for peaches canned in water. Canned food options are similarly nutritious as compared to fresh.

Overall, the evidence currently is that we don't need to feel guilty about buying canned foods, although given the changing landscape of scientific evidence, it may be prudent not to consume them at every meal. It's also worth noting that various phytonutrients have been shown to mitigate the toxic effect of BPA, including luteolin (found in parsley family vegetables, peppers, cabbage, broccoli and apples), naringin (found in citrus fruits), quercetin (found in green tea, apples, berries, and onions), and *N*-acetylcysteine (found in garlic).[148] That's another plus in the pro column for eating an abundance of fruits and veggies.

CITATIONS

[1] Ballantyne, C. “Strange but True: Drinking Too Much Water Can Kill.” *Scientific American*, June 21, 2007.

[2] Panacer, K., and Whorwell, P. J. 2019. “Dietary Lectin exclusion: The next big food trend?.” *World journal of gastroenterology*, *25*(24), 2973–2976. doi: 10.3748/wjg.v25.i24.2973

[3] Abdi, F., Zuberi, S., Blom, J. J., Armstrong, D., and Pinto-Sanchez, M. I. 2023. “Nutritional Considerations in Celiac Disease and Non-Celiac Gluten/Wheat Sensitivity.” *Nutrients*, *15*(6), 1475. doi: 10.3390/nu15061475

[4] Freed D. L. 1999. “Do dietary lectins cause disease?.” *BMJ (Clinical research ed.)*, *318*(7190), 1023–1024. doi: 10.1136/bmj.318.7190.1023

[5] Moreno, L., Garcés-Rimón M., and Miguel, M. 2022. “Antinutrients: Lectins, goitrogens, phytates and oxalates, friends or foe?.” Journal of Functional Foods. 89. 104938. doi: 10.1016/j.jff.2022.104938.

[6] Shi, L., Arntfield, S. D., and Nickerson, M. 2018. “Changes in levels of phytic acid, lectins and oxalates during soaking and cooking of Canadian pulses.” *Food research international (Ottawa, Ont.)*, *107*, 660–668. doi: 10.1016/j.foodres.2018.02.056

[7] Liu, W., Hu, B., Dehghan, M., Mente, A., Wang, C., Yan, R., Rangarajan, S., Tse, L. A., Yusuf, S., Liu, X., Wang, Y., Qiang, D., Hu, L., Han, A., Tang, X., Liu, L., Li, W., and PURE-China Investigators 2021. “Fruit, vegetable, and legume intake and the risk of all-cause, cardiovascular, and cancer mortality: A prospective study.” *Clinical nutrition (Edinburgh, Scotland)*, *40*(6), 4316–4323. doi: 10.1016/j.clnu.2021.01.016

[8] Bazzano, L. A., He, J., Ogden, L. G., Loria, C., Vupputuri, S., Myers, L., and Whelton, P. K. 2001. “Legume consumption and risk of coronary heart disease in US men and women: NHANES I Epidemiologic Follow-up Study.” *Archives of internal medicine*, *161*(21), 2573–2578. doi: 10.1001/archinte.161.21.2573

[9] Afshin, A., Micha, R., Khatibzadeh, S., and Mozaffarian, D. 2014. “Consumption of nuts and legumes and risk of incident ischemic heart disease, stroke, and diabetes: a systematic review and meta-analysis.” *The American journal of clinical nutrition*, *100*(1), 278–288. doi: 10.3945/ajcn.113.076901

[10] Aune, D., Keum, N., Giovannucci, E., Fadnes, L. T., Boffetta, P., Greenwood, D. C., Tonstad, S., Vatten, L. J., Riboli, E., and Norat, T. 2016. “Whole grain consumption and risk of cardiovascular disease, cancer, and all cause and cause specific mortality: systematic review and dose-response meta-analysis of prospective studies.” *BMJ (Clinical research ed.)*, *353*, i2716. doi: 10.1136/bmj.i2716

[11] Zhang, B., Zhao, Q., Guo, W., Bao, W., and Wang, X. 2018. “Association of whole grain intake with all-cause, cardiovascular, and cancer mortality: a systematic review and dose-response meta-analysis from prospective cohort studies.” *European journal of clinical nutrition*, *72*(1), 57–65. doi: 10.1038/ejcn.2017.149

[12] Aune, D., Keum, N., Giovannucci, E., Fadnes, L. T., Boffetta, P., Greenwood, D. C., Tonstad, S., Vatten, L. J., Riboli, E., and Norat, T. 2016. “Nut consumption and risk of cardiovascular disease, total cancer, all-cause and cause-specific mortality: a systematic review and dose-response meta-analysis of prospective studies.” *BMC medicine*, *14*(1), 207. doi: 10.1186/s12916-016-0730-3

[13] Grosso, G., Yang, J., Marventano, S., Micek, A., Galvano, F., and Kales, S. N. 2015. “Nut consumption on all-cause, cardiovascular, and cancer mortality risk: a systematic review and meta-analysis of epidemiologic studies.” *The American journal of clinical nutrition*, *101*(4), 783–793. doi: 10.3945/ajcn.114.099515

[14] Arya, S. S., Salve, A. R., and Chauhan, S. 2016. “Peanuts as functional food: a review.” *Journal of food science and technology*, *53*(1), 31–41. doi: 10.1007/s13197-015-2007-9

[15] Klein, L., Dawczynski, C., Schwarz, M., Maares, M., Kipp, K., Haase, H., and Kipp, A. P. 2023. “Selenium, Zinc, and Copper Status of Vegetarians and Vegans in Comparison to Omnivores in the Nutritional Evaluation (NuEva) Study.” *Nutrients*, *15*(16), 3538. doi: 10.3390/nu15163538

[16] Petroski, W., and Minich, D. M. 2020. “Is There Such a Thing as "Anti-Nutrients"? A Narrative Review of Perceived Problematic Plant Compounds.” *Nutrients*, *12*(10), 2929. doi: 10.3390/nu12102929

[17] Priyodip, P., Prakash, P. Y., and Balaji, S. 2017. “Phytases of Probiotic Bacteria: Characteristics and Beneficial Aspects.” *Indian journal of microbiology*, *57*(2), 148–154. doi: 10.1007/s12088-017-0647-3

[18] Karamad, D., Khosravi-Darani, K., Khaneghah, A. M., and Miller, A. W. 2022. “Probiotic Oxalate-Degrading Bacteria: New Insight of Environmental Variables and Expression of the oxc and frc Genes on Oxalate Degradation Activity.” *Foods (Basel, Switzerland)*, *11*(18), 2876. doi: 10.3390/foods11182876

