02: Food

asterisk

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Inside front cover: *Still Life with Fruit*
Jan Mortel, (Leyden c.1650–1719)
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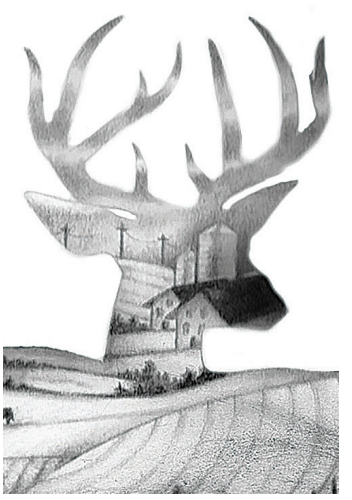
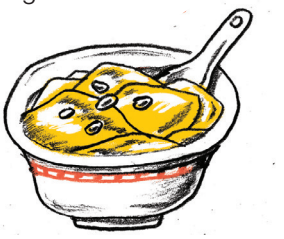
Inside back cover: *Still Life with Dressed Game, Meat and Fruit* (1734)
Alexandre François Desportes,
(French, 1661–1743)





Why do an issue about food? In the first place, food matters. At least for the moment, all of us need it to live. Food is complicated — from the technology we use to produce it, to the supply chains that bring it to our tables and its impact on our bodies. Food is interesting. It lets us tell stories about our families, cutting-edge science, and deeply held ethical principles.

Also, and more importantly, food makes people mad.

As the editors of a very new little magazine, of course, it's in our interests to touch the occasional emotional third rail. (Our readers may be brilliant and discerning, but 5,000-word essays on social science methodology only get us so many clicks.) Everyone has opinions about food, because everybody eats. And almost everyone cares if the things we choose to put in our mouths are bad for us, or bad for the world, or make us look bad in front of our neighbors.

We'll admit it: We like attention. But we also believe that when we're mad — or horrified, or defensive, or maybe just hungry — it's more important than ever to think clearly. The science of nutrition is hideously complicated, poorly understood, and frequently weaponized — but our health depends on getting it right. The Green Revolution is a strong contender for the most impactful event of the 20th century — but if you want to cause a fight in a roomful of development economists, just ask them how it went. We live in a world where billions of animals suffer horrifically at the hands of humans. We owe it to them to look at their experiences unflinchingly — and pragmatically. Do beef cattle have lives worth living? Is it possible — or desirable — to replace meat

consumption altogether? How many mice are poisoned for every ton of wheat harvested in North America? We don't know, and we'd like to find out.

In this issue, we've tried to bring together a selection of pieces that shed more light than heat on these important questions.

Our contributors have added up the indirect impacts of agriculture on wild animals, cut through the hype and cynicism around cultivated and plant-based meat, and learned how to make exploding-juice tofu. They've studied the ongoing impacts of the Green Revolution and tried to figure out how many people die because of misinformation about food and diets. They've asked why we still don't know the health effects of alcohol, whether oysters have feelings, how it took so long to learn that diarrheal diseases could be cured with water, sugar, and salt, and what it would take to feed the world if nuclear fallout blocked out the sun. And, yes, there are a couple of 5,000-word essays on social science methodology, because we just can't help ourselves.

Dig in. We hope you enjoy it.

6

The Forecast

What Comes After COVID?

Juan Cambiero

**The next pandemic is coming.
Is it possible to say when?**

From the beginning of agriculture 12,000 years ago to the early 20th century, infectious diseases have probably killed far more people than famine and violence combined.[1] When hunter-gatherers started to farm, they also built permanent settlements and domesticated animals — greatly increasing the likelihood of zoonotic spillover, which would in turn spread more readily in dense, interconnected human populations. Influenza, smallpox, and measles are just some of the infectious diseases that made their appearance in the human population during this period.

As late as 1900, infectious diseases were responsible for nearly half of all deaths in the United States. Infectious diseases continue to kill more people in low-income countries than noncommunicable diseases do. Worse yet, humanity as a whole faces the possibility of devastating future pandemics that could constitute an existential risk to humanity.

As we continue to grapple with the ongoing effects of COVID-19, we must start thinking about how to prepare for the next pandemic. The question is not whether it will occur, but when.

What Does It Mean to Forecast the "Next Pandemic"?

Before we can make any forecasts about the next pandemic, we have to be specific about *exactly* what that means. What counts as a "pandemic"? What's the time frame we're looking at? What in particular about the "next pandemic" do we want to know? I will use the following two specific questions.[2]

1. Will a pandemic caused by a novel pathogen begin between 2023 and 2032 and result in the deaths of more than 20 million people?
Since there is no officially recognized threshold for "pandemic," I'm defining it here as the spread of a pathogen that ultimately kills more than 20 million people and that is present worldwide.

Instead of looking at just confirmed deaths, which often undercount true fatalities, I prefer to use the number of excess deaths from all causes during the pandemic. *The Economist* estimates that COVID-19 caused 20.3 million excess deaths as of the end of 2022, compared to the World Health Organization's confirmed death count of 6.7 million.

To qualify, these 20 million-plus deaths should occur within a limited window of time — let's say three years — instead of over many decades. For example, a pandemic for which there are confirmed deaths beginning in February 2030 would have to result in 20 million-plus deaths by February 2033.

I set 20 million as my threshold because it may be of particular interest to ask about the probability of a COVID-like pandemic or worse.

2. If a pandemic begins in the next decade, what type of microorganism will be the causative agent?
This question is useful for thinking about countermeasures — for example, how we might want to focus prototype vaccine development. To avoid infohazard issues, I won't get into more detail than looking at different virus families. I've divided

1. Calculation by Charles Kenny in *The Plague Cycle*.

2. These questions are similar to two included in a biosecurity-specific forecasting tournament I launched on Metaculus.

potential causative agents into four categories: "Orthomyxoviridae virus family" (influenza); "Coronaviridae virus family" (coronaviruses); other known viruses; and nonviruses such as bacteria or fungi, as well as unknown viruses.

Initial Forecasting Process

To better understand the probability of a future pandemic, it is useful to look at the relevant reference class — in this case, the frequency and characteristics of past pandemics. The past is oftentimes an excellent guide to what might happen in the future.

But how far back do I want to go? All the way back to the Plague of Justinian in the sixth century? Probably not, for a few reasons: A lot about modern-day life is different (we now have antibiotics, for example) and our knowledge of infectious diseases has vastly improved (in particular, we now know that specific microorganisms cause particular diseases). We also have very sparse information about pandemics in the distant past, making it difficult to construct a useful data set.

A logical (and clean) cut-off is 1900. We have substantially more comprehensive data on pandemics or near-pandemics during this time. We also have high confidence about which pathogens caused the outbreaks that occurred after this point. For example, we've identified the virus that caused the Spanish flu as the A/H1N1 influenza strain, but we're not actually sure whether the 1889 Russian "flu" was, indeed, caused by a member of the Orthomyxoviridae family. This period is also characterized by a high degree of globalization, which makes it more applicable as a reference class.

Here, I include both events widely considered to be "pandemics" (rapid worldwide spread of a disease) and what I somewhat subjectively call near-pandemics: novel pathogens with high lethality potential that saw limited human-to-human transmission and were snuffed out or died out on their own before they reached the pandemic stage. I do this because these smaller outbreaks provide more data about the types of microorganisms that might be most likely to cause future pandemics.

The clustering of near-pandemics in recent decades is probably just because of an unfortunate lack of adequate public health surveillance in the early to mid-20th century — smaller outbreaks likely occurred but went unrecorded.

Next, let's take a look at our two questions in the context of the opposite historical data.[3]

1. Will a pandemic caused by a novel pathogen begin between 2023 and 2032 and result in the deaths of more than 20 million people?
In the 123 years between 1900 and 2022, there were a total of 12 known pandemics, epidemics, or outbreaks. Of these, two were pandemics that killed more than 20 million people within three years, for an annualized probability of ~1.6% in a given year.[4] Over 10 years, this would translate to a probability of ~16%. Thus, **16%** is my starting forecast.

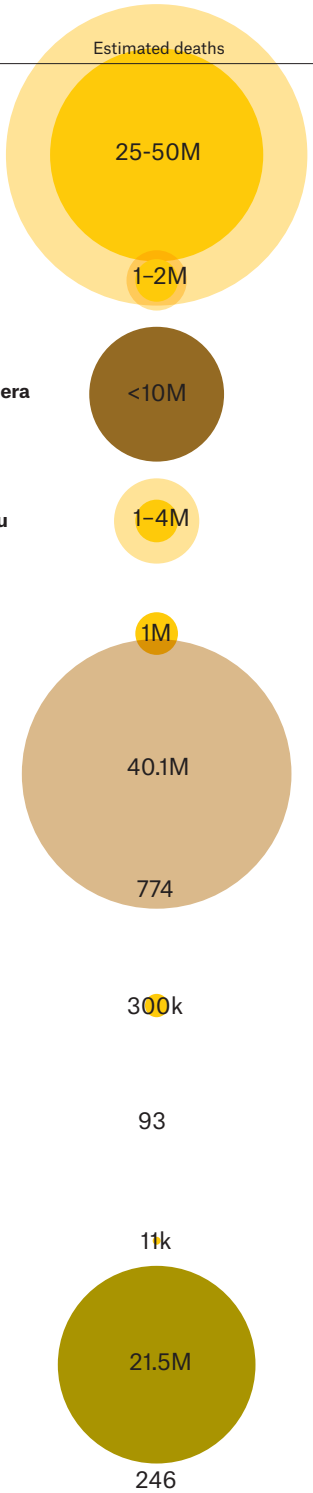
2. If a pandemic begins in the next decade, what type of microorganism will be the causative agent?
In the table I constructed, there are four general categories of microorganisms:

- **Orthomyxoviridae:** members of the influenza virus family, which caused $^{5}/_{12}$ events = **41.7%.** This includes $^{1}/_{2}$ of the events that meet my "pandemic" criteria.
- **Coronaviridae:** members of the coronavirus virus family, which caused $^{3}/_{12}$ events = **25.0%.** This includes $^{1}/_{2}$ of the events that meet my "pandemic" criteria.

3. Another thing to note: If I went back further in history, I'd probably want to adjust for the world population size. But because of the time scale we're looking at, it's not necessary to do this: It would not result in any additional events that meet my "pandemic" definition.

4. HIV/AIDS killed more than 20 million people, but not within the span of just three years — so it doesn't count.

Frequency and characteristics of past pandemics, 1900–2022



Name	Estimated deaths	Start/End	Microorganism
Spanish Flu	25-50M	1918/1920	Influenza A/H1N1
Asian Flu	1–2M	1957/1959	Influenza A/H2N2
Seventh Cholera pandemic	<10M	1961/ongoing	*Vibrio cholerae*
Hong Kong flu	1–4M	1968/1970	Influenza A/H3N2
Russian flu	1M	1977/1979	Influenza A/H1N1
HIV/AIDS	40.1M	1981/ongoing	HIV
SARS	774	2002/2003	SARS-CoV
Swine flu	300k	2009/2010	Influenza A/H1N1
MERS	93	2014/2014	MERS-CoV
Ebola	11k	2014/2016	Zaire ebolavirus
Covid-19	21.5M	2019/ongoing	SARS-CoV-2
MPV	246	2022/ongoing	Monkeypox virus

Microorganism type

- Orthomyxoviridae
- Vibrionaceae (bacteria)
- Other (Retroviridae, Filoviridae, Poxviridae)
- Coronaviridae

- **Other known virus:** viruses from any of the other 24 known human-infecting virus families, which were responsible for 3/12 events = **25.0%.**
- **Nonvirus or unknown virus:** any other microorganisms, including viruses from unidentified human-infecting virus families, bacteria, and fungi, which were responsible for 1/12 events (cholera) = **8.3%.**

From the reference class, we can clearly see that pandemics and near-pandemics have occurred fairly frequently throughout recent history and will likely continue to occur in the future. However, the probability of a future pandemic should also take into account the current state of technology and society — which is what we'll take on next.

Adjusted Forecast/Inside View

1. Will a pandemic caused by a novel pathogen begin between 2023 and 2032 and result in the deaths of more than 20 million people? I'll start with my initial forecast of 16% and adjust it based on factors I think are relevant.

Factors that *lower* the risk of a pandemic in the next decade:

- Better sanitation, hygiene, and general health: 16% → **13%**
- Increased likelihood of speedy detection of a novel pathogen and subsequent rapid development of vaccines/therapeutics: 13% → **10%**
- Improved medical practices and medical system infrastructure: 10% → **8.5%**
- Possible use of nonpharmaceutical interventions like widespread masking and physical distancing: 8.5% → **7.5%**

I ended up with a probability of 7.5%, down from my starting point of 16%. The most important factors here are better health and sanitation, increased likelihood of speedy detection, and the development of vaccines and therapeutics. Global rates of malnutrition, which greatly increases the likelihood of infection, are significantly lower than they were in 1900. In the realm of medicine, our response to COVID has shown what is possible: In the U.S., it took only 326 days from the first U.S. laboratory-confirmed case on January 20, 2020, until the first FDA-authorized vaccine on December 11, 2020. The COVID vaccines likely saved nearly 20 million lives worldwide by the end of 2021.

Biosafety Level 3 and 4 labs, where dangerous pathogens are handled and sometimes experimented on, are increasing in number. The continued democratization of biotechnological tools, meanwhile, is providing more and more actors with the capability to engineer dangerous pathogens.

However, there are other factors about the current context that increase the probability of a pandemic:

- Increased likelihood of unintentional lab leak of a naturally occurring pathogen or pathogen that underwent gain of function: 7.5% → **12%**
- Continued democratization of biotechnological tools that makes the ability to deliberately engineer deadly pathogens more accessible to bad actors: 12% → **16%**

- Increased interaction between humans and animals, which creates more opportunities for zoonotic spillover: 16% → **18%**
- Air travel enabling fast widespread transmission: 18% → **19%**

I updated from 7% all the way to 19%, largely because of the increased likelihood of an unintentional lab leak and the continued democratization of biotechnology. My concern for lab leaks is due to the fact that Biosafety Level 3 and 4 labs, where dangerous pathogens are handled and sometimes experimented on, are increasing in number. The continued democratization of biotechnological tools, meanwhile, is providing more and more actors with the capability to engineer dangerous pathogens. My final forecast for a pandemic killing more than 20 million people in the next decade is **19%**, or roughly a one-in-five chance.

2. If a pandemic begins in the next decade, what type of microorganism will be the causative agent?

I've arrived at a probability of 19% that a pandemic will start in the next decade and kills more than 20 million people. If this were to happen, what might the causative microorganism be? Eleven out of the 12 microorganisms in my reference class are viruses — five are influenza viruses (Orthomyxoviridae), three are coronaviruses (Coronaviridae), three are other known viruses, and one is a nonvirus. Viruses have historically been more likely than other microorganisms to cause a pandemic and are still epidemiologists' biggest concern, because of their high replication rate and the lack of a broad-spectrum antiviral.

Let's take each of these categories in turn. First, I'll adjust for the fact that events that met my definition of "pandemic" were caused once in 1918 by a flu virus and once in 2019 by a coronavirus. I'll give more weight to Orthomyxoviridae and Coronaviridae.