[19] Pujol, A., Sanchis, P., Grases, F., and Masmiquel, L. 2023. “Phytate Intake, Health and Disease: "Let Thy Food Be Thy Medicine and Medicine Be Thy Food".” *Antioxidants (Basel, Switzerland)*, *12*(1), 146. doi: 10.3390/antiox12010146

[20] López-González, A. A., Grases, F., Monroy, N., Marí, B., Vicente-Herrero, M. T., Tur, F., and Perelló, J. 2013. “Protective effect of myo-inositol hexaphosphate (phytate) on bone mass loss in postmenopausal women.” *European journal of nutrition*, *52*(2), 717–726. doi: 10.1007/s00394-012-0377-6

[21] Guimerà, J., Martínez, A., Bauza, J. L., Sanchís, P., Pieras, E., and Grases, F. 2022. “Effect of phytate on hypercalciuria secondary to bone resorption in patients with urinary stones: pilot study.” *Urolithiasis*, *50*(6), 685–690. doi: 10.1007/s00240-022-01357-8

[22] Sanchis, P., Rivera, R., Berga, F., Fortuny, R., Adrover, M., Costa-Bauza, A., Grases, F., and Masmiquel, L. 2018. “Phytate Decreases Formation of Advanced Glycation End-Products in Patients with Type II Diabetes: Randomized Crossover Trial.” *Scientific reports*, *8*(1), 9619. doi: 10.1038/s41598-018-27853-9

[23] Ikenaga, T., Kakumoto, K., Kohda, N., and Yamamoto, T. 2019. “Effect of Inositol Hexaphosphate (IP_6) on Serum Uric Acid in Hyperuricemic Subjects: a Randomized, Double-Blind, Placebo-Controlled, Crossover Study.” *Plant foods for human nutrition (Dordrecht, Netherlands)*, *74*(3), 316–321. doi: 10.1007/s11130-019-00735-9

[24] Fernández-Palomeque, C., Grau, A., Perelló, J., Sanchis, P., Isern, B., Prieto, R. M., Costa-Bauzá, A., Caldés, O. J., Bonnin, O., Garcia-Raja, A., Bethencourt, A., and Grases, F. 2015. “Relationship between Urinary Level of Phytate and Valvular Calcification in an Elderly Population: A Cross-Sectional Study.” *PloS one*, *10*(8), e0136560. doi: 10.1371/journal.pone.0136560

[25] Larvie, D. Y., and Armah, S. M. 2021. “Estimated Phytate Intake Is Associated with Improved Cognitive Function in the Elderly, NHANES 2013-2014.” *Antioxidants (Basel, Switzerland)*, *10*(7), 1104. doi: 10.3390/antiox10071104

[26] Ferraro, P. M., Bargagli, M., Trinchieri, A., and Gambaro, G. 2020. “Risk of Kidney Stones: Influence of Dietary Factors, Dietary Patterns, and Vegetarian-Vegan Diets.” *Nutrients*, *12*(3), 779. doi: 10.3390/nu12030779

[27] Loret, A., Jacob, C., Mammou, S., Bigot, A., Blasco, H., Audemard-Verger, A., Schwartz, I. V., Mulleman, D., and Maillot, F. 2023. “Joint manifestations revealing inborn metabolic diseases in adults: a narrative review.” *Orphanet journal of rare diseases*, *18*(1), 239. doi: 10.1186/s13023-023-02810-6

[28] Hoffman, G. S., Schumacher, H. R., Paul, H., Cherian, V., Reed, R., Ramsay, A. G., and Franck, W. A. 1982. “Calcium oxalate microcrystalline-associated arthritis in end-stage renal disease.” *Annals of internal medicine*, *97*(1), 36–42. doi: 10.7326/0003-4819-97-1-36

[29] Crivelli, J. J., Mitchell, T., Knight, J., Wood, K. D., Assimos, D. G., Holmes, R. P., and Fargue, S. 2020. “Contribution of Dietary Oxalate and Oxalate Precursors to Urinary Oxalate Excretion.” *Nutrients*, *13*(1), 62. doi: 10.3390/nu13010062

[30] Taylor, E. N., and Curhan, G. C. 2008. “Determinants of 24-hour urinary oxalate excretion.” *Clinical journal of the American Society of Nephrology : CJASN*, *3*(5), 1453–1460. doi: 10.2215/CJN.01410308

[31] Porrini, M., Riso, P., and Oriani, G. 2002. “Spinach and tomato consumption increases lymphocyte DNA resistance to oxidative stress but this is not related to cell carotenoid concentrations.” *European journal of nutrition*, *41*(3), 95–100. doi: 10.1007/s003940200014

[32] Kaufman, D. W., Kelly, J. P., Curhan, G. C., Anderson, T. E., Dretler, S. P., Preminger, G. M., and Cave, D. R. 2008. “Oxalobacter formigenes may reduce the risk of calcium oxalate kidney stones.” *Journal of the American Society of Nephrology : JASN*, *19*(6), 1197–1203. doi: 10.1681/ASN.2007101058

[33] Barghouthy, Y., and Somani, B. K. 202). “Role of Citrus Fruit Juices in Prevention of Kidney Stone Disease (KSD): A Narrative Review.” *Nutrients*, *13*(11), 4117. doi: 10.3390/nu13114117

[34] Hansen, T. H., Thomassen, M. T., Madsen, M. L., Kern, T., Bak, E. G., Kashani, A., Allin, K. H., Hansen, T., and Pedersen, O. 2018. “The effect of drinking water pH on the human gut microbiota and glucose regulation: results of a randomized controlled cross-over intervention.” *Scientific reports*, *8*(1), 16626. doi: 10.1038/s41598-018-34761-5

[35] Farvid, M. S., Ding, M., Pan, A., Sun, Q., Chiuve, S. E., Steffen, L. M., Willett, W. C., and Hu, F. B. 2014. “Dietary linoleic acid and risk of coronary heart disease: a systematic review and meta-analysis of prospective cohort studies.” *Circulation*, *130*(18), 1568–1578. doi 10.1161/CIRCULATIONAHA.114.010236

[36] Li, J., Guasch-Ferré, M., Li, Y., and Hu, F. B. 2020. “Dietary intake and biomarkers of linoleic acid and mortality: systematic review and meta-analysis of prospective cohort studies.” *The American journal of clinical nutrition*, *112*(1), 150–167. doi 10.1093/ajcn/nqz349

[37] Johnson, G. H., and Fritsche, K. 2012. "Effect of dietary linoleic acid on markers of inflammation in healthy persons: a systematic review of randomized controlled trials." *Journal of the Academy of Nutrition and Dietetics*, *112*(7), 1029–1041.e10415. doi: 10.1016/j.jand.2012.03.029

[38] Zhang, Y., Zhuang, P., Wu, F., He, W., Mao, L., Jia, W., Zhang, Y., Chen, X., and Jiao, J. 2021. "Cooking oil/fat consumption and deaths from cardiometabolic diseases and other causes: prospective analysis of 521,120 individuals." *BMC medicine*, *19*(1), 92. doi: 10.1186/s12916-021-01961-2

[39] Gharby S. 2022. "Refining Vegetable Oils: Chemical and Physical Refining." *TheScientificWorldJournal*, *2022*, 6627013. doi: 10.1155/2022/6627013

[40] Cravotto, C., Fabiano-Tixier, A. S., Claux, O., Abert-Vian, M., Tabasso, S., Cravotto, G., and Chemat, F. 2022. "Towards Substitution of Hexane as Extraction Solvent of Food Products and Ingredients with No Regrets." *Foods (Basel, Switzerland)*, *11*(21), 3412. doi: 10.3390/foods11213412

[41] Ligor, M., and Buszewski, B. 2008. "The comparison of solid phase microextraction-GC and static headspace-GC for determination of solvent residues in vegetable oils." *Journal of separation science*, *31*(2), 364–371. doi: 10.1002/jssc.200700303

[42] Debras, C., Chazelas, E., Sellem, L., Porcher, R., Druesne-Pecollo, N., Esseddik, Y., de Edelenyi, F. S., Agaësse, C., De Sa, A., Lutchia, R., Fezeu, L. K., Julia, C., Kesse-Guyot, E., Allès, B., Galan, P., Hercberg, S., Deschasaux-Tanguy, M., Huybrechts, I., Srour, B., and Touvier, M. 2022. "Artificial sweeteners and risk of cardiovascular diseases: results from the prospective NutriNet-Santé cohort." *BMJ (Clinical research ed.)*, *378*, e071204. doi: 10.1136/bmj-2022-071204

[43] Debras, C., Chazelas, E., Srour, B., Druesne-Pecollo, N., Esseddik, Y., Szabo de Edelenyi, F., Agaësse, C., De Sa, A., Lutchia, R., Gigandet, S., Huybrechts, I., Julia, C., Kesse-Guyot, E., Allès, B., Andreeva, V. A., Galan, P., Hercberg, S., Deschasaux-Tanguy, M., and Touvier, M. 2022. "Artificial sweeteners and cancer risk: Results from the NutriNet-Santé population-based cohort study." *PLoS medicine*, *19*(3), e1003950. doi: 10.1371/journal.pmed.1003950

[44] Fulgoni, V. L., 3rd, and Drewnowski, A. 2022. "No Association between Low-Calorie Sweetener (LCS) Use and Overall Cancer Risk in the Nationally Representative Database in the US: Analyses of NHANES 1988-2018 Data and 2019 Public-Use Linked Mortality Files." *Nutrients*, *14*(23), 4957. doi: 10.3390/nu14234957

[45] Yang, B., Glenn, A. J., Liu, Q., Madsen, T., Allison, M. A., Shikany, J. M., Manson, J. E., Chan, K. H. K., Wu, W. C., Li, J., Liu, S., and Lo, K. 2022. "Added Sugar, Sugar-Sweetened Beverages, and Artificially Sweetened Beverages and Risk of Cardiovascular Disease: Findings from the Women's Health Initiative and a Network Meta-Analysis of Prospective Studies." *Nutrients*, *14*(20), 4226. doi: 10.3390/nu14204226

[46] Zhang, Y. B., Jiang, Y. W., Chen, J. X., Xia, P. F., and Pan, A. 2021. "Association of Consumption of Sugar-Sweetened Beverages or Artificially Sweetened Beverages with Mortality: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies." *Advances in nutrition (Bethesda, Md.)*, *12*(2), 374–383. doi: 10.1093/advances/nmaa110

[47] Yang, Q., Zhang, Z., Gregg, E. W., Flanders, W. D., Merritt, R., and Hu, F. B. 2014. "Added sugar intake and cardiovascular diseases mortality among US adults." *JAMA internal medicine*, *174*(4), 516–524. doi: /10.1001/jamainternmed.2013.13563

[48] Gibson, S., Gunn, P., Wittekind, A., and Cottrell, R. 2013. "The effects of sucrose on metabolic health: a systematic review of human intervention studies in healthy adults." *Critical reviews in food science and nutrition*, *53*(6), 591–614. doi: 10.1080/10408398.2012.691574

[49] Zhang, Y. B., Chen, J. X., Jiang, Y. W., Xia, P. F., and Pan, A. 2021. "Association of sugar-sweetened beverage and artificially sweetened beverage intakes with mortality: an analysis of US National Health and Nutrition Examination Survey." *European journal of nutrition,* 60(4), 1945–1955. doi: 10.1007/s00394-020-02387-x

[50] Onakpoya, I. J., and Heneghan, C. J. 2015. "Effect of the natural sweetener, steviol glycoside, on cardiovascular risk factors: a systematic review and meta-analysis of randomised clinical trials." *European journal of preventive cardiology*, *22*(12), 1575–1587. doi: 10.1177/2047487314560663

[51] Walbolt, J., and Koh, Y. 2020. "Non-nutritive Sweeteners and Their Associations with Obesity and Type 2 Diabetes." *Journal of obesity & metabolic syndrome*, *29*(2), 114–123. doi: 10.7570/jomes19079

[52] Oplatowska-Stachowiak, M., and Elliott, C. T. 2017. "Food colors: Existing and emerging food safety concerns." *Critical reviews in food science and nutrition*, *57*(3), 524–548. doi: 10.1080/10408398.2014.889652

[53] Miller, M. D., Steinmaus, C., Golub, M. S., Castorina, R., Thilakartne, R., Bradman, A., and Marty, M. A. 2022. "Potential impacts of synthetic food dyes on activity and attention in children: a review of the human and animal evidence." *Environmental health : a global access science source*, *21*(1), 45. doi: 10.1186/s12940-022-00849-9

[54] Gentry, R., Greene, T., Chappell, G., Lea, I., Borghoff, S., Yang, C., Rathman, J., Ribeiro, J. V., Hobocienski, B., Mostrag, A., Rodricks, J., and Clewell, H. 2021. "Integration of evidence to evaluate the potential for neurobehavioral effects following exposure to USFDA-approved food colors." *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association*, *151*, 112097. doi: 10.1016/j.fct.2021.112097

[55] Bradman, A., Castorina, R., Thilakaratne, R., Gillan, M., Pattabhiraman, T., Nirula, A., Marty, M., and Miller, M. D. 2022. "Dietary Exposure to United States Food and Drug Administration-Approved Synthetic Food Colors in Children, Pregnant Women, and Women of Childbearing Age Living in the United States." *International journal of environmental research and public health*, *19*(15), 9661. doi: 10.3390/ijerph19159661