- **Orthomyxoviridae:** 41.7% → **50.0%**
- **Coronaviridae:** 25.0% → **30.0%**
- **Other known virus:** 25.0% → **15.0%**
- **Nonvirus or unknown virus:** 8.3 → **5.0%**

On the other hand, while we have experience developing vaccines for influenza viruses and coronaviruses, we do not have a prototype vaccine for 11 of the 26 human-infecting viral families. Many of these other human-infecting viral families are also generally less well characterized, which increases the danger they pose. So I want to increase the likelihood of outbreak from the other known virus and nonvirus or unknown virus categories. I also want to account for the fact that we are actively concerned about specific flu viruses that can spread between mammals. I think overall this should negate about a third of my previous adjustment for Orthomyxoviridae and fully negate it and then some for Coronaviridae, while substantially increasing other known virus and nonvirus or unknown virus.

- **Orthomyxoviridae:** 50.0% → **47.2%**
- **Coronaviridae:** 30.0% → **20.8%**
- **Other known virus:** 15.0% → **23.0%**
- **Nonvirus or unknown virus:** 5.0% → **9.0%**

So, according to my forecast, there is roughly a one-in-two chance of the causative agent of the next pandemic being an influenza virus, a one-in-five chance of it being a coronavirus, a one-in-four chance of it being some other virus from a known human-infecting viral family, and a one-in-11 chance of it being some other microorganism.

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The devastation caused by previous pandemics, including COVID-19, serves as a reminder of the destructive power of infectious diseases. We do not know when the next pandemic will strike, or what form it will take, but by approaching the question with a probabilistic mindset, we can give ourselves the best chance of meeting it prepared.

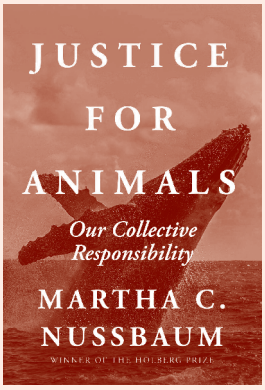
12

Review

The Virtue of Wonder: Martha Nussbaum's *Justice for Animals*

Ozy Brennan

Martha Nussbaum's latest book challenges us to change the way we think—and feel—about animals. What role can wonder and awe play when pathos comes up short?



Simon and Schuster

Early in Martha Nussbaum's new book *Justice for Animals: Our Collective Responsibility*, she writes in loving detail about a house finch that she listens to through a web database of bird songs: "Jean-Pierre is compelling to look at: such delicate gradations of color in his plumage, so active and intelligent as he socializes with other birds — and, above all, entrancing to hear as he spins his complicated warbling compositions. He never tires of singing."

If you've heard of any contemporary academic philosopher, there is a decent chance that it is Martha Nussbaum. She is prolific (29 books) and prolifically decorated (63 prizes, 65 honorary degrees). She has written on — among other things — Hellenistic philosophy, political philosophy, international development, feminism, literature, disability, sex, and opera. Foremost, she is a philosopher of emotions. Since her early career as a classical philologist, Nussbaum has been interested in vulnerability, grief, anger, disgust, and love — what she herself refers to as our animal natures.

In this sense, *Justice for Animals* is a continuation of her long-term project: using philosophy, the stereotypical preserve of pure reason, to illuminate the parts of life and the living beings long considered less than rational. A sense of love pervades *Justice for Animals* which was written in honor of Nussbaum's late daughter Rachel, an animal welfare attorney. Nussbaum loves the fastidious cleanliness of the pig, the echolocation skills of a dolphin who may even be able to tell that a human is pregnant before the human knows, the art of a bowerbird, which incorporates flowers and plastic with equal ingenuity, and the complex calls of a chickadee which have their own syntax. And she wants you to love them, too.

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Nussbaum highlights three essential virtues in thinking about animals: wonder, which draws our attention to the value of animals; compassion, which alerts us to suffering; and outrage without the desire for retribution, which motivates us to improve the world. Compassion and outrage are common and valued in the animal advocacy community, but wonder is rarer.

The virtue of wonder is both amazement at animals' unique ways of life and curiosity about why they behave the way they do. When we wonder at an animal, we recognize that their behavior has a purpose, that there is something it is like to be them, and we try to understand. Wonder, she writes, "takes us out of ourselves and toward the other... [It has] nothing to do with our own personal search for well-being. It is connected to our original joy at life itself."[1]

Nussbaum's approach to animal ethics is the "Capabilities Approach." Originally developed by Nussbaum and economist Amartya Sen as a political philosophy about humans, the Capabilities Approach says that societies should protect a set of basic "central capabilities" which are necessary for each individual to flourish. Although any individual might not wish to exercise any particular capability, the individual should still be able to, if they choose. For humans, these capabilities are as varied as eating nutritious food, reading, voting for those in power over them, planning the course of their lives, and relating to animals and the natural world. The Capabilities Approach is a theory of justice: Nussbaum argues that, as reasoning beings with inviolable dignity, we are entitled to the ability to exercise these central capabilities.

1. Martha C. Nussbaum, *Justice for Animals: Our Collective Responsibility* (New York: Simon and Schuster, 2023), 10.

Nussbaum provocatively argues that animals are also reasoning beings with inviolable dignity, and so are entitled to the protection of their central capabilities. Factory farming is not merely a harm to animals; it is an injustice. In principle, allowing a wild animal to die of a treatable illness is no different from allowing a child to die of a treatable illness.[2] Both are unjust.

Many readers — even animal advocates — will find this view challenging. Instead of looking collectively at species or ecosystems, the Capabilities Approach requires us to treat each animal as an individual moral subject. Protecting the dignity of wild antelopes, cockatoos, and hammerhead sharks would require massive and costly interventions into nature. It is not clear how the Capabilities Approach treats the incommensurate central capabilities of predator and prey. It grants no special status to humans.

Nussbaum might respond to these challenges by reminding us that she is a political philosopher, not an ethicist. The Capabilities Approach is not, and is not trying to be, a definitive answer to the question of animal ethics, but an attempt to provide the basis for deliberations which will one day shape policy. It does not tell us how to advocate for animals, or even what goals we should advocate for — only the attitude to adopt before we start.

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Nussbaum's strongest disagreement with other strains of animal advocacy is with what she calls the "So Like Us" approach, which grounds animal justice in certain animals' similarity to humans. Some people, such as animal-rights attorney Steven Wise, argue that we shouldn't hurt gorillas because gorillas can be taught to use sign language to indicate their emotions. Because they can communicate with us in a way that we intuitively understand, they must be morally valuable. But even gorillas who use sign language don't use it with each other. It's a trick played with humans. Instead of valuing gorillas because they can be taught to playact as humans, using language in a similar way to us, we should value gorillas for the unique ways that they express empathy *as gorillas*, as well as the ways that they build nests, use tools, and wander across large ranges. If we say that birdsong and whalesong indicate that birds and whales are valuable because they sing just like humans do, then we miss the opportunity to appreciate birdsong and whalesong as unique forms of art created by minds that are very different from our own.

Nussbaum cares about justice for animals both because of how similar they are to us and because of how different they are to us. Animals are fundamentally unlike us, in everything from their mode of life to their sensory capabilities. Nevertheless, like us, they set goals and pursue them; like us, they struggle for life and fulfillment in a hostile world. Our amazement at the diversity of ways of being creates a desire for those ways of being to be lived out more fully.

In an earlier essay, Nussbaum describes her work on animal justice as "a neo-Aristotelian approach containing Kantian elements."[3] From Kant, modulated by the work of her own former student Christine Korsgaard, she borrows the principle that sentient beings are ends in themselves; from Aristotle, the importance of attending to each species's distinctive way of flourishing. What it is not, Nussbaum insists, is utilitarian.

Unlike classical Benthamite utilitarianism, the Capabilities Approach emphasizes the needs of members of each individual species to exercise their typical species capabilities. An elephant must have the capability to travel through a range thousands of miles wide; this ability is of no use to a house cat. Dolphins must be able to form social groups; polar bears have no such requirement. Utilitarianism, conversely, emphasizes the universal need of all animals to experience pleasure and avoid pain.

In line with her emphasis on a species' capabilities, Nussbaum, therefore, grounds

2. Nussbaum acknowledges other differences between the cases. Treating a wild animal's illness, for example, may have complex effects on the ecosystem that we do not understand which, on balance, makes the treatment harmful.

3. Martha Nussbaum, "The Capabilities Approach and Animal Entitlements," in *The Oxford Handbook of Animal Ethics*, eds. Tom L. Beauchamp and R. G. Frey (Oxford: Oxford University Press, 2014), 2.

our concern for animals in "significant striving," the ability to pursue the goals that matter most while setting aside those which are inconsequential. Utilitarians, however, care about whether an animal can suffer. Nussbaum argues that this distinction makes little difference in practice, because animals evolved to feel pain and pleasure so that they could prioritize between goals and pursue them in a flexible manner. Any organism that has the traits that the Capabilities Approach cares about, she claims, has the traits that utilitarians care about. However, this doesn't fully justify her point. It is conceivable that some organisms, such as shrimp, are able to suffer without necessarily having what we would call a significant aim. Would the Capabilities Approach be indifferent to their pain?

However, this disagreement is smaller than it seems — at least, smaller than it seems to Nussbaum. Under the Capabilities Approach, some central capabilities are shared by all animals, such as the capability to eat adequate and nutritious food.[4] Most utilitarians subscribe to a theory of animal welfare like the Five Freedoms Approach.[5] However, the Five Freedoms include "the freedom to express normal behavior," that is, the behavior typical of a particular species. While the emphasis is different, the recommendations converge. Nussbaum herself seems to underestimate this convergence by arguing that utilitarians would accept (say) an elephant being fed and given adequate health care but denied a social group. Yet, loneliness is a pain, and social company is a pleasure. Utilitarian animal advocates take the ability of an animal to perform species-typical behavior very seriously. Perhaps Nussbaum's underestimation is an attempt to differentiate her view from utilitarianism.

The primary distinction, I think, is one of attitude. The virtue of the utilitarian is compassion. The utilitarian grieves the suffering of (say) a lonely and isolated dolphin, calling out for podmates who aren't there. The virtue of the follower of the Capabilities Approach is wonder. The follower of the Capabilities Approach has a deep respect for the way of being of the dolphin — their alien senses and ways of moving through the world, and yet how they — like us — have desires and longings, strivings and frustrations, and achievements. From that wonder grows an outrage that such a beautiful thing can be destroyed.

To some extent, it doesn't matter what reason a person has to help animals as long as they help. But I think that wonder can provide a more robust motivation for animal advocacy. If we are simply concerned about suffering, then the enormity of the injustice done to animals (companion animals, research animals, farmed animals, wild animals) can lead to despair and a sense of helplessness. Rather, wonder allows us to experience a balancing joy in an animal's life well-lived. We don't just have something to avoid; we have something to aim for.

Dolphins can detect buried mines in harbors, a feat that human-developed sonar is incapable of. Octopuses in a lab squirt water at lightbulbs in order to burn them out and experience their preferred darkness. Chimpanzees have cultures: some groups have different grooming, courtship, tool use, and nest-building practices than others because of multi-generational social learning, not generational differences. The natural world is a place of wonder.

Show a young child a documentary about animals and you will see that the natural response to the diversity of animals — so strange from our parochial human view — is awe. But by adulthood, the awe, in this as in so many other areas of life, is stamped out. If we cultivate the wonder of a child, perhaps it will give us the curiosity, the compassion, and the outrage we need to begin to treat animals with justice.

4. Martha Nussbaum does suggest that her list of human central capabilities can be expanded to describe the central capabilities of animals of all species. I find this an uncharacteristic deviation from her careful attention to difference and do not think it is actually implied by the Capabilities Approach.

5. For more information on the Five Freedoms approach, see Melissa Elischer, "The Five Freedoms: A history lesson in animal care and welfare," *Michigan State University*, September 6, 2019, https://www.canr.msu.edu/news/an_animal_welfare_history_lesson_on_the_five_freedoms.

16

Interview

Feeding the World Without Sunlight

Mike Hinge

In 1815, the largest volcanic eruption in recorded history led to harvest failures across the globe. Today, a nuclear winter could bring the global food system crashing down. Is it possible to feed the world in the aftermath of a catastrophe?

Asterisk: *Your background is as an agricultural economist and, among other things, you've studied the former USSR. So to start out, I wanted to talk a little bit about why the Russian invasion of Ukraine caused such severe shocks to the global food system.*

Mike: The conflict in Ukraine has had huge impacts across many supply chains, and it comes on the heels of the COVID pandemic, which had already disrupted them. Ukraine is a big exporter and an important supplier of food for a large number of countries in the Mediterranean. Russia is also a very big exporter — of grains as well as of fertilizers and fertilizer precursors in the form of natural gas, potassium, and phosphorus. So the disruption has been twofold: Sanctions in Russia have disrupted the supply. And, particularly early in the conflict, food prices spiked very sharply because of disruptions to the port of Odessa.

Only about 12 percent of grains are traded internationally. The majority of production remains within borders. But the countries that do import grains are reliant on them. They have very little slack. Lebanon, Egypt, Tunisia, and other Middle Eastern and North African countries were facing serious difficulties without Ukrainian shipments. Luckily, it's now partially resolved.

This is a humanitarian concern that needs to be addressed today, but it's also a warning sign that future global supply shocks can result in rapid disruptions of large magnitude. Somewhere between 2 percent and 3 percent of global calories were disrupted, but that led to a spike of about 40 or 50 percent in grain prices.

A: *I'm thinking of the 2007 to 2008 global food-price spike, which involved a lot of things that were much less extreme than one major grain exporter invading another country that is an even bigger grain exporter, but still added up to this huge global disruption.*

M: Many factors contribute to price spikes, which is what makes understanding and predicting them hard. Agriculture is what we call "lumpy"— it doesn't have a continuous supply of crops because it's seasonal. How much of a harvest is stored depends on a number of factors, and that in turn influences the impact of supply shocks. A 2 percent supply shock could be negligible if you have very high stocks and rock-bottom prices, or a 2 percent shock could be coming on largely empty stores, which was what happened in '07 to '08. And in that case, it's critical because within a harvest, it's very difficult to get extra food once it's in the ground. With these complicated supply chains you've negotiated potentially a year or two in advance for your contracts for certain crops and the inputs needed for them. So to balance the supply and demand, you have to bring demand down. That can lead to some very high prices.

A: *You mentioned COVID as a cause leading to this price shock, so let's talk about what COVID did to the global food-supply chain.*

M: First there was panic. Countries were looking to secure their own supply. Supply chains themselves were under threat because quarantine measures were being introduced with strokes of pens, and people were working at high speed to try to work out how they would function. Ports were disrupted. For example, crew changes couldn't occur, and an entire bulk carrier can be taken out by having two or three key employees not available. At the same time, countries had to ensure that they had sufficient food supply for their own population, so many places imposed or considered export restrictions and bans just as a precaution — another thing that was linked to the 2007 to 2008 crisis. And then you can have a cascade where concerns about export availability cause exporters to cut back and importers to import more, which means those who are least able to afford it are left carrying the shock.

Now, these issues were resolved — maritime organizations managed to get people to ports, supply situations were fixed, and the EU and Japan said that they weren't planning to impose export restrictions and that any orders placed would be honored. In the end, countries committed to meeting the needs of the market, which was another strategy that helped in the '07 to '08 crisis. But the concern is that this method only works when the few countries that can step up and make these commitments have the stocks to meet the shortage. If it was a very large shortage, that wouldn't be the case.

A: *How common do you think shocks like this are going to be in the future?*

M: That's a very difficult question. Historically, severe food shocks that have taken out, say, 3 to 4 percent of global calories have been quite rare. Shocks within a certain region can be very severe, but they tend to not be correlated to the global level. We can trade between surplus areas and deficit areas, and even between bread baskets and key producing regions.

But volatility is likely to rise. Climate change is already leading to more climate volatility, and we're likely to see events that previously occurred once in 20 or 100 years occurring once in every 5 or 10 years. That becomes much harder to manage through trade. And the second thing is that there are much larger shocks that could also occur, which I believe we'll talk about later.