[56] Zhang, Y., and Giovannucci, E. L. 2022. "Ultra-processed foods and health: a comprehensive review." *Critical reviews in food science and nutrition*, 1–13. Advance online publication. doi: 10.1080/10408398.2022.2084359

[57] Martini, D., Godos, J., Bonaccio, M., Vitaglione, P., and Grosso, G. 2021. "Ultra-Processed Foods and Nutritional Dietary Profile: A Meta-Analysis of Nationally Representative Samples." *Nutrients*, *13*(10), 3390. doi: 10.3390/nu13103390

[58] Rico-Campà, A., Martínez-González, M. A., Alvarez-Alvarez, I., Mendonça, R. D., de la Fuente-Arrillaga, C., Gómez-Donoso, C., and Bes-Rastrollo, M. 2019. "Association between consumption of ultra-processed foods and all cause mortality: SUN prospective cohort study." *BMJ (Clinical research ed.)*, *365*, l1949. doi: 10.1136/bmj.l1949

[59] Chen, X., Chu, J., Hu, W., Sun, N., He, Q., Liu, S., Feng, Z., Li, T., Han, Q., and Shen, Y. 2022. "Associations of ultra-processed food consumption with cardiovascular disease and all-cause mortality: UK Biobank." *European journal of public health*, *32*(5), 779–785. doi: 10.1093/eurpub/ckac104

[60] Suksatan, W., Moradi, S., Naeini, F., Bagheri, R., Mohammadi, H., Talebi, S., Mehrabani, S., Hojjati Kermani, M. A., and Suzuki, K. 2021. "Ultra-Processed Food Consumption and Adult Mortality Risk: A Systematic Review and Dose-Response Meta-Analysis of 207,291 Participants." *Nutrients*, *14*(1), 174. doi: 10.3390/nu14010174

[61] Taneri, P. E., Wehrli, F., Roa-Díaz, Z. M., Itodo, O. A., Salvador, D., Raeisi-Dehkordi, H., Bally, L., Minder, B., Kiefte-de Jong, J. C., Laine, J. E., Bano, A., Glisic, M., and Muka, T. 2022. "Association Between Ultra-Processed Food Intake and All-Cause Mortality: A Systematic Review and Meta-Analysis." *American journal of epidemiology*, *191*(7), 1323–1335. doi: 10.1093/aje/kwac039

[62] Shin, J. S., Lee, K. G., Lee, H. H., Lee, H. J., An, H. J., Nam, J. H., Jang, D. S., and Lee, K. T. 2016. "α-Solanine Isolated From Solanum Tuberosum L. cv Jayoung Abrogates LPS-Induced Inflammatory Responses Via NF-κB Inactivation in RAW 264.7 Macrophages and Endotoxin-Induced Shock Model in Mice." *Journal of cellular biochemistry*, *117*(10), 2327–2339. doi: 10.1002/jcb.25530

[63] Mensinga, T. T., Sips, A. J., Rompelberg, C. J., van Twillert, K., Meulenbelt, J., van den Top, H. J., and van Egmond, H. P. 2005. "Potato glycoalkaloids and adverse effects in humans: an ascending dose study." *Regulatory toxicology and pharmacology : RTP*, *41*(1), 66–72. doi: 10.1016/j.yrtph.2004.09.004

[64] Korpan, Y. I., Nazarenko, E. A., Skryshevskaya, I. V., Martelet, C., Jaffrezic-Renault, N., and El'skaya, A. V. 2004. "Potato glycoalkaloids: true safety or false sense of security?." *Trends in biotechnology*, *22*(3), 147–151. doi: 10.1016/j.tibtech.2004.01.009

[65] Friedman M. 2002. "Tomato glycoalkaloids: role in the plant and in the diet." *Journal of agricultural and food chemistry*, *50*(21), 5751–5780. doi: 10.1021/jf020560c

[66] Delbrouck, J. A., Desgagné, M., Comeau, C., Bouarab, K., Malouin, F., and Boudreault, P. L. 2023. "The Therapeutic Value of Solanum Steroidal (Glyco)Alkaloids: A 10-Year Comprehensive Review." *Molecules (Basel, Switzerland)*, *28*(13), 4957. doi: 10.3390/molecules28134957

[67] Ghavipour, M., Saedisomeolia, A., Djalali, M., Sotoudeh, G., Eshraghyan, M. R., Moghadam, A. M., and Wood, L. G. 2013. "Tomato juice consumption reduces systemic inflammation in overweight and obese females." *The British journal of nutrition*, *109*(11), 2031–2035. doi: 10.1017/S0007114512004278

[68] Widjaja, G., Doewes, R. I., Rudiansyah, M., Sultan, M. Q., Ansari, M. J., Izzat, S. E., Al Jaber, M. S., Kzar, H. H., Mustafa, Y. F., Hammid, A. T., Turki Jalil, A., and Aravindhan, S. 2022. "Effect of tomato consumption on inflammatory markers in health and disease status: A systematic review and meta-analysis of clinical trials." *Clinical nutrition ESPEN*, *50*, 93–100. doi: 10.1016/j.clnesp.2022.04.019

[69] Mazidi, M., Katsiki, N., George, E. S., and Banach, M. 2020. "Tomato and lycopene consumption is inversely associated with total and cause-specific mortality: a population-based cohort study, on behalf of the International Lipid Expert Panel (ILEP)." *The British journal of nutrition*, *124*(12), 1303–1310. doi: 10.1017/S0007114519002150

[70] Wong, C., Roberts, S. M., and Saab, I. N. 2022. "Review of regulatory reference values and background levels for heavy metals in the human diet." *Regulatory toxicology and pharmacology : RTP*, *130*, 105122. doi: 10.1016/j.yrtph.2022.105122

[71] Balali-Mood, M., Naseri, K., Tahergorabi, Z., Khazdair, M. R., and Sadeghi, M. 2021. "Toxic Mechanisms of Five Heavy Metals: Mercury, Lead, Chromium, Cadmium, and Arsenic." *Frontiers in pharmacology*, *12*, 643972. doi: 10.3389/fphar.2021.643972

[72] Barone, G., Storelli, A., Meleleo, D., Dambrosio, A., Garofalo, R., Busco, A., and Storelli, M. M. 2021. "Levels of Mercury, Methylmercury and Selenium in Fish: Insights into Children Food Safety." *Toxics*, *9*(2), 39. doi: 10.3390/toxics9020039

[73] Ralston, N. V. C., Kaneko, J. J., and Raymond, L. J. 2019. "Selenium health benefit values provide a reliable index of seafood benefits vs. risks." *Journal of trace elements in medicine and biology : organ of the Society for Minerals and Trace Elements (GMS)*, *55*, 50–57. doi 10.1016/j.jtemb.2019.05.009

[74] Ralston, N. V., and Raymond, L. J. 2010. "Dietary selenium's protective effects against methylmercury toxicity." *Toxicology*, *278*(1), 112–123. doi: 10.1016/j.tox.2010.06.004

[75] Ralston N. V. 2008. "Selenium health benefit values as seafood safety criteria." *EcoHealth*, *5*(4), 442–455. doi: 10.1007/s10393-008-0202-0

[76] Jiang, L., Wang, J., Xiong, K., Xu, L., Zhang, B., and Ma, A. 2021. "Intake of Fish and Marine n-3 Polyunsaturated Fatty Acids and Risk of Cardiovascular Disease Mortality: A Meta-Analysis of Prospective Cohort Studies." *Nutrients*, *13*(7), 2342. doi: 10.3390/nu13072342

[77] Wan, Y., Zheng, J., Wang, F., and Li, D. 2017. "Fish, long chain omega-3 polyunsaturated fatty acids consumption, and risk of all-cause mortality: a systematic review and dose-response meta-analysis from 23 independent prospective cohort studies." *Asia Pacific journal of clinical nutrition*, *26*(5), 939–956. doi: 10.6133/apjcn.072017.01

[78] Wan, Y., Zheng, J., Wang, F., and Li, D. 2017. "Fish, long chain omega-3 polyunsaturated fatty acids consumption, and risk of all-cause mortality: a systematic review and dose-response meta-analysis from 23 independent prospective cohort studies." *Asia Pacific journal of clinical nutrition*, *26*(5), 939–956. doi: 10.6133/apjcn.072017.01

[79] Starling, P., Charlton, K., McMahon, A. T., and Lucas, C. 2015. "Fish intake during pregnancy and foetal neurodevelopment--a systematic review of the evidence." *Nutrients*, *7*(3), 2001–2014. doi: 10.3390/nu7032001

[80] Su, L. J., Chiang, T. C., and O'Connor, S. N. 2023. "Arsenic in brown rice: do the benefits outweigh the risks?." *Frontiers in nutrition*, *10*, 1209574. doi: 10.3389/fnut.2023.1209574

[81] Rintala, E. M., Ekholm, P., Koivisto, P., Peltonen, K., and Venäläinen, E. R. 2014. "The intake of inorganic arsenic from long grain rice and rice-based baby food in Finland - low safety margin warrants follow up." *Food chemistry*, *150*, 199–205. doi: 10.1016/j.foodchem.2013.10.155

[82] Meharg, A. A., Sun, G., Williams, P. N., Adomako, E., Deacon, C., Zhu, Y. G., Feldmann, J., and Raab, A. 2008. "Inorganic arsenic levels in baby rice are of concern." *Environmental pollution (Barking, Essex : 1987)*, *152*(3), 746–749. doi: 10.1016/j.envpol.2008.01.043

[83] Zavala, Y. J., and Duxbury, J. M. 2008. "Arsenic in rice: I. Estimating normal levels of total arsenic in rice grain." *Environmental science & technology*, *42*(10), 3856–3860. doi: 10.1021/es702747y

[84] Abt, E., Fong Sam, J., Gray, P., and Robin, L. P. 2018. "Cadmium and lead in cocoa powder and chocolate products in the US Market." *Food additives & contaminants. Part B, Surveillance*, *11*(2), 92–102. doi: 10.1080/19393210.2017.1420700

[85] Yuan, S., Li, X., Jin, Y., and Lu, J. 2017. "Chocolate Consumption and Risk of Coronary Heart Disease, Stroke, and Diabetes: A Meta-Analysis of Prospective Studies." *Nutrients*, *9*(7), 688. doi: 10.3390/nu9070688

[86] Ried, K., Fakler, P., and Stocks, N. P. 2017. "Effect of cocoa on blood pressure." *The Cochrane database of systematic reviews*, *4*(4), CD008893. doi: 10.1002/14651858.CD008893.pub3

[87] Gong, F., Yao, S., Wan, J., and Gan, X. 2017. "Chocolate Consumption and Risk of Heart Failure: A Meta-Analysis of Prospective Studies." *Nutrients*, *9*(4), 402. doi: 10.3390/nu9040402

[88] Rostami, A., Khalili, M., Haghighat, N., Eghtesadi, S., Shidfar, F., Heidari, I., Ebrahimpour-Koujan, S., and Eghtesadi, M. 2015. "High-cocoa polyphenol-rich chocolate improves blood pressure in patients with diabetes and hypertension." *ARYA atherosclerosis*, *11*(1), 21–29.

[89] Kord-Varkaneh, H., Ghaedi, E., Nazary-Vanani, A., Mohammadi, H., and Shab-Bidar, S. 2019. "Does cocoa/dark chocolate supplementation have favorable effect on body weight, body mass index and waist circumference? A systematic review, meta-analysis and dose-response of randomized clinical trials." *Critical reviews in food science and nutrition*, *59*(15), 2349–2362. doi: 10.1080/10408398.2018.1451820

[90] Winter, C. K., and Katz, J. M. 2011. "Dietary exposure to pesticide residues from commodities alleged to contain the highest contamination levels." *Journal of toxicology*, *2011*, 589674. doi: 10.1155/2011/589674

[91] Vigar, V., Myers, S., Oliver, C., Arellano, J., Robinson, S., and Leifert, C. 2019. "A Systematic Review of Organic Versus Conventional Food Consumption: Is There a Measurable Benefit on Human Health?." *Nutrients*, *12*(1), 7. doi 10.3390/nu12010007

[92] Baudry, J., Méjean, C., Péneau, S., Galan, P., Hercberg, S., Lairon, D., and Kesse-Guyot, E. 2015. "Health and dietary traits of organic food consumers: results from the NutriNet-Santé study." *The British journal of nutrition*, *114*(12), 2064–2073. doi 10.1017/S0007114515003761

[93] Andersen, J. L. M., Frederiksen, K., Raaschou-Nielsen, O., Hansen, J., Kyrø, C., Tjønneland, A., and Olsen, A. 2022. "Organic food consumption is associated with a healthy lifestyle, socio-demographics and dietary habits: a cross-sectional study based on the Danish Diet, Cancer and Health cohort." *Public health nutrition*, *25*(6), 1543–1551. doi: 10.1017/S1368980021001270

[94] Smith-Spangler, C., Brandeau, M. L., Hunter, G. E., Bavinger, J. C., Pearson, M., Eschbach, P. J., Sundaram, V., Liu, H., Schirmer, P., Stave, C., Olkin, I., and Bravata, D. M. 2012. "Are organic foods safer or healthier than conventional alternatives?: a systematic review." *Annals of internal medicine*, *157*(5), 348–366. doi 10.7326/0003-4819-157-5-201209040-00007

[95] Dangour, A. D., Lock, K., Hayter, A., Aikenhead, A., Allen, E., and Uauy, R. 2010. "Nutrition-related health effects of organic foods: a systematic review." *The American journal of clinical nutrition*, *92*(1), 203–210. doi 10.3945/ajcn.2010.29269

[96] Hoefkens, C., Vandekinderen, I., Meulenaer, B., Devlieghere, F., Baert, K., Sioen, I., Henauw, S., Verbeke, W., and Camp, J. 2009. "A literature-based comparison of nutrient and contaminant contents between organic and conventional vegetables and potatoes." *British Food Journal*. 111. 1078-1097. doi: 10.1108/00070700910992934.