A: *What policies do you think countries should adopt now to prepare for these shocks going forward?*

M: There are a few options. Holding additional stocks is possible but expensive. So there are other potential reforms that could be quite valuable. If we can't get more supply within a given year and we need to therefore cut back demand, we can try to put policies in place to make sure that the demand flex is in nonhuman consumption. There are many that could be cut down without reducing human caloric availability — animal feed, for example. There's also a significant volume in biofuels. But this gets complicated — if you simply abolish the biofuels policy altogether, the land would probably fall out of use.

A: *The policy being biofuel mandates.*

M: Yes. This is where governments mandate that a certain volume of their fuel has to be from biofuel sources, typically instead of diesel or petrol. These policies were introduced for a number of reasons. Yield growth was outstripping human demand for crops, so governments created additional demand. There are complex arguments about whether this is good for the climate and whether it's sensible to maintain this land under crops at all, but it does potentially give us a cushion for climate shocks. For example, if key grains are being made into these biofuels, we could feed them to humans during a crisis.

A: *What about financial technologies — things like reforming futures markets to increase price stability?*

M: I think there's some potential there. Futures markets allow farmers to prepare for shortages in the short run. They can sell their crops ahead and use that money to buy inputs — in essence, it gives farmers access to capitalization to respond to where deficits are and target where their crops are most needed. But financial instruments will likely only be useful in the case of small shocks; they'd be overwhelmed by very large ones.

A: *I have a grain futures question I've been dying to ask someone. The 2022 wheat futures started spiking right around February 24, when Russia invaded Ukraine. This is confusing because warnings of an invasion began in late 2021. You'd think if anybody would be paying attention to that and pricing that into their purchases earlier, it would be the people trading on these markets. I'm very curious why that didn't happen.*

M: The markets were creeping up a bit before, but just a bit. And the only explanation is that traders were assigning a low or a fairly low probability to an invasion — closer to 30 percent than 70 percent. I myself was looking at the Metaculus question of whether Russia would invade, and one of the factors I looked into was how those markets were moving.

A: *It's one of the very few cases where you can take a Metaculus question and compare it directly to a real market. Naively, you might expect that the real market would beat Metaculus, but in this case, Metaculus outperformed the futures markets.*

M: I think the market struggles with these weird tail risks. In January and February the U.S. was releasing huge amounts of information daily saying, "In the next few days Russia will be doing this …" — and then Russia did it. The level of confidence that the invasion would occur should have been closer to 70 percent than 30 percent. Markets aren't perfect.

A: *Speaking of undervaluing tail risk, let's talk about ALLFED. At ALLFED, you mostly think about much more extreme scenarios, things like nuclear winters. I'm interested*

in how the response to supply shocks is different in that sort of scenario. What would the immediate impact be on food systems and how would we make sure there's enough food?

M: ALLFED began when our founder, David Denkenberger, read an article on how mushrooms would thrive in a nuclear winter. David thought to himself almost as a joke, "Why don't we just eat the mushrooms?" So he tried to calculate how many mushrooms we'd need to eat to sustain the population. It turns out it's a lot. And then he thought, "Okay, what can we actually do?"

ALLFED itself now looks at understudied food shocks. We don't just study very high-magnitude shocks, but much of what we do looks at large disasters because they're so neglected. The primary threat class is abrupt sunlight reduction scenarios (ASRS): things that disrupt the amount of sunlight arriving at the Earth's surface. There's three main possibilities, which would be a volcanic eruption, an asteroid impact, or a nuclear winter. In each of these cases, material is ejected high enough into the atmosphere such that it will persist for an extended period of time because it rises above the level where moisture naturally occurs, so it won't get rained out. As they diffuse, these materials would persist for years and result in a loss of agricultural output — around 5 to 10 percent for the solutions we're talking about to be necessary.

The eruption of Mt. Tambora in 1815, for instance, led to the year without summer in 1816, when global temperatures decreased between 0.4 and 0.7 degrees Celsius. There are interesting anecdotes in relation to it. *Frankenstein* was written because of the terrible summer that year — Mary Shelley spent much of her holiday in Geneva indoors because of it. And lots of J. M. W. Turner's paintings have a unique style because of what happened to the sky.

Tambora was classified as a VEI-7 (volcanic explosivity index) eruption, but there is also the possibility of a VEI-8 eruption. This level of eruption hasn't occurred in the history of agriculture.

These scenarios could last for up to a decade. In a nuclear winter, the disruptions would get steadily worse up to about year two and three before gradually recovering up to about year 10 to 12. Over that kind of period, it's not just an issue of food equity. Even if we perfectly distributed and shared our food, which is an impossible task, there wouldn't be enough. So we need to find ways of producing that food.

A: *Let's walk through some of those. Let's say we do everything right — what are the mainstays of our diet? Where are our calories coming from?*

M: The specifics would vary significantly depending upon your location, but almost certainly the vast majority of it would still come from plants grown on land. We would have to shift to simpler products, but it would still be largely crop based. We like to think in terms of resilient foods — foods that are less affected by the loss of sunlight than average. There would be a shift to cold-tolerant varieties of outdoor crops, and to potatoes and wheat rather than soybeans and maize. We'd want to deploy greenhouses as deeply and widely as possible to raise

Joseph Mallord William Turner 1775-1851, *Sunset.*

The vivid long-lasting sunsets and sunrises caused by the cloud of sulphuric acid in the stratosphere after the Mount Tambora eruption influenced a number of landscape painters, including Turner.

temperatures and increase yields. We'd also have to radically drop the amount of meat simply by necessity.

The grain surplus we have now goes to feed cattle for a start, but if there's a shortage for humans, it would be, quite frankly, gross to feed that to cattle rather than a person. So we would be destocking sharply. From preliminary calculations, we could maintain dairy stocks if we used material that's inedible to humans — residues, grasses, things like that. There'd be less after the disaster, but there would be some, and dairy is the most efficient conversion of that material into human-edible food. And then beyond that, you could have things at the margins such as seaweed, cellulosic sugars, and single-cell proteins.

A: What are cellulosic sugars and single-cell proteins?

M: Cellulosic ethanol is produced when you break down cellulose (the stringy fiber of a plant, typically inedible) into its sugars, primarily

glucose and fructose, and then ferment those into ethanol fuel. Although the technology exists, it's just far too expensive to produce fuel in any kind of competitive way compared with conventional biofuels, which are created by fermenting maize. So these programs were scaled back in the U.S., and these advanced biofuels were not adopted as planned. But facilities such as a paper mill contain something like 80 percent of the material you need for this process. In a disaster, all we'd have to do is take a paper mill, complete the pulping process, and then add an enzyme to that pulp. Producing food this way would be expensive today because sugar is cheap, but perfectly affordable for the majority of people after a disaster.

Single-cell proteins are produced when you feed bacteria on a number of feedstocks, including natural gas or hydrogen. These are very high in protein. There are proposals now for pilots to produce fish feed and chicken feed this way in countries like Qatar and Saudi Arabia, which are energy rich but lack natural resources in the form of food. And if these are viable commercially today, that will make it much easier to scale them up in a disaster if they are needed.

We may have a situation where the countries in high latitudes have cold-resistant crops, but their ground is frozen solid. Meanwhile tropical countries that are cultivating hot-temperature crops would be simply too cold for a yield to occur.

A: *Presumably the reason we want these things is because a diet of just potatoes and wheat is not nutritionally complete. How much more expensive is it to achieve nutritionally complete diets compared with simply producing the minimum number of calories we need to survive?*

M: What we have looked at so far is the cost of producing different foods at current prices and input costs. At current costs, the cheapest way of getting enough calories should be about 50 U.S. cents per capita — that's at 2018 prices. Obviously you can't spend all of your budget on food, but if you are making a dollar a day, you could afford the calories. The cheapest diet that also supplies sufficient macronutrients — that is, fat and protein in addition to carbohydrates — would be 80 cents to a dollar. So that suggests if you're making about $1.50, you could afford it. A diet that is truly nutritionally complete, including all necessary micronutrients, might be somewhere closer to $2 or $2.50. A good part of sub-Saharan Africa would struggle to meet that and, in fact, struggles to meet that today. And a disaster would significantly reduce food affordability.

Many low-income countries might struggle to subsidize their entire population, so this would likely require international cooperation and transfers. But

then the second problem is just how large the disruptions are going to be post-war. There may be the kind of panics we've seen from the conflicts in Ukraine, but it would be orders of magnitude higher. And so this could rapidly jam up the supply chains needed to supply or to actually produce these foods.

Will there be international cooperation? Will people trade? Will supply chains break down from instability? There are a lot of questions regarding economics, sociology, and other factors here.

A: *In a post-disaster world, what do you think will happen to the cost of energy and other inputs? What are the biggest bottlenecks?*

M: Right now agriculture, forestry, and fishing together are something like 3.5 to 4 percent of global gross domestic product. We're not devoting massive resources to agriculture today. For many of these, we would expect resources in the system to approximately double for half the output, which would result in food on average being four times more expensive to produce. In some cases we've done quite detailed estimates — do we have enough nails, do we have enough wood, could we substitute different materials? What's the cheapest greenhouse we can produce en masse? What's our plastic-extrusion capacity? Do we have enough rope for the seaweed farms? We'd be all right if food production only requires 10 to 20 percent of a certain resource, or if that resource can be scaled up quickly. Perhaps the only saving grace of an ASRS is that the main climate impact arrives at some point between eight months and a year after the event, so we'd have enough time to start. You can take some actions if you use that time well.

A: *All right. Let's talk then about international cooperation — what would be necessary and what are the major obstacles to it going smoothly?*

M: One of the key problems we would face in a disaster is that our resources may not be very useful where they're currently located. Farmers very carefully tailor their crops to their local conditions — the soil, the amount of light they get, whether they're on the different slopes of a hill. But in an ASRS, that expertise would be diminished by the climate shock. We may have a situation where the countries in high latitudes have cold-resistant crops, but their ground is frozen solid. Meanwhile tropical countries that are cultivating hot-temperature crops would be simply too cold for a yield to occur. This may lead to a collapse in agricultural output, which modeling on nuclear winter suggests is almost guaranteed in the more severe scenarios — assuming we don't respond by moving the cold-tolerant crops, either within or between countries. For example, India grows a variety of crops across its own territory. China as well, with wheat and potatoes in the north and rice in the south.

If we shifted wheat and potatoes to the global tropics, we could significantly increase output. That may well require the movement of the seeds, as well as assistance for farmers who have never grown these crops before, and potentially also the inputs and machinery necessary to support them. And the other benefit we'd have is that if fertilizer output survives the disaster, we would likely have

enough fertilizer for all of our area to be intensively farmed, simply because so much of our farming area would be nonviable. But we'd have to transport the fertilizer. At the moment, the U.S. applies fertilizer more intensely by a factor of 10 than they do in many parts of Africa, and that would have to change.

A: *So the U.S. might want to send seeds to Tanzania or Guatemala or somewhere. How would they ensure that they get crops back at the end of that?*

M: Yes. There are real challenges with this, particularly depending upon the nature of the disaster. The global financial system and even basic communications may be severely damaged. Money and contracts may have little value. What if there's less food output than expected? Would there be trust in this scenario, especially given that a conflict may have damaged many of these key economies significantly? The next issue is that countries may want to retreat into autarky — trying to feed themselves instead of participating in risky trade agreements. To avoid this, we advocate that countries think about these scenarios in advance, particularly where partnerships already exist. The EU has partnerships into Africa and the U.S. has the U.S.-Canada-Mexico trade agreement. These existing structures could at least be the seed of future agreements.

A: *What's the likelihood of an ASRS occurring from a volcano?*

M: A VEI-7, something like Tambora, has about a 15 to 20 percent probability of happening per century, and that would cause crop losses in the range of 5 to 20 percent. VEI-8 events are less frequent, but have occurred once in somewhere between every 17,000 to 50,000 years.

A: *And the last thing I wanted to talk about is your report on U.S. domestic policy levers for preparing for an ASRS — things that a government could do a bit more unilaterally than trying to set up international trade agreements.*

M: The U.S. is in a unique position simply because it has the volume of resources and the degree of agricultural diversity to allow it to respond largely within its own borders. It stretches from a cold north to quite a hot south, it's a major agricultural exporter, and has many other relevant industries. But this only matters if these resources can be deployed effectively, which may require significant preparation.

So let's think about policy. Let's think about any industry that's commercially viable today and could be of use in the disaster. The government could use pilot schemes and licensing to promote viable industries around seaweed, single-cell proteins, et cetera. And beyond that, the U.S. has some in-house expertise that could be developed and expanded upon — for example, the USDA has climate-modeling data and translates it into actionable advice for farmers in the U.S. Farmers will need to know what's going to happen to their land, and we have projections for this. Nuclear-winter modeling exists. Volcanic modeling is also now starting to arrive in high detail.

The difficulty is that these models are typically at a global level — predicting regional differences is far harder. Any advances we can make ahead of time would be very valuable. Beyond that, there's many different recommendations that are hard to break out individually. For example, just how is the U.S. going to communicate with its population?

A: *I got a real World War II vibe, actually, as I was reading — there's all this advice on how to save food and do more domestic vegetable gardening. It feels very 1943.*

M: The experience of World War II is a very interesting one in terms of food, because many countries saw their food output fall sharply. And the tragic thing is, in many cases this was a deliberate and cold choice. There were some real crimes committed during the war, but there are also some real achievements. People switched entire agricultural industries at short notice. Mauritius, for example, was heavily focused on exporting sugar and importing food that they needed, and suddenly shipping was constantly attacked and there was no market for their sugar. So they had to quickly switch to supplying their own domestic markets. Australia — similar issues with meat and milk. The experience of World War II is one of the reasons why I am hopeful something can be done. It's not always the case that people fall apart. Countries made significant sacrifices on behalf of each other.

A: *Are there any major pragmatic and logistical lessons from how countries in World War II handled food shortages that have informed your policy advice?*

M: One of the key lessons is the importance of a palatable diet. In the United Kingdom, it was decided that potatoes and carrots were the most efficient way to feed people. But if you were doing hard work, you couldn't eat enough potatoes in a day and digest them to meet a 4,000-calorie workload. Fat was one of the things most complained about — people were constantly chafing at fat restrictions. So producing a diet that people want to eat is also an important part of this.

Second, the availability of shipping and logistics is very important. Refrigerated shipping was a severe bottleneck in many wartime cases. Potatoes are very difficult to move, whereas bulk grains are easier; in general energy-dense foods are easier to move than energy-light foods. We have an advantage today, which is that the sheer volume of shipping we have available is far beyond anything in World War II. It's not the case that it's all atrophied — we do produce more food per capita than ever before, which is an incredible achievement. The challenge today is making sure that we can get it to people. And the challenge in the future will be making sure we can always produce that food.

26

Interview

Beyond Staple Grains

Prabhu Pingali

The Green Revolution saved a billion lives, but it left a legacy of homogenous diets and distorted agricultural markets. What impact has this had on global health—and how can we move forward?

Asterisk: *You argue that the nutritional gains of the Green Revolution have been uneven. Although overall calorie consumption has increased in some areas, dietary diversity has decreased, and micronutrient deficiencies and stunting still remain common. Can you describe this process, using India as an example?*

Prabhu: When the Green Revolution began, India was facing massive hunger and starvation. The focus of the Green Revolution was a major boost to the calorie supply, and the new varieties of rice and wheat helped to do that. But the government was focused on just these two crops. All the infrastructure that was built, the policy environment, and the incentives for farmers were focused on these crops only. That resulted in the crowding out of more traditional crops that are higher in nutrition, such as millets and pulses.

As the hunger problem was solved, incomes started to rise through small-farm productivity growth. But then we also found that although the demand for dietary diversity was rising, the supply wasn't keeping up for foods like fruits, vegetables, pulses, and livestock products. The policy environment still focused on the big staple crops.

But all this happened in the regions where the Green Revolution was successful and incomes were rising. With rising income, people could trade with other parts of the country where other foods were grown, bringing some of that diversity into local markets. But if you were in the regions that are much poorer — the Green Revolution did not take root as strongly in the eastern part of India, for example — you did not see either an increase in the demand for diversity or an increased supply of diversity to markets. Those are the places that ended up with very high levels of malnutrition and child stunting, which continue to be persistent.

A: *Can you say more about why there was better support for wheat and rice as opposed to millet or lentils and what forms that support took?*

P: Beginning in the '60s, there was a search for crops that could see a rapid increase in overall yields. This was an international effort involving large experiments that focused on very particular crops. The U.S. and Europe had a history of research on wheat, and yields were already rising as a result of that crop-improvement research. The challenge was to make crop-improvement research applicable to the subtropical conditions, such as the Indo Gangetic plains in India. That was the work that made Norman Borlaug very famous, resulting in the Nobel Prize in 1970. Wheat materials developed in Mexico were then brought to India, China, and many other countries.

It was a similar story with rice. Japan, Korea, and other Asian countries had a history of rice-improvement research, but these were all japonica-type varieties. The challenge was to bring that crop improvement into rice varieties grown in the tropics, such as the indica varieties. That was done at the International Rice Research Institute in the Philippines and resulted in high-yielding rice varieties, which then very rapidly spread across Asia.

Why wasn't the same thing done for millet, sorghum, or other traditional crops? None of these crops were grown in the West. There was no history of

research on them, and the history of agriculture research played a major role in which crops were chosen.

Today we are now saying we need higher-yielding varieties of millets, pulses, et cetera. There's quite a bit of effort happening on this front, including at ICRISAT (the International Crops Research Institute for the Semi-Arid Tropics) in India. But the improvements haven't been as dramatic as we've seen for rice and wheat. Rice and wheat productivity went from one (metric) tonne per hectare to four, five, even six times that. In the case of millet, we're still talking about going from a tonne to maybe two.

A: *Why did Green Revolution crops fail to be as successful in Africa compared with Latin America or Asia?*

P: It's important to separate out the crops themselves. Wheat can be grown fairly well in areas like Ethiopia, Zimbabwe, or South Africa, and these countries have seen widespread adoption of modern wheat varieties. But much of what's being produced goes to urban markets and urban populations. High-yielding varieties of rice are also now slowly coming to West Africa, in swampy areas especially.

But maize has been more disappointing and there are many reasons for that. When Asia was undergoing the Green Revolution in the '60s and '70s, land was scarce and population densities were high. So the emphasis there was on how to increase yields on existing lands. Africa did not have that same land scarcity issue. At that time, it was still very sparsely populated, with large land areas available for expansion. As a result, much of the donor focus was on increasing labor productivity rather than crop productivity. So instead of increasing productivity per unit of land, funding emphasis was on mechanization and ways to expand land area under cultivation. At that time, it seemed like a better strategy.

The problem is that if you look at Africa today, population densities in many areas are very similar to those in Asia in the '70s and '80s. Moreover, it's growing much more rapidly than Asia is growing now. So one would anticipate that right now you should see more intensification and adoption of higher-yielding varieties.

That's happening to some extent, but not as rapidly as one would expect. One reason for the slow progress is that the infrastructure investments have been very poor in Africa relative to other regions. The second is that after the formation of the World Trade Organization in 1995, international trade in food became very prevalent. In many of the big population centers in Africa, it's often cheaper to import food from other countries than it is to grow domestically. The terms of trade have made it very hard to create a competitive supply system from within the continent.

A: *Could you expand on how intensive agriculture became a stepping stone for further development?*

P: Much of Asian agriculture has traditionally been smallholder, where farmers own one or two hectares and traditionally grow one crop a year. One crop of rice or millets traditionally yielded about a tonne per hectare. After a farmer keeps

what is needed for the family, there's very little to sell. The margin is small and in many years — because of weather or climatic issues — farmers would end up with less than one tonne and have a food deficit as a result.

So the opportunities for agriculture as a growth sector, to lead to increased incomes, were limited. As new crop varieties and new technologies came in, farmers could grow four or five times what they'd been able to in the past. After you kept what was necessary for your own needs, you still had a significant amount to sell.

Another factor was that these crop varieties had a much shorter growing period compared with the older traditional varieties. So you could grow two or three crops on the same piece of land. That then created an enormous boost in productivity, which then boosted market surplus. As that happened, it generated income that could be invested in better housing, purchase of consumer goods, education, etc. In addition, productivity increased land values of small farms, so farmers sold their land and invested it outside of agriculture. And that triggered an overall economic growth process.

A: *And places like Africa that are importing grain don't have that same beneficial flywheel effect.*

P: Exactly. In the hinterlands of sub-Saharan Africa, farmers continue to eke out a ton per hectare. So the opportunity for growth there is very limited.

A: *You mentioned earlier that demand for dietary diversity is increasing, but supply of diverse foods has not kept up with demand. Why?*

P: As incomes rise, the demand for diversity in your food consumption increases also. Very poor households will consume large amounts of basic, starchy staples and very little of vegetables, fruit, livestock products, et cetera. As incomes rise, the share of the staples in your overall diet begins to decline. In agricultural economics, this is referred to as Bennet's law.

But the supply hasn't matched that demand. And one of the reasons I think that's the case is that policy tends to be very sticky. Policy hasn't been nimble enough to redirect itself as the demand conditions have changed. Even today, for instance, much of the food and agriculture policy in India is focused on the big staples. There is some lip service to promoting diversity, but the essentials remain the same: price supports, procurement of grain, subsidies for inputs, subsidized credit.

We don't have a level playing field for other crops. A farmer can't say, for example, "I'm getting a better price for onions in the market, so maybe I should switch from rice to onions." The onion production doesn't have the support system that rice production does, so onion production tends to be much riskier. In addition, we don't have infrastructure built around non-staples. Combine that with a lack of incentives, and the switch to non-staple crops has been very limited.

One last point here is that the people who have been most successful in growing staple crops have also benefited the most from the supports. They're not

going to give those supports up easily. So there's a big political economy issue here. How do you make the transition for them as well as making the transition for the food system itself?

A: *You've called this "crop-neutral agricultural policy." Have you seen any movement away from strong support for staple grains toward nutrition-sensitive agriculture on a policy level, or is policy still too sticky?*

P: There's a lot more *talk* about nutrition-sensitive agriculture and a lot more pronouncements about why this is important. However, most governments see this as an add-on, not a substitution. Rather than removing the existing supports or reducing the existing supports for staples, governments have just added supports for other crops. That creates some marginal improvement for some of the other crops, but your fundamentals don't change. The crop-neutrality argument says: Treat all these crops on a level playing field and let market signals determine the supply responses.

A: *One barrier here is that access to markets is often very poor in a lot of the developing world. What kinds of policy interventions and private investments do you think are important to make sure markets are well-developed for diverse foods?*

P: This is where the private sector needs to be playing a much bigger role than it does today. When we talk about nutrition-sensitive crops, we're talking about perishable crops and perishable products. You need cold-storage systems, quality controls, safety controls, et cetera. These require massive investments from the private sector. And encouraging the private sector to take on these roles is really important.

Many governments have been shy about doing that because much of the historical procurement policies and support policies have been led by governments or government parastatals rather than by private sector companies. But unless you make that transition, you're not going to see that supply response coming in.

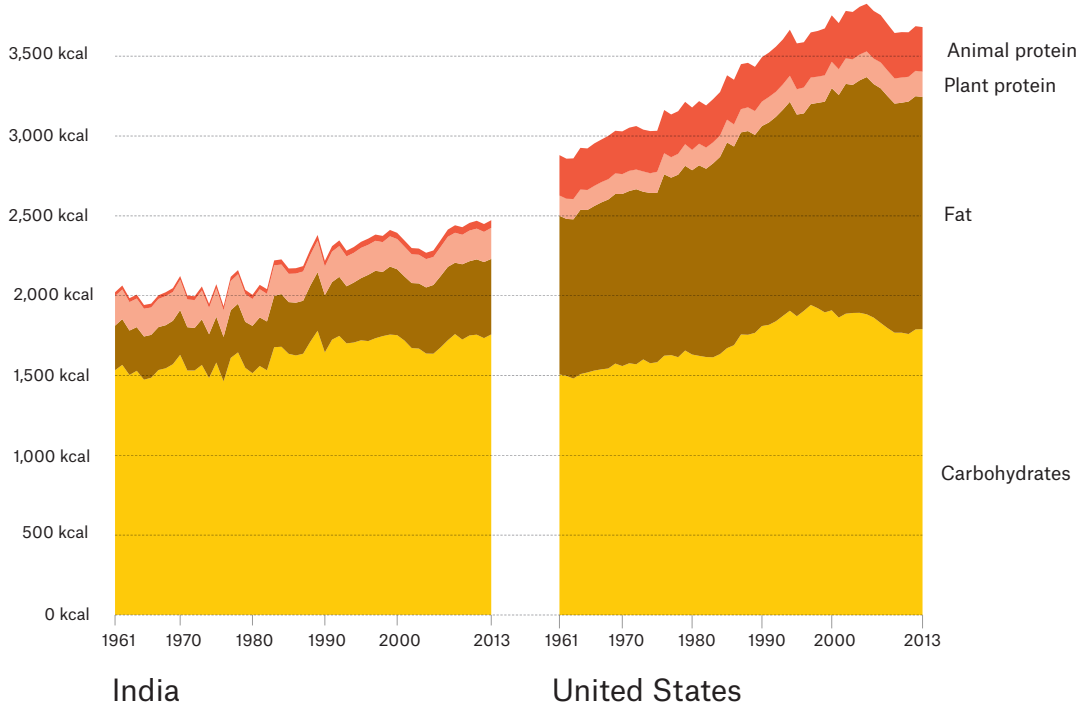
A: *What do you see as the role for bio-fortified crops, which tend to receive a lot of interest? Something like orange-fleshed sweet potatoes can marginally increase vitamin A status for women and children. But other bio-fortified crops — for example golden rice — have received a lot of pushback. What are the benefits and what are the drawbacks of bio-fortifcation, compared with targeting dietary diversification for nutrition outcomes?*

P: When we think about bio crops, we have to be very careful to say we're not talking about GMOs, because a large proportion of bio-fortified crops are done through traditional breeding, not through genetic modification. Golden rice, of course, is a GM crop, and that's where it received pushback, particularly from civil-society groups.

But for the rest — orange-fleshed sweet potato for vitamin A, zinc-enhanced wheat or rice, et cetera — there's been a lot of research and public investment to

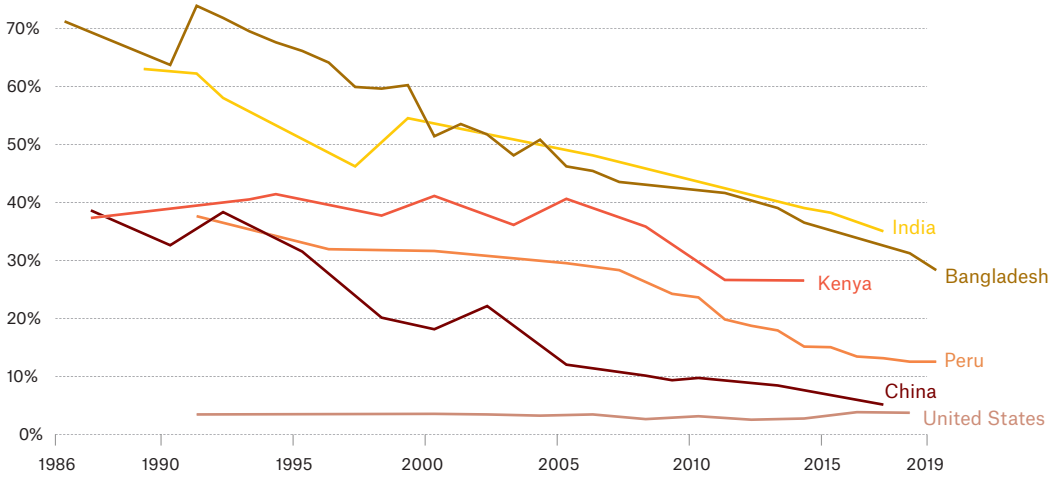
Daily caloric supply derived from carbohydrates, protein and fat, 1961 to 2013

The average per capita supply of calories derived from carbohydrates, protein and fat, all measured in kilocalories per person per day.



Malnutrition: Share of children who are stunted

The share of children younger than five years old that are defined as stunted. Stunting is when a child is significantly shorter than the average for their age, as a consequence of poor nutrition and/or repeated infection.



Top Source: Food and Agriculture Organization of the United Nations / Our World in Data
Bottom Source: UNICEF, World Health Organization and World Bank / Our World in Data

try to promote these crops, particularly in Africa. Orange-fleshed sweet potato has made some inroads. But outside of Africa it's been very limited. There's been little adoption of most bio-fortified crops. They're available but farmers don't choose them.

I think one big reason for the lack of adoption is that there's no way to physically differentiate a bio-fortified crop from a non-bio crop. They look the same. The color is the same. And once they're out in the field, they all get mixed up and it's hard to tell them apart. As a result, there's very little price difference.

The incentives, therefore, in investing in bio-fortified crops are limited for farmers. And the fact that it's more nutritious is not a particularly persuasive argument for them. Getting the same nutrients from other sources, such as fortified products, is often easier.

A: *We've been talking about crops specifically, but animal-sourced foods are one of the best sources of a lot of key nutrients. How do you think about the trade-offs between animal welfare and nutrition outcomes?*

P: From a food-policy point of view, there's been a lot more attention to livestock issues than, say, millets and vegetables. Much more attention is being given to improving livestock productivity, and there have been significant improvements.

Milk and dairy production has gone up dramatically over the last few decades in Asia, although less so in Africa. Access to nutrients from those products is improving significantly.

Meat has been a challenge for many reasons. One, there are cultural issues around meat consumption, and therefore supply of meat has been limited. But the other factor has been that overall infrastructure around meat production, including meat marketing, has been limited. Here again, we come back to perishable-food issues — cold storage, et cetera— so we haven't seen supply rise to meet demand.

A: *Obtaining accurate information on nutrition and agriculture seems really hard. Even in high-income contexts, getting good food-consumption data is a pretty tricky problem. I'm curious what the biggest challenges are in your research and how they impact the kinds of conclusions you can draw about nutrition.*

P: Data is a big challenge for all of us. In my public lectures, I typically spend at least 10 minutes complaining about lack of data, especially when there are policy makers in the audience. I keep telling them that they have to do something about this.

Many countries have these periodic nationally representative surveys that look at income and consumption and try to track what's happening. Many of them are done on a recall basis and the time periods between surveys can be as much as 10 years or more.

Recently, other groups have established their own surveys. One of them is the Living Standards Measurement Study of the World Bank, part of which is the Integrated Agricultural Assessment. That survey attempts to capture some of the

consumption data, which is helpful. But again, it's periodic — every five years or so, which makes it difficult to track what's happening over time. In India there's what's known as CMIE data, which tracks monthly expenditures across food groups for 60,000 households around the country. So these expenditure surveys are giving us some more real-time tracking ability to look at what's happening with food consumption.