[97] Worthington V. 2001. "Nutritional quality of organic versus conventional fruits, vegetables, and grains." *Journal of alternative and complementary medicine (New York, N.Y.)*, *7*(2), 161–173. doi 10.1089/107555301750164244

[98] Koh, E., Charoenprasert, S., and Mitchell, A. E. 2012. "Effect of organic and conventional cropping systems on ascorbic acid, vitamin C, flavonoids, nitrate, and oxalate in 27 varieties of spinach (Spinacia oleracea L.)." *Journal of agricultural and food chemistry*, *60*(12), 3144–3150. doi: 10.1021/jf300051f

[99] Reganold, J. P., Andrews, P. K., Reeve, J. R., Carpenter-Boggs, L., Schadt, C. W., Alldredge, J. R., Ross, C. F., Davies, N. M., and Zhou, J. 2010. "Fruit and soil quality of organic and conventional strawberry agroecosystems." *PloS one*, *5*(9), e12346. doi 10.1371/journal.pone.0012346

[100] Montgomery, D., and Biklé, A. 2021. "Soil Health and Nutrient Density: Beyond Organic vs. Conventional Farming." *Frontiers in Sustainable Food Systems*. 5. doi: 10.3389/fsufs.2021.699147.

[101] Paśko, P., Okoń, K., Krośniak, M., Prochownik, E., Żmudzki, P., Kryczyk-Kozioł, J., and Zagrodzki, P. 2018. "Interaction between iodine and glucosinolates in rutabaga sprouts and selected biomarkers of thyroid function in male rats." *Journal of trace elements in medicine and biology : organ of the Society for Minerals and Trace Elements (GMS)*, *46*, 110–116. doi: 10.1016/j.jtemb.2017.12.002

[102] Paśko, P., Krośniak, M., Prochownik, E., Tyszka-Czochara, M., Fołta, M., Francik, R., Sikora, J., Malinowski, M., and Zagrodzki, P. 2018. "Effect of broccoli sprouts on thyroid function, haematological, biochemical, and immunological parameters in rats with thyroid imbalance." *Biomedicine & pharmacotherapy = Biomedecine & pharmacotherapie*, *97*, 82–90. doi: 10.1016/j.biopha.2017.10.098

[103] Paśko, P., Zagrodzki, P., Okoń, K., Prochownik, E., Krośniak, M., and Galanty, A. 2022. "Broccoli Sprouts and Their Influence on Thyroid Function in Different In Vitro and In Vivo Models." *Plants (Basel, Switzerland)*, *11*(20), 2750. doi: 10.3390/plants11202750

[104] Chartoumpekis, D. V., Ziros, P. G., Chen, J. G., Groopman, J. D., Kensler, T. W., and Sykiotis, G. P. 2019. "Broccoli sprout beverage is safe for thyroid hormonal and autoimmune status: Results of a 12-week randomized trial." *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association*, *126*, 1–6. doi: 10.1016/j.fct.2019.02.004

[105] Shapiro, T. A., Fahey, J. W., Dinkova-Kostova, A. T., Holtzclaw, W. D., Stephenson, K. K., Wade, K. L., Ye, L., and Talalay, P. 2006. "Safety, tolerance, and metabolism of broccoli sprout glucosinolates and isothiocyanates: a clinical phase I study." *Nutrition and cancer*, *55*(1), 53–62. doi: 10.1207/s15327914nc5501_7

[106] Aune, D., Giovannucci, E., Boffetta, P., Fadnes, L. T., Keum, N., Norat, T., Greenwood, D. C., Riboli, E., Vatten, L. J., and Tonstad, S. 2017. "Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality-a systematic review and dose-response meta-analysis of prospective studies." *International journal of epidemiology*, *46*(3), 1029–1056. doi: 10.1093/ije/dyw319

[107] Liu, B., Mao, Q., Lin, Y., Zhou, F., and Xie, L. 2013. "The association of cruciferous vegetables intake and risk of bladder cancer: a meta-analysis." *World journal of urology*, *31*(1), 127–133. doi: 10.1007/s00345-012-0850-0

[108] Liu, X., and Lv, K. 2013. "Cruciferous vegetables intake is inversely associated with risk of breast cancer: a meta-analysis." *Breast (Edinburgh, Scotland)*, *22*(3), 309–313. doi: 10.1016/j.breast.2012.07.013

[109] Wu, Q. J., Yang, Y., Vogtmann, E., Wang, J., Han, L. H., Li, H. L., and Xiang, Y. B. 2013. "Cruciferous vegetables intake and the risk of colorectal cancer: a meta-analysis of observational studies." *Annals of oncology : official journal of the European Society for Medical Oncology*, *24*(4), 1079–1087. doi: 10.1093/annonc/mds601

[110] Bandera, E. V., Kushi, L. H., Moore, D. F., Gifkins, D. M., and McCullough, M. L. 2007. "Fruits and vegetables and endometrial cancer risk: a systematic literature review and meta-analysis." *Nutrition and cancer*, *58*(1), 6–21. doi: 10.1080/01635580701307929

[111] Wu, Q. J., Yang, Y., Wang, J., Han, L. H., and Xiang, Y. B. 2013. "Cruciferous vegetable consumption and gastric cancer risk: a meta-analysis of epidemiological studies." *Cancer science*, *104*(8), 1067–1073. doi: 10.1111/cas.12195

[112] Kirsh, V. A., Peters, U., Mayne, S. T., Subar, A. F., Chatterjee, N., Johnson, C. C., Hayes, R. B., and Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial. 2007. "Prospective study of fruit and vegetable intake and risk of prostate cancer." *Journal of the National Cancer Institute*, *99*(15), 1200–1209. doi: 10.1093/jnci/djm065

[113] Han, B., Li, X., and Yu, T. 2014. "Cruciferous vegetables consumption and the risk of ovarian cancer: a meta-analysis of observational studies." *Diagnostic pathology*, *9*, 7. doi: 10.1186/1746-1596-9-7

[114] Li, L. Y., Luo, Y., Lu, M. D., Xu, X. W., Lin, H. D., and Zheng, Z. Q. 2015. "Cruciferous vegetable consumption and the risk of pancreatic cancer: a meta-analysis." *World journal of surgical oncology*, *13*, 44. doi: 10.1186/s12957-015-0454-4