A lot of people use dietary diversity scores, which ask how many times you've had this food or that food. I find those are shaky and not very useful, but that's the information that there is on the nutrition-status side.

A: *You've written about the double burden of malnutrition — high undernutrition, high numbers of the overweight and obese. In India, rates of stunting are still more than 30 percent. But overweight and obesity numbers are inching up to 20 or 30 percent as well.*

In general, we don't have much evidence of countries that have been able to eliminate undernutrition at the same time that they minimize overnutrition. How are those problems connected? And if there are countries that have evidence of maintaining a stable ground, what are the characteristics of those?

P: It all comes back to dietary diversity. What happens is that countries that have been successful in increasing staple-grain productivity end up with large volumes of staple grains. These grains are relatively cheap, which leads to surplus being used by the processed-food industry, which leads in turn to a drop in the relative price of processed foods. The other issue is oils, sugars, and sugary beverages. It's incredible that for the same countries where we talk about access to good food there's no poor access to bad food. Bad-food access is easy, even in very remote areas.

Countries that have been successful in managing the nutrition transition are countries that very quickly shifted from staples to a more diversified food basket.

A: *I'm curious about the kinds of interventions you think are effective at addressing some of these issues.*

P: Behavioral change plays a big role. Just getting consumers to demand better quality food and more diversity of food plays a big role. Even middle-class populations haven't been as quick to change their diets and consumption practices as much as economic theory suggests they should be. Behavioral-change campaigns have been a big part of the nutrition work that's happening. But these are not easy campaigns. They can't be done at scale and they tend to be expensive.

Now, there are few models. One is the Got Milk? campaign in the U.S. I think that had a big impact on U.S. consumer behavior relative to some of the other campaigns around meat consumption and reducing meat consumption.

So these broad messages at scale through media and through advertising can have an impact, but I don't think the nutrition community has really used these tools to create behavioral change in developing countries. That's something I think is possible.

34

Interview

Animal Welfare in the Anthropocene

Jordan Hampton

Wild animals outnumber farmed animals by orders of magnitude. Are we obligated to help them? And even if we wanted to, do we know how?

ILLUSTRATION BY
Melody Newcomb

Asterisk: *One of the major themes in your work is the consequentialist approach to conservation. Can you talk about this approach and what sets it apart from other ways people think about conservation, and in particular how we interact with wild animals?*

Jordan: My particular niche is trying to find a place for animal welfare. This is a relatively modern entrant into the values that are prioritized when it comes to wildlife management, but one that's become increasingly important, particularly in countries like Australia, New Zealand, and the United Kingdom. There's been a real focus on the welfare of individual animals in ecosystems, not just populations, species, or biodiversity. That's where some of my work has entered the fray.

Any time we talk about intervening in the lives of wild animals beyond those species that we target — if, for example, we're particularly concerned about wild horses or kangaroos and decide that we should do something for them — there's the need to not only consider the direct consequences of those actions, but the indirect impacts that might affect nontarget species in that ecosystem. Consequences might be those that affect other species via trapping or shooting or roundup.

Trapping or shooting have obvious consequences, but there are subtle effects that occur when we change ecosystems. Some well-meaning efforts to improve the lives of wild animals — for example fencing — have yielded unintentional and negative consequences. The framing of consequentialism reminds anyone involved in these decisions that there are implications beyond those that are intentional and designed to improve the lives of animals that people care about.

A: *It's complicated to track the many impacts of any of these interventions. I'd love to talk about some of some of the case studies that you've done in a little more detail, like some of your work on using predators to control herbivores. It's really fascinating to me in terms of the trade-offs that come up there.*

J: I think it's going to remain one of our prime dilemmas as we're collectively more interested in trying to restore our ecosystems, particularly the apex predators that sit within those ecosystems. These are animals that have important benefits for ecosystems, but on occasion they will eat us. They'll eat our kids. They'll eat our pets. So there are real-world negatives for us in terms of convenience and safety in having these predators provide these services to the ecosystem.

That's the case in Australia. We have large populations of introduced herbivores, mostly ungulates or hoofed mammals. A lot of land managers, whether they're conservationists or farmers, would like to have some or all of these animals removed. One idea is that rather than shooting, poisoning, or trapping a large number of animals, we could use more "natural" control methods. This is where predators come in. When a native or established predator has been eradicated, like in the case of wolves in Yellowstone National Park, people start thinking, "we could just reintroduce this animal, it naturally lived here." That's

been the case with wolves in many places. It's been discussed with dingoes in Australia. But from an animal welfare perspective, well, how are these top predators achieving these desirable outcomes of less herbivores in the landscape or less grazing pressure? And the obvious reality is that they're chasing, attacking, and eating animals.

A: *Do you think that the reintroduction of wolves to Yellowstone ultimately had an overall positive or negative welfare impact on animals in that ecosystem? Or, if that's not possible to answer, how would we go about trying to answer that?*

J: Animal welfare is a pretty young science, and there are some unavoidably subjective components to it. We don't have a good scientific basis to understand what's going on with consciousness in humans, so it's quite difficult with animals. But let's talk about at least three ways we can conceive of animal welfare.

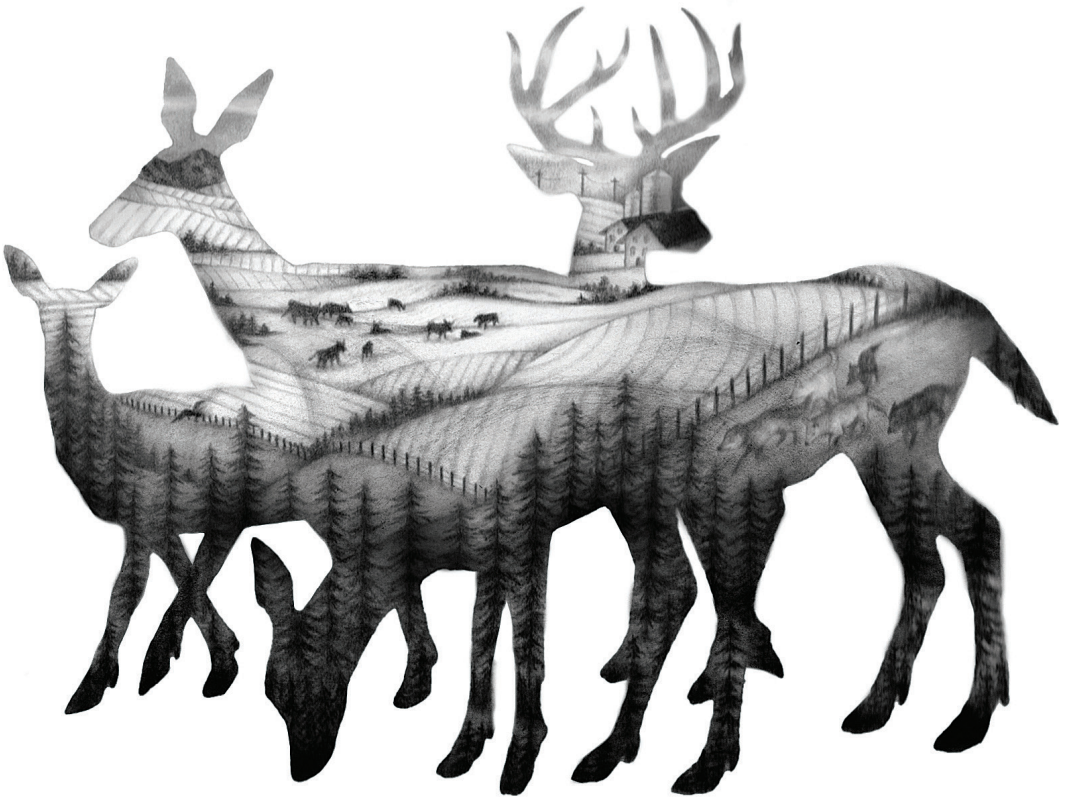
One is a net balance of positive to negative feelings. A second way of thinking about it is whether animals are performing natural behaviors. The third way is thinking about biological functioning, or just having good health. There could be an argument made that it's good for the welfare of wild herbivores to interact again with a predator they've evolved with on an individual animal level. I accept that the prospect of being run down and bitten and eaten alive doesn't sound appealing, but nonetheless we are talking about a natural relationship that's evolved over a long period of time. But if we think about the feelings approach to animal welfare, it's very hard to avoid the conclusion that it's going to be bad.

A: *The cortisol studies and the stress response studies just seem pretty compelling evidence that the experience for the animals is negative. It's hard to see how this consequentialist way of looking at it could square with a natural behaviors approach.*

J: The interesting thing about studies that utilize cortisol or other stress hormones is that there's a growing recognition that they really just measure levels of arousal, not necessarily of negative experience. Cortisol will certainly go up during long-term painful experiences, but they'll also go up during generally pleasurable experiences like sex and eating. So we have a tool that's useful for looking at how aroused animals are, but not necessarily whether that arousal is associated with something that's positive or negative.

And yes, different ways of thinking about ethics and welfare often don't overlap a lot. A natural-behavior benefit for an animal doesn't always mean that there's going to be an associated improvement in their subjective experiences.

A: *This also ties into your work on wildlife contraception. I think there is a sense among people who don't follow this closely that contraception is more humane than lethal control methods. But you've written about how hormonal contraception and endocrine disruptors really get in the way of animals expressing natural behaviors. It even changes them physiologically, and we don't understand the welfare effects of this.*



J: Most thinking around animal welfare came from laboratory livestock or pet animal scenarios — animals for which humans had a widely understood duty of care, animals that lived in very unnatural conditions. For most of us that own pets, fertility control is widely seen to be a good thing, certainly preferable to having mass numbers of animals killed. But with wildlife, there are other considerations. First, there's the logistics. It's quite difficult to make it effective at a population scale unless we have small islands and fenced populations. I think most of the fertility control came about from a distaste for killing. There has been a growing global movement towards mutualism and thinking that, rather than having dominion over wild animals and killing them whenever they're inconvenient to us, perhaps we can learn to live with them.

But treating animals with a surgical procedure, or an implant, or a vaccine designed to reduce their reproduction is going to have impacts on their physiology and on population demographics. There's some evolutionary concern about the selection pressures imposed if we do start using fertility control widely. What traits will be selected for amongst those animals that remain fertile? Even at an individual animal level, if we're using hormonal products that do markedly change the physiology of an animal, that might mean that they're less capable of competing with rivals. We use chemicals that reduce the body size or muscle mass of male animals or that prevent fertilization in females, leading

to prolonged estrus periods associated with the stress and the competition of mating seasons. And then there's longer term indirect impacts that we're really not quite sure about right now.

A: *Some of the studies that try to use more subjective models seem, intuitively, to me as a human, that they overweight the suffering associated with very quick deaths. Take leopards, which tend to kill in less than sixty seconds. In a model like the Five Domains Model, this is rated as very high suffering, because those few seconds before the animal dies are presumably quite painful. But it's over so quickly. It seems less bad than some ways I as a human with good medical care might expect to die, and it's certainly less bad than most ways that animals could die in the wild. I'm curious about some of the intuitions that go into trying to quantify these effects and weigh them against each other.*

J: I think intuitions is the key word there. A real stumbling block for all of this science is that it's hard to separate our own tastes or distaste for what we'd like to happen to us from what we think is good or bad for an animal. Prey animals have an evolved aversion to the idea of being attacked and eaten. It's hard for us to sit back and say, "well, you know, I don't think that would be so bad," without putting ourselves in that position of being hunted down by a pack of ravenous animals. On the other hand, there are killing methods that have been shown from our objective measures to be relatively quick, efficient, and painless. Here I'm thinking about methods like the shooting of kangaroos at night time in Australia, where the animals are required to be shot in the head. Ninety-eight or ninety-nine percent of animals probably have no experience of it beyond seeing a bright light. Most people intuitively still don't like the idea of that, and if they're forced to think about the welfare impact, they generally score it as quite high suffering. So this is a limitation of relying on expert opinion and thinking about subjective experiences.

A: *Speaking of intuitions, let's talk about hunting. I think a lot of people, including myself, have the intuition that it's this across-the-board more humane alternative to eating farmed meat. But you have some interesting work on how the welfare impacts of hunting vary a lot depending on the hunting technique.*

J: When we compare food production methods on animal welfare grounds or biodiversity or anything else, it's all about land clearing. Any food production method that doesn't require the clearing of land is going to yield better outcomes for individual animals. That's where hunting and other forms of wildlife harvesting have a genuine advantage over our traditional widespread clearing, fencing, monoculture cropping, or livestock grazing regimes. But obviously it involves the killing of animals, so there are always going to be animal welfare impacts. We have seen an incredible evolution in hunting methods used over the last few centuries.

Still, there are a number of techniques in modern recreational hunting that involve serious animal welfare concerns. Take the use of dogs to hunt large

mammals. First, we have concerns there for the animal being hunted — say a deer being pursued through a forested area for several miles — and for the dogs themselves. There's also been a long-term concern about wounding. It's relatively easy to hit a duck but not kill it outright. How long do they survive for and how impeded are they?

And then there's a really broad group of indirect impacts that come about from nearly all hunting methods. Lead has been used widely in ammunition for as long as we've had guns, and it's a really nasty toxicant. There's been a move internationally to replace some of the lead used in ammunition so that we reduce the nontarget impacts on wildlife species.

When we compare food production methods on animal welfare grounds or biodiversity or anything else, it's all about land clearing. Any food production method that doesn't require the clearing of land is going to yield better outcomes for individual animals.

A: *In a lot of animal welfare work, there is, I can sense, a real need to be sensitive to the concerns of hunters, ranchers, farmers, wildlife managers, of all of these people who have stakes in how we treat wild animals, but for whom animal welfare is not their first priority.*

J: My PhD supervisor used to say to me, "if you want to improve animal welfare, you have to start by being inside the tent." You need to have enough rapport to be part of the conversations and have your suggestions taken seriously if you want to see any improvements made. A lot of really strong emotions and opinions come out in animal welfare. There are some ethical views that are really aligned with abolition of all animal use practices, whether that's farming or hunting or even pet ownership. But the disadvantage of some of the more extreme views is that those groups have been marginalized, and their voices haven't been considered when management or regulatory decisions are made.

A: *Abolition is an interesting concept. It seems very nonobvious to me that wild animals have higher welfare lives than domesticated animals.*

J: And I would say that many people would disagree with you directly.

A: *What do you think?*

J: My feeling is that globally we're moving towards a situation where most people that are influential within animal welfare feel that livestock have better lives.

And I think increasingly we're seeing wildlife managers, veterinarians, and other biologists trying to treat wild animals more like we would treat domestic pets or livestock. There's more discussion of supplementary feeding during cold winters or after bushfires, more discussion of parasitism, of whether we should intervene to save animals if they're drowning in a river or a flood. And even if that's not a conscious decision, I think it's being manifested in how we manage wildlife. We've moved from the older days of "nature red in tooth and claw" to the attitude that we're in the Anthropocene now and everything that happens on the globe is within our sphere of influence.

A: *So in your personal opinion, what is the lowest-suffering diet a person could eat?*

J: I did a project with a few colleagues on a very conceptual overview of this question. We settled on foraging for wild plants and wild fungi. If you could make it nutritionally balanced, that would negatively impact the fewest animals. Beyond that, we started moving down the rankings, and we found that if you can harvest abundant wildlife species in a way that results in a very quick death, that's going to really yield very few animal welfare impacts. But anything that involves the clearing of land fencing, irrigation, or fertilizers is going to impact millions and millions of animals, often in indirect or invisible ways.