[115] Liu, B., Mao, Q., Cao, M., and Xie, L. 2012. "Cruciferous vegetables intake and risk of prostate cancer: a meta-analysis." *International journal of urology : official journal of the Japanese Urological Association*, *19*(2), 134–141. doi: 10.1111/j.1442-2042.2011.02906.x

[116] Bosetti, C., Negri, E., Kolonel, L., Ron, E., Franceschi, S., Preston-Martin, S., McTiernan, A., Dal Maso, L., Mark, S. D., Mabuchi, K., Land, C., Jin, F., Wingren, G., Galanti, M. R., Hallquist, A., Glattre, E., Lund, E., Levi, F., Linos, D., and La Vecchia, C. 2002. "A pooled analysis of case-control studies of thyroid cancer. VII. Cruciferous and other vegetables (International)." *Cancer causes & control : CCC*, *13*(8), 765–775. doi: 10.1023/a:1020243527152

[117] Aune, D., Giovannucci, E., Boffetta, P., Fadnes, L. T., Keum, N., Norat, T., Greenwood, D. C., Riboli, E., Vatten, L. J., and Tonstad, S. 2017. "Fruit and vegetable intake and the risk of cardiovascular disease, total cancer and all-cause mortality-a systematic review and dose-response meta-analysis of prospective studies." *International journal of epidemiology*, *46*(3), 1029–1056. doi: 10.1093/ije/dyw319

[118] Kwok, C. S., Gulati, M., Michos, E. D., Potts, J., Wu, P., Watson, L., Loke, Y. K., Mallen, C., and Mamas, M. A. 2019. "Dietary components and risk of cardiovascular disease and all-cause mortality: a review of evidence from meta-analyses." *European journal of preventive cardiology*, *26*(13), 1415–1429. doi: 10.1177/2047487319843667

[119] Zhang, X., Shu, X. O., Xiang, Y. B., Yang, G., Li, H., Gao, J., Cai, H., Gao, Y. T., and Zheng, W. 2011. "Cruciferous vegetable consumption is associated with a reduced risk of total and cardiovascular disease mortality." *The American journal of clinical nutrition*, *94*(1), 240–246. doi: 10.3945/ajcn.110.009340

[120] Steinberg, F. M., Murray, M. J., Lewis, R. D., Cramer, M. A., Amato, P., Young, R. L., Barnes, S., Konzelmann, K. L., Fischer, J. G., Ellis, K. J., Shypailo, R. J., Fraley, J. K., Smith, E. O., and Wong, W. W. 2011. "Clinical outcomes of a 2-y soy isoflavone supplementation in menopausal women." *The American journal of clinical nutrition*, *93*(2), 356–367. doi: 10.3945/ajcn.110.008359

[121] Sosvorová, L., Mikšátková, P., Bičíková, M., Kaňová, N., and Lapčík, O. 2012. "The presence of monoiodinated derivates of daidzein and genistein in human urine and its effect on thyroid gland function." *Food and chemical toxicology : an international journal published for the British Industrial Biological Research Association*, *50*(8), 2774–2779. doi: 10.1016/j.fct.2012.05.037

[122] Domínguez-López, I., Yago-Aragón, M., Salas-Huetos, A., Tresserra-Rimbau, A., and Hurtado-Barroso, S. 2020. "Effects of Dietary Phytoestrogens on Hormones throughout a Human Lifespan: A Review." *Nutrients*, *12*(8), 2456. doi: 10.3390/nu12082456

[123] Messina M. 2010. "Soybean isoflavone exposure does not have feminizing effects on men: a critical examination of the clinical evidence." *Fertility and sterility*, *93*(7), 2095–2104. doi: 10.1016/j.fertnstert.2010.03.002

[124] Reed, K. E., Camargo, J., Hamilton-Reeves, J., Kurzer, M., and Messina, M. 2021. "Neither soy nor isoflavone intake affects male reproductive hormones: An expanded and updated meta-analysis of clinical studies." *Reproductive toxicology (Elmsford, N.Y.)*, *100*, 60–67. doi: 10.1016/j.reprotox.2020.12.019

[125] Oliveira, F. R. K., Gustavo, A. F. S. E., Gonçalves, R. B., Bolfi, F., Mendes, A. L., and Nunes-Nogueira, V. D. S. 2021. "Association between a soy-based infant diet and the onset of puberty: A systematic review and meta-analysis." *PloS one*, *16*(5), e0251241. doi: 10.1371/journal.pone.0251241

[126] Rizzo, G., Feraco, A., Storz, M. A., and Lombardo, M. 2022. "The role of soy and soy isoflavones on women's fertility and related outcomes: an update." *Journal of nutritional science*, *11*, e17. doi: 10.1017/jns.2022.15

[127] Boutas, I., Kontogeorgi, A., Dimitrakakis, C., and Kalantaridou, S. N. 2022. "Soy Isoflavones and Breast Cancer Risk: A Meta-analysis." *In vivo (Athens, Greece)*, *36*(2), 556–562. doi: 10.21873/invivo.12737

[128] Otun, J., Sahebkar, A., Östlundh, L., Atkin, S. L., and Sathyapalan, T. 2019. "Systematic Review and Meta-analysis on the Effect of Soy on Thyroid Function." *Scientific reports*, *9*(1), 3964. doi: 10.1038/s41598-019-40647-x

[129] Nachvak, S. M., Moradi, S., Anjom-Shoae, J., Rahmani, J., Nasiri, M., Maleki, V., and Sadeghi, O. 2019. "Soy, Soy Isoflavones, and Protein Intake in Relation to Mortality from All Causes, Cancers, and Cardiovascular Diseases: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies." *Journal of the Academy of Nutrition and Dietetics*, *119*(9), 1483–1500.e17. doi: 10.1016/j.jand.2019.04.011

[130] Rietjens, I. M. C. M., Louisse, J., and Beekmann, K. 2017. "The potential health effects of dietary phytoestrogens." *British journal of pharmacology*, *174*(11), 1263–1280. doi: 10.1111/bph.13622

[131] Petrine, J. C. P., and Del Bianco-Borges, B. 2021. "The influence of phytoestrogens on different physiological and pathological processes: An overview." *Phytotherapy research : PTR*, *35*(1), 180–197. doi: 10.1002/ptr.6816

[132] Villegas, R., Gao, Y. T., Yang, G., Li, H. L., Elasy, T. A., Zheng, W., and Shu, X. O. 2008. "Legume and soy food intake and the incidence of type 2 diabetes in the Shanghai Women's Health Study." *The American journal of clinical nutrition*, *87*(1), 162–167. doi: 10.1093/ajcn/87.1.162