In any context, the indirect harms are going to dwarf anything that we do directly, and they're not always intuitive. Whatever our understanding is of the harms being created by cropping or fencing or clearing, it's likely that we're missing a lot.

A: *I've been having a bit of a crisis about wheat since I read in a paper that around five-hundred mice are poisoned for every ton of wheat harvested in Australia. And rodent poison is usually a horrifically painful way to die.*

J: What happens to those species that live in the paddock really is significant, particularly with mice that will congregate en masse when there's grain spilled on the ground or stored in a silo or grain elevator, and it's quantifiable. A few studies have had eye-watering results about the number of small mammals that are killed.

But if you want to minimize the animal welfare impacts from how you get your food, land clearing alone is much better than first clearing the land and then putting cattle on it. There are impacts on the cattle themselves, and then there might be predator control to prevent the cows from being eaten, and fertilizer and irrigation and fencing. These consequences just add up and up and

up. In the paper we did, we ended up with intensive dairy farming as one of the worst systems.

A: *I thought that dairy cattle themselves had some of the better lives among intensively farmed animals.*

J: There is diversity in dairy production systems, but it's certainly an industry that involves daily interference in the lives of animals and quite a lot of external inputs required for the system to work.

A: *So, order of magnitude, do you think that the direct harm done to farmed animals is more or less than the indirect harm done to other species that are affected by land clearing?*

J: In any context, the indirect harms are going to dwarf anything that we do directly, and they're not always intuitive. Whatever our understanding is of the harms being created by cropping or fencing or clearing, it's likely that we're missing a lot. In Australia, something that looks relatively benign, like the use of fertilizer, causes outbreaks of blue-green algae because the extra nitrogen is ending up in our creeks and our rivers, which is in turn causing the mass death of fish and profound impacts to marine and estuarine ecosystems. If we're going to think about animals in a relatively egalitarian sense, in that they all have lives or welfare status that's roughly equal, the indirect harms are just astonishingly elevated beyond what we do directly.

A: *What do you think the most underaddressed issues in wild animal welfare research are right now?*

J: I've been researching pollutants for the last few years, and I'm amazed at how widespread they've become, from Arctic ecosystems through to the tropics, and the diversity of pollutants, from pharmaceuticals to heavy metals. I think over time we're going to find that these chemicals are having harmful impacts on the lives of animals. But a lot of the time they're difficult to study.

I think it's easy to get emotional about seeing a rat caught in a trap or a kangaroo shot, but I don't think those direct impacts are the bigger story. The indirect stuff we're doing through climate, through the spread of species and infectious agents and chemicals, are probably having really profound and accelerating impacts. My feeling is we're going to start seeing more and more of that the deeper we dig.

42

What I Won't Eat

Georgia Ray

A reflection on ethics, animal cognition, and chocolate cake.

ILLUSTRATION BY
Karol Banach

To answer the question of "What should I eat for dinner?" you must first answer, "What does it mean to suffer?" (This is a joke. Answer it *after* you eat dinner. You'll need brain fuel.)

Like most people, I require calories to live. I'm lucky to be part of a powerful culture that has a vast infrastructure set up to sate this. However, this infrastructure also includes billions and billions of animals purposefully kept in situations where, if you were watching an edgy action movie and saw the villains doing these things to a dog, you'd think, "Yikes, we get that they're evil, they didn't need to do that." I've put a lot of thought into how to proceed from here.

Some principles that outline the dilemma:

1. Suffering is bad.
(I care about other things too, but this is the biggest. I'll debate the ethics of preserving heritage livestock breeds or bringing beings into existence just to kill them down the line, *once we stop amputating body parts without anesthesia*. There's some really interesting nuance in what it means to own a sentient being, even a family pet, for instance, but — hey, is that a baby lamb? Where are you going with that knife? *Get back here!*)

2. Any plausible diet in my current society will entail *some* suffering and some death.
(We can and should reduce this — see Principle 1 — but there's no perfect score. *If nothing else,* animals live in my crops and die during harvesting and processing. Brian Tomasik points out that a couple of copepods — microscopic water arthropods — are killed in each liter of purified tap water. It's the invertebrates' planet. We're just also here.)

3. I'm a person with limited means, energy, and knowledge, and I'm strongly in favor of my own survival and flourishing.
(Theoretically, with years of dedication and study, I could be satisfied that no part of my diet is killing or hurting any animal. I'm not going to do that. It's unrealistic to expect that of anyone. I care about other things more. I hope most of the good in my life will come from work other than my diet.)

I don't necessarily mean this as a manifesto. You might look at the question of suffering differently from me. You might have different dietary needs. I make some compromises that you might not have to. But for now, this is where I stand and why.

Animals

Here are some questions researchers ask to study pain in animals: Does its nervous system, especially parts that fire when the animal is injured or damaged, look like the human nervous system? (Do human analgesics change its behavior?) If the animal is injured, does it act differently overall? If a small part of the animal is injured, will it treat that part differently — groom it or avoid use of it or be especially sensitive to touch there? Can the animal learn things? Can it learn associations in ways that probably aren't evolved?

There are different kinds of learning. A creature might react to chemical traces of predators or damage signals from its fellow conspecifics by becoming more cautious and willing to take defensive actions. We could call this a kind of learning from its environment, but a very straightforward one — it could be a preprogrammed if-then statement. Plants do forms of this. But if the same creature can learn in the face of other arbitrary stimuli that don't have the same meaning in its natural environment — the color red, a certain chemical added to food, a sound — that suggests something more generalized. Broad input processed in the pursuit of a goal — perhaps something like a desire.

Go even a step further. Can the animal learn to take actions that were not evolutionarily conscribed? Can it make tradeoffs between rewards and harms? At that point, a generalized evolutionary response to harm is doing something similar to an animal to what it does to me — it makes us want to avoid it. Call it an incentive to avoid damage, a sense that "something is wrong." Neurons are costly compared to other cell types; without the ability to learn, there's no reason to have that system. At that point, to me, postulating an experience of "suffering" starts to answer questions rather than cause them. In the murky terrain of consciousness and minds very different from my own, this is where I draw the line.

Unfortunately, we humans have not tried to answer these questions for a lot of animal species. Mice? Yes. Fish? Of the kinds we've studied, yes. But numerically, vertebrates are a minority of earth life. *Especially* understudied are the smaller animals that comprise most of animal life: copepods, springtails, nematodes, arrow worms. Fortunately, people don't go out of their way to grow and consume springtails or arrow worms, so we can sidestep them for this analysis.

What people have studied — not a lot, but some — are familiar cultivated invertebrates like shrimp or bees. This evidence implies some fairly nuanced learning and differentiation based on negative stimulus — prawns tend their injuries, less so when given novocaine. Honeybees learn complicated spatial maps and make judgment calls about resources, and when they've escaped from simulated predator attacks, they get warier and pessimistic. Which is to say, the answers to the questions above, about sentience, are mostly yes. As far as I know, all the fish species anyone has bothered to look at are similar in this regard. That's enough cognition to make me think there's probably something going on in there, and to take all vertebrates and familiar invertebrates literally off the table. Surely it's best to be careful.

Now that we've established any capacity for suffering, the question is: *How much?*

We have "ability to learn" as a starting point for the scale. But above that things start to get weird. I feel pretty strongly that an ant is less morally important than a cow. Do I think it is *half* as important? A tenth? A millionth? Here I falter — a million is *so much*. A million ants still *weigh less* than a cow, but have *many more*

brain cells. Does that mean anything?

What am I even measuring at that point? How sure am I that "capacity for suffering" scales alongside cognition? I'm a self-important animal with a penchant for existentialism, and my literal worst nightmares are about being chased by something that wants to kill me. That has to be the number one shrimp nightmare scenario too. What if "intensity of suffering" is directly correlated with that incentive to escape death? What if a mouse gets exactly as scared running from a cat as I would running from a murderer? A human suffering intensely at least has a conception of time and severity and even, at worst, death — the comfort that "it will be over some day." I'm not sure any other animal has that last one. There's no reason it would evolve.

All this to say: I'm confused. This argument about animals having equal moral importance doesn't *sound* right, but I don't have a good counterargument either. I'm definitely biased by the ominous other side of that equation: that if killing an ant is as bad as killing a cow, everything starts to get a lot more horrible. Brian Tomasik has done some calculations related to this, e.g., investigating the total impact on animal lives from raising and feeding a beef cow, as well as for cropland. I invite the reader to investigate further.

In the meantime, here are some edible animals I'm *pretty sure* aren't sentient: oysters, saltwater mussels, jellyfish.

Adult oysters or mussels are sessile, meaning that their mobile larvae settle into one place and live stuck there for the rest of their lives. The choices afforded to these animals are few. Their nerves are centralized but not to the extent of full brains. They probably have fewer total neurons than, say, an ant. And a hearty mussel or oyster is *much, much* larger than an ant. That's a lot of meat per brain. That's pretty good eating!

All this to say: I'm confused. This argument about animals having equal moral importance doesn't *sound* right, but I don't have a good counterargument either. I'm definitely biased by the ominous other side of that equation: that if killing an ant is as bad as killing a cow, everything starts to get a lot more horrible.

Other clams or scallops aren't immobile; they swim or dig — and then now that they have the option to escape certain death, we circle back to: Where does suffering begin? So I steer clear. But I'd still rather eat a scallop than a cricket.

Jellyfish are even simpler animals, the earliest drafts of mobile animals, nervous systems minimal and not remotely centralized. They're big in East Asian cuisines.

Given all of the above, it will not surprise you to learn that I am, aside from the stray oyster or jellyfish, a vegetarian.

What About Animals That *Aren't* from Factory Farms?

I could talk about happy food animals. I could tell you about the summer I bought eggs from my boss, who had twenty

chickens in his backyard, or the day I spent on a friend's small commercial fishing boat in Alaska, where they hauled hooked salmon up to the surface within minutes and killed them quickly — not awesome, but you could do a whole lot worse. I don't want to pick a fight here. These people care about animal well-being; largely, we are on the same side.

But they're in the minority.

Polls find that most people don't support factory farms. Everyone likes the idea of treating animals well. Still, 99% of farmed animals live in factory farms. I can talk about grass-fed beef or cage-free chickens but that's *very few of the farmed animals*. Buy them carefully or don't buy them; look, that's great. But let's not get distracted from the 99%.

Humane husbandry is sometimes offered as a selling point or a compromise. Now, call it the by-product of an alternative liberal arts college education or call it common sense, but I don't trust corporations. More accurately, I trust them to maximize their own profits, and that's it. Factory farms are like that because they are *extraordinarily* cost-efficient. If they can lie to me or misrepresent themselves to me to upcharge me on eggs, I expect they will.

What to do? I could find a new guy with twenty chickens. I could find a farm where I can *go look at the chickens* and *verify that they aren't in tiny cages and can do chicken business*. But mostly, because I'm on a budget, and because none of my neighbors have twenty chickens, I buy tofu.

And how about wild animals? Compassionate hunting might be fine, but numerically, the wild animals eaten in greatest quantities are fish and shrimp. There are no legal mandates anywhere on earth that food fish or shrimp be killed in a minimally painful way. Often, they asphyxiate after being hauled into boats. It can take hours. Tofu is cheap. So are beans.

Human people

"Ethical cannibalism" is the idea that — wait, I'm kidding, come back. I've talked about everything from battery cages to zooplankton. What about the actual humans who produce the food? Well, I care about them too. I try to keep up with boycotts, to buy slavery-free chocolate, etc. But Principle 3 applies: My energy and time is finite. I focus on animals for three reasons:

1: There are *many more* animals involved, and the things that happen to those animals *are worse* than the things happening to humans. If there's some industry where humans are regularly subject to surgery without anesthesia or kept in cages or for that matter *selectively bred as workers*, please let me know.

2: Other people are on this — organizing boycotts, working on political improvements for migrant laborers, etc. Fish or shrimp have fewer advocates.

3: Agency. I don't mean to imply that everyone in awful working conditions can just leave if they want — it's not that simple. But disenfranchised people still have voices and can report on their own state of being. A person *can* choose to opt into some suffering in lieu of a different outcome or for a benefit later, even on the scale of years. Nonhuman animals can't do either of these. If these systems regularly mistreat the humans who operate them, do you trust them with billions of animals?

Animal Products

I try moderately hard to avoid eggs and mildly to avoid milk. Some context: There are egg-laying and meat chickens. Similarly, cows are bred in separate

lineages for milk and meat. A milk cow makes a lot of milk during its life, but a beef cow only makes beef once — by opting for milk instead, you're still contributing economically to a cow's life and death on a farm, but you are contributing *less*.

But these categories aren't clear-cut: Male chicks whose sisters are destined as egg-laying chickens are ground and sold as animal feed; old dairy cows and laying chickens are sold as low-quality meat. The unfortunate truth is that dairy funds the beef industry, and eggs fund the chicken meat industry. Say what you will about the current agricultural system, but it's pretty good at using the entire animal.

Your standard battery hen lays one egg a day for most of the year — put differently, a single egg represents one to two days of battery hen life. That's a heavy price. When I bend on this, it's often because of gifted food (I rarely look a gift baked good in the mouth) or an abiding love of diner cuisine. This isn't very principled of me. I mention it only because it is the truth, and because if you aren't always principled either, well, you're not alone.

Dairy is my more defensible compromise. It's better for two reasons.

First, while an egg is a chicken's entire daily output, a glass of milk is less than 1% of a U.S. dairy cow's average daily output. (Incorporating the interchange between dairy and beef, as described above, the outlook becomes worse, but not *a lot worse*.) Even the worst conditions for dairy cows seem better than the worst conditions for chickens.

Second, I've *tried* going full vegan. I stopped. I sometimes have trouble eating enough food, and often a bit of cheese is cheaper and easier and more tempting than anything else. Hopefully, once I'm better-funded or my tastes change, I'll revisit this compromise and will be approximately at peace with my diet. Until then, I'll be buying soy milk alongside cheddar cheese, and then I will eat dinner.

Hopefully, once I'm better-funded or my tastes change, I'll revisit this compromise and will be approximately at peace with my diet. Until then, I'll be buying soy milk alongside cheddar cheese, and then I will eat dinner.

(The actually principled compromise would be to sometimes eat beef but vehemently avoid eggs…but *that's* tough too, because vegetarianism is a well-known label that usefully explains most of my dietary preferences. "In short, I'm a vegetarian; in long, there's this article in *Asterisk Magazine*…")

As a rule, vegans avoid honey. I don't — not because I'm convinced bees don't suffer or that beekeeping is definitely good for bees, but the rest of my or anyone's plant-based diet subsidizes honeybee agriculture. In the U.S., honeybee keepers make 30% of their profits from honey and 70% from renting them out for pollinating dozens of crop species. May as well get something sweet from it.

Less-Expected Animal Products

I care *less* about trace additives in processed foods than major components, but not zero. On one hand, there might be less

than 1% of these in any given product. On the other hand, humanity may not have nailed vegan cheeses yet, but we *absolutely have* dyes or gelling agents or what have you that aren't made from animals. I tried gelatin-free gummy worms last month! They were fine! Get it together, Haribo!

Gelatin is made from bones. You knew that, right? Did you know that confectioner's glaze/resinous glaze/food glaze/shellac is made from the secretions of the shellac beetle? It's in candy as well as wood glazes, pharmaceuticals, wax for fresh fruits, and various other products. It's not clear that the harvesting process is *terribly* harmful. Beetles are mostly *not* killed during it, and they're not domesticated — but they are cultivated, in the billions, so I am concerned.

In the face of my own ignorance, I'm falling back on suspicion and the fact that most people underrate insect suffering to decide: I don't like it! Prove to me that you're doing right by these insects, shellac industry. I don't usually double-check products for this, because I hadn't realized how common it was until right now. Uh-oh. I think I'll start.

...But again, they put this stuff on *apples*. I don't think I can avoid it entirely. Compromise is a bitter game. But unless you grow literally everything you eat, you *are* playing.

A Note on Joy

Now that I've made myself sound like the most obnoxious dinner guest of all time, allow me to defend myself. Yes, I think about this very often. Yes, it's as exhausting as it sounds — unless you find research papers about shrimp interesting, as I do, in which case, it's exhausting peppered with points of intrigue.

But the thing is: I love food. I cook and bake. You'll notice my policies are dotted with exceptions for gifts or dinners out. For me, that's where love is: providing for other people, in sharing meals and being fed. This love is *why* I put so much thought into what I eat. How could I *not?*

Anyway, to show that caring and compromise is not so joyless, I offer this, my go-to, the easiest cake I know how to make. It's adapted from the 1997 edition of *The Joy of Cooking*.

The Only Chocolate Cake

- Grease a 9-inch square cake pan.
- Mix 1 1/2 cups flour, 1 cup sugar, 6 tablespoons cocoa powder, 1 teaspoon baking soda, and 1/4 teaspoon salt.
- In another bowl, stir 1 cup water, 1/4 cup vegetable oil, 1 tablespoon vinegar, and 2 teaspoons vanilla.
- Combine and mix until it's homogeneous, but no longer. Pour into pan. Bake at 350°F for 25-30 minutes, until a toothpick stabbed into the middle of the cake comes out clean.
- Let it sit for 10 minutes and turn it out of the pan. Once the cake is totally cool, frost it, or for dinner party panache, use a mesh strainer to dust confectioner's sugar or cocoa powder over the top. Enjoy!

50 Cows vs. Chemists: The Health Debates Over Plant-Based Meat

Jake Eaton

Everyone wants to know if plant-based meats are good for you. Despite what you might read, no one has a definitive answer.


BEYOND BURGER
PLANT-BASED PATTIES
35% LESS SATURATED FAT
THAN A 4 OZ PATTY OF 80/20 GROUND BEEF
20g OF PROTEIN PER SERVING | NO SOY GLUTEN
2 - 4 OZ PATTIES NET WT 8 OZ (226g)
PERISHABLE: KEEP REFRIGERATED
IF PURCHASED REFRIGERATED, BEST BEFORE:
RETAILER: APPLY REFRIGERATED "BEST BEFORE" DATE
NON GMO Project VERIFIED
IMPOSSIBLE
BURGER PATTIES
MADE FROM PLANTS
19g PROTEIN
NO ANIMAL HORMONES OR ANTIBIOTICS
2 PATTIES ¼lb EACH
NET WT. 8 OZ (227g)
87% LESS WATER
89% LESS EMISSIONS
96% LESS LAND

Last May, Kim Kardashian debuted as Beyond Meat's chief taste consultant. In a commercial posted to Instagram, Kim takes a selfie with a taco, inhales deeply over a breakfast sausage link, and swoons while chewing an apparent mouthful of Beyond Burger — except, as many fans noticed, the burger half in her hands remains pristinely cut, evidently untasted. In fact, across the thirty-second clip, Kim never actually bites into anything. For this, she got dragged in the comments. The media pounced too: "Kim Kardashian Is Being Roasted for Her Beyond Meat Advert," ran the *BuzzFeed* headline.

But not all of the near 20,000 comments were on Kim's eating habits. In many, the skepticism centered on the rise — and the healthfulness — of plant-based meats. They implicated Beyond's products (in no particular order) in indigestion, cellulite, and cancer. Fans implored other fans to "just read the ingredients," that Beyond Meat is, among other things, "full of chemicals" ("really bad chemicals," "a chemical shitstorm"), "unnatural," and "freaky." The products are "engineered, specifically, to fool our senses into thinking they're whole foods," when in reality they're full of "toxic fats" and "high carbs" and lacking in "real nutrients." Other commenters veered down the now well-worn algorithmic path to misinformation, the narrative running something like: Beyond Meat is a plot to take over American ranchland. It's lab meat — "poison" — funded by Bill "Satan" Gates. And it's now being promoted by Kim, who only play-acts vegan; in reality, we know she's an omnivore because she eats small children.

Reactions to Kim Kardashian's social media may not, of course, be totally representative for market research. But in hindsight, the eighth most popular person on Instagram getting ratioed over a 30-second clip augured what would become a less than encouraging year for the plant-based meat industry.

Before 2022, of course, the momentum had been building. The Impossible Burger debuted in 2016 to praise and optimism: Mark Bittman called it "impressive." Ezra Klein called it "life-changing." Restaurants in coastal cities served the then-limited supply on a first-come, first-served basis. McDonald's, Burger King, and Dunkin' debuted plant-based sandwiches. Both Impossible Foods and Beyond Meat struggled to meet demand.

As retail availability expanded, sales increased steadily, around 10% per year. During the height of the pandemic, they exploded. In 2020, sales grew 45%, and the industry eclipsed the $1 billion mark for the first time.[1] Beyond Meat became a meme stock. Plant-based meats were heralded, at least in some corners of the internet, as a silver bullet, one of the best options to promote food system sustainability, combat global food insecurity, and minimize pandemic risk.[2] Sales held steady in 2021. For a moment, it felt like plant-based meat really was the future.

But 2022 was a bad year. Grocery sales dropped 14% by volume and restaurant orders

1. Sales for conventional meat were $81.8 billion.

2. The Good Food Institute's 2021 *Plant-Based State of the Industry* report states that "alternative proteins offer some of the most game-changing research opportunities with potential for global societal impact — stabilizing the climate and preserving biodiversity while eliminating food's contribution to pandemic risk and antibiotic resistance."

were down nearly 10% from their 2019 peak. The press grew progressively worse, particularly for Beyond: McDonald's ended their US trials of Beyond Meat's McPlant (poor sales),[3] one factory was cited for "mold, listeria, and other food-safety issues," and the company fired 19% of its employees.[4] (Impossible Foods announced in January 2023 that they too would be laying off 20% of their staff). Many reporters seemed eager to attack, the headlines oscillating between skepticism and eulogy: "Industry Possibly Suffering Perception Problem"; "Plant-Based Meat May Be All Hat, No Cattle"; "Fake Meat Was Supposed to Save the World. It Became Just Another Fad."

What changed?

One answer is that the health halo around plant-based meats is dimming. In 2020, the Food Industry Association's *Power of Meat* study found that 50% of consumers chose plant-based meat because they consider it healthier. Deloitte's 2021 *Future of Fresh* survey put that number at 68%. But in 2022, health perceptions dropped: 15 percentage points in the *Power of Meat* survey, to 35%, and 8 percentage points in the *Future of Fresh* survey, to 60%.[5]

3. The McPlant and the Double McPlant are still on menus in the UK and Northern Ireland.

4. To say nothing of September, when Beyond's COO left the company following a battery arrest for assault, in which he, to the delight of ironists everywhere, bit off a piece of another motorist's nose.

5. In Deloitte's survey, there was also a 5% drop in consumers who considered plant-based food more environmentally sustainable.

6. The actual quote is "We can understand, too, that natural species are chosen not because they are 'good to eat' [*bonnes à manger*] but because they are 'good to think' [*bonnes à penser*]."

7. Concern for the environment was a factor for 70% (49% major/21% minor), food safety for 65% (43%/22%), and animal welfare for 65% (41%/24%).

There's a Claude Lévi-Strauss quote that's gone through a game of telephone as it's been passed down through college syllabi. In its now garbled form, it's become something of an axiom in food studies: *good to eat, good to think*.[6] The basic idea: Food must first seem palatable to our values, must fit into our culture, before it's deemed fit for consumption. And consumers appear to be of many minds when it comes to plant-based meat.

Skeptics see a fabrication unlikely to escape the uncanny valley; foodies want a product that tastes better. Everyone wants a better price. But optimists look past the taste and see plant-based meats at scale: better for the planet, better for animals, and better for public health. Bruce Friedrich of the Good Food Institute, a nonprofit think tank dedicated to expanding the alternative protein market, includes two components in his theory of change: Plant-based meat won't compete with animal agriculture until it costs the same or less and tastes as good or better. But there's one "better" that's missing from that formulation, the component a majority of consumers think about the most: better health.

Health Matters

People who eat fewer animal products do so because they think it's better for them. In a 2019 Gallup poll, 23% of Americans reported reducing meat consumption in the prior year (5% were eating *more*). Of those eating less meat, 90% cited health reasons, and fully 70% named health a major concern — sizable gaps over the environment, food safety, or animal welfare.[7] And global surveys by Euromonitor and Veylinx show similar patterns.

As the name suggests, plant-based meats have capitalized on the plant-based diet trend, and no company more so than Beyond Meat. The company's IPO prospectus detailed the company's "strong belief" that Beyond products can "help address concerns related to human health, climate change, resource conservation and animal welfare." Ethan Brown, the company's CEO, leans into health claims in particular. In 2021, he told *The New York Times*

that "a No. 1 priority" is to "make sure people understand that our products are actually better for them than animal protein."[8]

But critics — and there are many — describe plant-based meats as ultra-processed foods (UPFs): highly energy-dense, "hyper-palatable" products. They slam the high sodium content, the ingredient list full of additives, or the heme iron found in Impossible.[9] And they are piggybacking off a growing body of evidence that links higher UPF consumption with pretty much everything bad: from all-cause mortality to decreased sperm motility. Michael Pollan's advice — "Eat food. Not too much. Mostly plants." — became a mantra of the food movement. By food, he meant "real" food, what your grandmother would recognize. Critics tap into this ethos: Meat is not a plant, but plant-based meat is not food. The Beyond Burger is, in Pollanian formulation, an edible foodlike substance, an intricate product of food science.[10]

The health critique is being lobbed in some places you'd expect. Mark Bittman's blog *Heated* published a series of critiques of plant-based meat — "less like a salad, more like a Pringle." Former Whole Foods CEO John Mackey has expressed reservations about the health impacts of plant-based meat, despite introducing Beyond Meat to the retail market. Academics worry the plant-based association obscures what could otherwise be a diet full of junk. But skepticism is also growing on the side of the aisle known to frequent Chick-fil-A and eat McDonald's in the White House.

Since 2019, the Center for Consumer Freedom, a PR firm headed by Rick Berman,[11] has been leading a campaign against plant-based meats. Late in 2019, the organization placed full-page ads in *The New York Times*, The *Wall Street Journal*, and *USA Today* that raised health concerns over plant-based meats. The ads directed readers to CleanFoodFacts.com, where articles include "Bill Gates Wants You to Eat Ultra-Processed Goop," "Quiz: Veggie Burger or Dog Food?" and "Titanium Dioxide in Meat: What Is It?" This January, the top "rising" topic searched in conjunction with plant-based meat on Google Trends was titanium dioxide. And if Kim's Instagram comments are indicative of anything, it's that the themes are catching on.

Berman and other opponents have seen an opening. Taking a page from Steve Bannon's playbook, the Center for Consumer Freedom's strategy has been to flood the zone with shit — in this case, using evidence and language from nutrition science to run negative advertising in the form of full-page newspaper ads, a Super Bowl spot, even a campaign to force plant-based meats to include a cancer warning under California's Proposition 65.

And that strategy seems to be working, because the zone's been flooded with shit for a long time.

Definitive Evidence is Elusive

The nutrition debates[12] over plant-based meat typically center around one of two arguments: 1) Meat, especially red meat, is bad for you. Replacing beef with plant-based meats must therefore be better. This is the position of Beyond Meat and the Good Food Institute, among others. 2) Ultra-processed foods are bad for you, so plant-based meats are bad for you too. This is the where the Center for Consumer

8. Impossible Foods, perhaps smartly, is more circumspect. From an Impossible blog post titled "Are Impossible Products Healthy?": "Categorizing foods as 'healthy' or 'unhealthy' is a virtually impossible task, as all foods provide nutrients, all of which are needed to some degree for health."

9. Impossible's heme iron is made using a yeast genetically engineered with the gene for soy leghemoglobin, which is derived from soy plants.

10. "By my standards, it's not food," Pollan said in an interview in 2018. "Doesn't mean I'm against it."

11. A possible inspiration for Nick Naylor in *Thank You for Smoking*, Berman first cut his teeth fighting smoking limitations in restaurants. In the past, the Center for Consumer Freedom has coordinated efforts critical of, among others, the CDC, PETA, the Center for Science in the Public Interest, and Mothers Against Drunk Driving.

12. In keeping with the average American, I will ignore environmental and animal welfare arguments in this piece.

Freedom falls,[13] but it's also the position of a constellation of actors that don't necessarily want plant-based meat to fail. These include Carlos Monteiro, a professor at the University of São Paulo credited with spearheading research into food processing, and the International Panel of Experts on Sustainable Food Systems, whose recent report *The Politics of Protein* criticizes the framing of plant-based meats as a silver-bullet solution.

This debate will not be resolved in the short term. To understand why, it's worth a short detour through the methods of nutrition science. We'll look first at the evidence base around dietary patterns before diving into the specific research on plant-based meat. My goal is not to convince you that one position is right. It's to show that because the literature is so messy, arguments on either side rely on spin as much as evidence.

The first issue is that nearly all studies purporting to show health consequences of eating (usually red) meat or health benefits of plant-based diets are observational. Observational studies are the backbone of nutrition science; they outnumber controlled trials in one estimate by more than 7-to-1. The basic idea is to follow people over a long time, record what they eat, and identify what foods and/or dietary patterns are associated with a range of health outcomes. Bigger studies and longer time frames equate to more statistical power and higher accuracy. But the limitations are considerable.

These studies have the same weakness as all observational research: showing that some health outcome is associated with a particular diet isn't enough to prove that diet caused the outcome. And in the world of nutrition, confounding is massive. People who eat healthier diets tend to look very different from those who don't. Are improved health outcomes among vegetarians (if they are found, which is not always) due to the absence of meat or to a higher-quality diet? Or could they be the result of demographic factors — higher income and education? Or is it something else entirely: higher health consciousness, even religion? One meta-analysis of studies comparing heart disease between vegetarians and the general population found that beneficial effects for vegetarian diets was driven primarily by data from Seventh-Day Adventists; "the effect of vegetarian diet in other non-Adventist cohorts remains unproven."

In addition to the challenges of observational research, nutrition science has a very difficult time accurately capturing dietary intake. How often did you eat bananas in the past year?[14] What about melons, strawberries, cooked greens, raw greens, stuffing, dressing, or dumplings? Vary the time scales in the questions, repeat for 140 foods, and you've completed a food frequency questionnaire. The most commonly used dietary assessment tools are bad. Like, open-secret, mostly unreliable bad. In 2013, Edward Archer, an obesity theorist, published an analysis of the data used in the CDC-sponsored National Health and Nutrition Examination Survey (NHANES) data set that showed that 60% of reported dietary intakes were physiologically implausible. Elsewhere, he's called the data pseudoscientific and inadmissible in scientific research.

These challenges are part of why finding consensus in nutrition science is so difficult. Many observational studies indicate an association between meat consumption and negative health outcomes. Many do not. If you have strong priors, it's extremely easy to confirm them by looking at isolated studies. One analysis of NHANES data demonstrated that high animal protein consumption led to increased mortality risk; another, using the same data, did not. Even meta-analyses are often unclear.

The strongest evidence of any risk is between processed meat and colorectal cancer. In 2015, the WHO took a strong position

13. If they can be said to have a position on anything, it's mostly just opposition.

14. On the low end, your options are one to six times per year. On the high end, two or more times per day. There are eight frequency options in between.