[133] Zhu, B., Sun, Y., Qi, L., Zhong, R., and Miao, X. 2015. "Dietary legume consumption reduces risk of colorectal cancer: evidence from a meta-analysis of cohort studies." *Scientific reports*, *5*, 8797. doi: 10.1038/srep08797

[134] Fan, Y., Wang, M., Li, Z., Jiang, H., Shi, J., Shi, X., Liu, S., Zhao, J., Kong, L., Zhang, W., and Ma, L. 2022. "Intake of Soy, Soy Isoflavones and Soy Protein and Risk of Cancer Incidence and Mortality." *Frontiers in nutrition*, *9*, 847421. doi: 10.3389/fnut.2022.847421

[135] Nachvak, S. M., Moradi, S., Anjom-Shoae, J., Rahmani, J., Nasiri, M., Maleki, V., and Sadeghi, O. 2019. "Soy, Soy Isoflavones, and Protein Intake in Relation to Mortality from All Causes, Cancers, and Cardiovascular Diseases: A Systematic Review and Dose-Response Meta-Analysis of Prospective Cohort Studies." *Journal of the Academy of Nutrition and Dietetics*, *119*(9), 1483–1500.e17. doi: 10.1016/j.jand.2019.04.011

[136] Oldewage-Theron, W., and Egal, A. 2013. "The effect of consumption of soy foods on the blood lipid profile of women: a pilot study from Qwa-Qwa." *Journal of nutritional science and vitaminology*, *59*(5), 431–436. doi: 10.3177/jnsv.59.431

[137] Liu, Z. M., Ho, S. C., Chen, Y. M., Ho, S., To, K., Tomlinson, B., and Woo, J. 2014. "Whole soy, but not purified daidzein, had a favorable effect on improvement of cardiovascular risks: a 6-month randomized, double-blind, and placebo-controlled trial in equol-producing postmenopausal women." *Molecular nutrition & food research*, *58*(4), 709–717. doi: 10.1002/mnfr.201300499

[138] Delclos, K. B., Camacho, L., Lewis, S. M., Vanlandingham, M. M., Latendresse, J. R., Olson, G. R., Davis, K. J., Patton, R. E., Gamboa da Costa, G., Woodling, K. A., Bryant, M. S., Chidambaram, M., Trbojevich, R., Juliar, B. E., Felton, R. P., and Thorn, B. T. 2014. "Toxicity evaluation of bisphenol A administered by gavage to Sprague Dawley rats from gestation day 6 through postnatal day 90." *Toxicological sciences: an official journal of the Society of Toxicology*, *139*(1), 174–197. doi: 10.1093/toxsci/kfu022

[139] Rogers L. D. 2021. "What Does CLARITY-BPA Mean for Canadians?." *International journal of environmental research and public health*, *18*(13), 7001. doi: 10.3390/ijerph18137001

[140] Lakind, J. S., and Naiman, D. Q. 2011. "Daily intake of bisphenol A and potential sources of exposure: 2005-2006 National Health and Nutrition Examination Survey." *Journal of exposure science & environmental epidemiology*, *21*(3), 272–279. doi: 10.1038/jes.2010.9

[141] Lorber, M., Schecter, A., Paepke, O., Shropshire, W., Christensen, K., and Birnbaum, L. 2015. "Exposure assessment of adult intake of bisphenol A (BPA) with emphasis on canned food dietary exposures." *Environment international*, *77*, 55–62. doi: 10.1016/j.envint.2015.01.008

[142] Teeguarden, J. G., Calafat, A. M., Ye, X., Doerge, D. R., Churchwell, M. I., Gunawan, R., and Graham, M. K. 2011. "Twenty-four hour human urine and serum profiles of bisphenol a during high-dietary exposure." *Toxicological sciences : an official journal of the Society of Toxicology*, *123*(1), 48–57. doi: 10.1093/toxsci/kfr160

[143] EFSA Panel on Food Contact Materials, Enzymes and Processing Aids (CEP), Lambré, C., Barat Baviera, J. M., Bolognesi, C., Chesson, A., Cocconcelli, P. S., Crebelli, R., Gott, D. M., Grob, K., Lampi, E., Mengelers, M., Mortensen, A., Rivière, G., Silano Until December, V., Steffensen, I. L., Tlustos, C., Vernis, L., Zorn, H., Batke, M., Bignami, M., Corsini, E., FitzGerald, R., Gundert-Remy, U., Halldorsson, T., Hart, A., Ntzani, E., Scanziani, E., Schroeder, H., Ulbrich, B., Waalkens-Berendsen, D., Woelfle, D., Al Harraq, Z., Baert, K., Carfì, M., Castoldi, A.F., Croera, C., and Van Loveren, H. 2023. "Re-evaluation of the risks to public health related to the presence of bisphenol A (BPA) in foodstuffs." *EFSA journal. European Food Safety Authority*, *21*(4), e06857. doi: 10.2903/j.efsa.2023.6857

[144] Lehmler, H. J., Liu, B., Gadogbe, M., and Bao, W. 2018. "Exposure to Bisphenol A, Bisphenol F, and Bisphenol S in U.S. Adults and Children: The National Health and Nutrition Examination Survey 2013-2014." *ACS omega*, *3*(6), 6523–6532. doi: 10.1021/acsomega.8b00824

[145] Prudencio, T. M., Swift, L. M., Guerrelli, D., Cooper, B., Reilly, M., Ciccarelli, N., Sheng, J., Jaimes, R., and Posnack, N. G. 2021. "Bisphenol S and Bisphenol F Are Less Disruptive to Cardiac Electrophysiology, as Compared With Bisphenol A." *Toxicological sciences : an official journal of the Society of Toxicology*, *183*(1), 214–226. doi: 10.1093/toxsci/kfab083

[146] Nevoral, J., Kolinko, Y., Moravec, J., Žalmanová, T., Hošková, K., Prokešová, Š., Klein, P., Ghaibour, K., Hošek, P., Štiavnická, M., Řimnáčová, H., Tonar, Z., Petr, J., and Králíčková, M. 2018. "Long-term exposure to very low doses of bisphenol S affects female reproduction." *Reproduction (Cambridge, England)*, *156*(1), 47–57. doi: 10.1530/REP-18-0092

[147] Thoene, M., Dzika, E., Gonkowski, S., and Wojtkiewicz, J. 2020. "Bisphenol S in Food Causes Hormonal and Obesogenic Effects Comparable to or Worse than Bisphenol A: A Literature Review." *Nutrients*, *12*(2), 532. doi: 10.3390/nu12020532

[148] Akash, M. S. H., Rasheed, S., Rehman, K., Imran, M., and Assiri, M. A. 2023. "Toxicological evaluation of bisphenol analogues: preventive measures and therapeutic interventions." *RSC advances*, *13*(31), 21613–21628. doi: 10.1039/d3ra04285e