Plant or animal?

a.

b.

c.

a. Beyond Burger; b. hamburger; c. Impossible

in classifying processed meat as carcinogenic.[15] But in 2019, a large analysis in the *Annals of Internal Medicine* looked at the same evidence combined with four new studies and concluded it was too weak; the consortium of researchers ultimately recommended that adults continue their current meat consumption. Harvard scientists attempted to refute that. And then it emerged that the lead researcher behind the *Annals of Internal Medicine* studies and recommendation had in the past accepted funding from a trade group with ties to the meat industry. This goes on ad nauseam.

The debate persists largely because, across a wide body of observational research relating to meat consumption and vegetarian dietary patterns, the evidence is inconsistent, the effect sizes are generally small, and the quality of evidence is very low. If you want to make a claim supporting meat consumption or vegetarianism, there are many studies — even many meta-analyses — you can choose from.

In experimental trials, we stand on somewhat firmer ground. And it's here that we have direct evidence of some of the health impacts of plant-based meat.

Experimental studies have major advantages over observational research. Careful trial design can help tease out which foods actually impact our health, and shorter time scales permit researchers a more accurate look at what their subjects eat. Kevin Hall's lab has pioneered the use of inpatient trials in a controlled environment where dietary intake and metabolism can be accurately monitored. Most notably, Hall demonstrated that a diet composed of ultra-processed foods results in increased energy intake and weight gain compared to unprocessed foods: If given no restrictions, people just eat more calories when they're consuming UPFs. But most other experimental studies take place out in the real world.

Because these kinds of studies are costly and difficult to conduct over longer periods — very few people want to try experimental diets for months on end, let alone years — they can usually only track changes in short-term health outcomes or biomarkers like cholesterol or blood pressure. But a further challenge is that it's extremely difficult to trust studies funded with industry support.

Over half of all industry-sponsored studies find favorable results, compared to 10% of studies without involvement. Sometimes the practice appears benign: When, for instance, when the California Strawberry Commission sponsors research into adult cognition. But it has also been insidious: Throughout the 1960s and '70s, for instance, the sugar industry sponsored a research program that, according to a *JAMA Internal Medicine* article, "successfully cast doubt about the hazards of sucrose while promoting fat as the dietary culprit" in coronary heart disease.[16] Marion Nestle, professor emirata of nutrition, food studies, and public health at New York University, has written that industry funding has become so rampant that "health professionals and the public may lose confidence in basic dietary advice," to say nothing about specific food products.

But public funding for nutrition trials is limited and industry interests nearly limitless. And most trials sponsored by industry actors seem tailored to support specific talking points for marketing teams. That's one way to read the most well-known trial on plant-based meat.

The SWAP-MEAT Trial

The most widely cited study on plant-based meats is the "Study With Appetizing Plantfood-Meat Eating Alternative Trial" — or, in the grand tradition of medical acronyms, SWAP-MEAT.

15. The WHO quantifies the risk: every 50-gram portion of processed meat eaten daily increases the risk of colorectal cancer by about 18%. NB: This report also includes experimental data in animals, so it is not purely observational data.

16. The American Society for Nutrition cites this event as eroding trust in the field.

A brief summary[17]: SWAP-MEAT was a randomized crossover trial in which 36 participants ate two servings a day of either animal meat (ground beef, pork sausage, or chicken breast) or plant-based meat (Beyond products matched to the animal equivalents — Crumbles for ground beef, etc.). Each participant consumed the plant or animal diet for eight weeks, then switched to the other. Half began in the plant phase, half in the animal phase. The study's primary outcome — the biomarker it measured — was fasting serum trimethylamine-N-oxide (TMAO, which we'll get to shortly). Secondary outcomes were levels of cholesterol, triglycerides, glucose, insulin, blood pressure, and weight.

At the study's end, TMAO was significantly lower during the plant phase than the animal phase. Participants in the plant phase also had significantly lower LDL (bad) cholesterol (on average 109.9 mg/dL compared to 120.7mg/dL) and weighed significantly less (on average 78.7 kg compared to 79.6 kg). The abstract concludes: "Among generally healthy adults, contrasting Plant with Animal intake, while keeping all other dietary components similar, the Plant products improved several cardiovascular disease risk factors, including TMAO; there were no adverse effects on risk factors from the Plant products."

The Good Food Institute hailed SWAP-MEAT as "a critical milestone for alternative proteins." Nestle, on her blog, was skeptical. She concluded that: "two servings a day of Beyond Meat is unlikely to be harmful. Whether substituting Beyond Meat for real meat is truly useful for health in the absence of other dietary changes remains to be confirmed, hopefully by independently funded research."

The point, once again, is that your takeaway is likely to depend on your priors. And so in an effort to illustrate how much space there could be between positions, what follows is my most good faith argument between both positions.

Optimist: *Bottom line: This study shows modest improvements in cardiometabolic biomarkers when plant-based meat is compared to the real thing. First, the differences in TMAO were huge! A 2017 systematic review of nearly 20,000 individuals showed that elevated concentrations of TMAO are associated with increased risk of both heart attacks and all-cause mortality. Several other studies, including a 2022* JAMA Network Open *article, conclude the same. These are big studies in prestigious journals with large effect sizes. Now we have experimental evidence indicating the causal role played by meat, and plant-based products come out better.*

Skeptic: *The evidence on TMAO is unclear at best, meaningless at worst. TMAO is not a universally accepted biomarker of disease; no large health bodies condone its use as a diagnostic, and for good reasons. To nitpick one: TMAO is elevated in people with chronic kidney diseases, who we know have poor health outcomes — that correlation could explain some of those effects.*

Even were that not the case, the use of TMAO as an indicator of disease is misleading. TMAO is produced when gut bacteria consume choline and carnitine, nutrients present in large quantities only in animal-sourced foods. Plant-based meats match animal meat on some nutrients, like iron, but they don't have carnitine or choline. Saying that eating meat leads to higher TMAO relative to plants is something like saying that eating Twizzlers leads to insulin spikes relative to kale. Christopher Gardner, the study's PI, admitted this in an interview when he described the TMAO result as a "foregone conclusion."[18]

Last point: Some fish are known to increase TMAO more than any other animal-sourced food — in one study, forty times more than red meat. Taking the logic of SWAP-MEAT at face value, we should also limit fish

17. It's worth reading the abstract at minimum, and the whole paper if you're particularly interested in the hair-splitting to come.

18. Researchers at McGill are currently recruiting for a very similar trial, using TMAO concentrations after one week. I would anticipate that headlines will read "Eating Plant-Based Meat Improves Signs of Cardiac Health in Just One Week."

consumption — but fish is about the one thing most nutritionists agree is healthy.

***O:** Then let's ignore TMAO, as, indeed, most write-ups of the trial have. On secondary outcomes, we stand on more solid ground. Body weights were lower during the plant phase of the trial (~2 pounds, on average). That's a small but consistent difference — it wouldn't have been significant otherwise. This finding provides evidence that counters the idea that plant-based meats will lead people to overeat because they're "ultra-processed." They might even lose weight!*

***S:** But this result was only true for the group that received the plant intervention first. What's more — and this is buried in the supplementary data — the plant-to-animal group gained weight on both diets. Meanwhile, the animal-to-plant group lost weight on both diets. Even if the main point of the study is to compare the plant and animal phases, it's disingenuous not to discuss how the findings might generalize. If we care about real-world impacts shouldn't we actually be looking at changes from baseline?*

In addition (and forgive me for being a little conspiratorial here), the authors listed waist circumference as an outcome in their registration at ClinicalTrials.gov, but for some reason that isn't included in the final report. I'm not necessarily calling foul — perhaps they concluded it wasn't important — but I'm also not not calling foul. Two pounds may be statistically significant, but it's hard to say it's clinically meaningful, or likely to have an impact on health outcomes; it would be great to see another measure.

***O:** Fair. But the strongest evidence is that during the plant phase, participants' LDL cholesterol was 10 mg/dL lower. Unlike 2 pounds of weight loss or gain, this one really matters. Meta-analyses have shown that a 10% decrease in LDL reduces all-cause mortality by something like 10%.*

***S:** That's true. But again, looking at baseline LDL levels suggests there's noise within the signal. The plant-to-animal group came into the trial with mean LDL levels of 130. These dropped to 112 in the plant phase (a big drop!) before they rose to 122 in the animal phase. But even during the animal phase, their LDL levels were still lower than baseline. This is confusing because, before starting the trial, they were eating one serving of meat per day on average, compared to two during the trial. Somehow, when they were eating more meat, their cholesterol was still lower.*

The animal-to-plant group, meanwhile, began the trial at 113 on average, rising only 4 points to 117 during the animal phase before falling to 106 in the plant phase. The plant phase showed better LDL cholesterol overall, but the dose response is inconsistent enough to make me wonder what would happen in a bigger trial.

That said, I do think it's clear that LDL cholesterol was lower in the plant phase, so the bigger question is: What about the fact that there were no differences in triglycerides or blood pressure? Or Insulin-like Growth Factor 1, which the authors hypothesized would change in their trial registration?

***O:** Plant-based meats have higher sodium, so the fact that the study found no meaningful differences in blood pressure is probably more in their favor. And macronutrients were fairly well matched in overall diets, so it's not surprising that there weren't larger differences in triglycerides.*

***S:** I'm just not sure that's conclusive enough to say that plant-based meat "improved several cardiovascular disease risk factors." Regardless, a final point: Even if you think the findings are valid, they're still an incomplete picture. In another study (which is similarly narrow, I'll admit!), Itkonen et al. compared the impacts of varying ratios of animal to plant protein on bone health. After 12 weeks, participants in the plant-based diet had significantly higher markers of bone resorption and formation — risk factors for bone disease. We need so much more research!*

The SWAP-MEAT study was specifically designed to make Beyond Meats look good, and it did so by choosing very specific biomarkers, only three of which showed changes, and even then the dose-response relationships were unclear. It was conducted by Christopher Gardner, who is vegan (no offense, Chris). And it was paid for through an

unrestricted research gift from Beyond Meat to Stanford University. How do you tease out bias here?

***O:** The lack of restrictions on the research gift means Beyond had no involvement in any aspect of the study. And Gardner is a respected scientist with a track record of publishing null results. He wrote to Marion Nestle to tell her the study was coming. He's well aware he might be called a vegan shill. The point of this study was to answer questions specifically about plant-based meat compared to conventional meat. At worst, this study proves that, over a short period of time, eating plant-based meat is not bad for you. At best, it's an indication that plant-based meats might be better.*

The Limits of Reductionism

So, it's hard to say that plant-based meats are healthier than animals. What of the argument that, as ultra-processed foods, they might actually be worse?

Over the past decade, the number of studies looking at food processing has exploded. It's somewhat strange this didn't start earlier — presumably our grandmas have been telling us all along that chips and Twinkies are bad for us — but the reason is that until 2010, we didn't have a good way of thinking about degrees of processing. In that year, Carlos Monteiro first published the NOVA classification system for food processing, which now defines four processing categories[19]: unprocessed and minimally processed foods; processed culinary ingredients; processed foods; and ultra-processed foods. Unlike minimally processed and processed foods, UPFs are not modified whole foods; they are, under NOVA, "industrial formulations made mostly or entirely with substances extracted from foods, often chemically modified, and from additives, with little if any whole food added." Most plant-based meats, including Impossible and Beyond, fall into this category.

Part of the reason we didn't have good ways of thinking about food processing is that nutrition science had traditionally favored what's usually called the *reductionist* approach — trying to understand how single compounds impact human physiology. This enabled massive strides in identifying and addressing micronutrient deficiencies, but it has more limited application to diet-related chronic disease. Beriberi is a thiamine deficiency, straightforwardly treated with a B1 supplement. The causes of coronary heart disease are multifactorial: stress, physical activity, air quality, smoking, diet, and potentially many more. They are difficult to tease out from one another, and it remains quite unclear how dietary substitutions impact the disease's course. A Google Scholar search of "saturated fat" returns over 1.3 million articles, the top 10 of which are not in agreement. On a daily basis, this stuff leads to Twitter fights among grown adults.

The reductionist approach helped to transform the food landscape by incentivizing product reformulation. The canonical example is margarine, promoted as an alternative to saturated-fat-rich butter, the media's favorite flip-flopping nutrition finding. After a series of articles showed small or neutral effects of butter on health outcomes, Time Magazine proudly proclaimed, "Eat Butter." Those weary of the debate may prefer how Joan Dye Gussow, former chair of the nutrition education Program at Teachers College, put it: "I prefer butter to margarine, because I trust cows more than chemists."

What's glaringly absent within the reductionist paradigm — indeed, within much of nutrition science — is theory. Without it, much of nutrition science comes to resemble a frequentist fishing expedition amid a vast sea of data. This was memorably demonstrated in a 2013 article, "Is Everything We Eat Associated with Cancer?" Selecting 50 ingredients at random from a cookbook, including beef,

19. Full categorization here: https://educhange.com/wp-content/uploads/2018/09/NOVA-Classification-Reference-Sheet.pdf

lobster, corn, cinnamon, and rum, Jonathan Schoenfeld and John Ioannidis found that 80% had articles reporting on their cancer risk. Of 264 identified studies across the 50 ingredients, nearly three-quarters — 72% — showed statistically significant associations, including 103 of which showed increased risks for cancer. Theory demands causal mechanisms, but the status quo of nutrition science is to rely on previously reported associations.

This approach has seeped into the popular comparisons between beef and plant-based meat. In a piece in *Wired*, Hannah Ritchie argues that the backlash against processing unfairly characterizes plant-based meats. She compares the nutrition profile of grass-fed beef and plant-based meats, concluding, based on macronutrients, that plant-based meats are "probably a bit better for our health than their meat equivalents." But that analysis only incorporates protein, fat, saturated fat, and sodium. The Good Food Institute does a similar, selective comparison, which additionally includes cholesterol and fiber. But these products should not be viewed as nutritionally interchangeable even where nutrition panels appear similar. An analysis of plant-based meat and grass-fed beef showed substantial differences in nutrients between meat and plant-based meat, despite the nutrition panels on packaging showing comparable nutrient profiles.[20]

Moreover, the nutritional content of a food is not a perfect indicator of its health benefits. An analysis of 44 different meat substitutes available for purchase in Sweden found that while they contained similar amounts of iron to animal meat, this iron was in a form that's much harder for our bodies to absorb. Phytate, present in many plant products, inhibits absorption of many nutrients, including iron. Generally, diets in high-income countries are sufficient in most nutrients for this not to matter, but where major micronutrient deficiencies remain common, phytate-to-nutrient ratios remain a concern.[21]

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Nutrient reductionism only tells us about specific nutrients in specific populations. That's good for marketing claims, but it cuts both ways. It's surprising that Big Beef hasn't yet conducted a controlled trial of beef vs. plant-based meat in women with anemia, or even in children with stunting. But that may be because they don't yet see a sufficient threat from the plant-based meat industry.

The SWAP-MEAT trial, to its credit, avoids nutrient reductionism. Others don't. Good Food Institute's *Plant-Based Meat and Your Health: The Facts* favorably compares the Impossible Whopper to a conventional Whopper: "less total fat," "more complex carbohydrates," and "fewer calories." Let's

20. This analysis was funded, it should be noted, by the North Dakota Beef Association.

21. This is the main reason that adherents of the carnivore diet recommend avoiding vegetables.

ignore the fact that the differences in nutrients are quite small and focus on the larger health concern, which is that the Impossible Whopper from Burger King is an Impossible Whopper from Burger King. The same document, in a section that explains the "truth about processed food," equates ruminant digestion to industrial food processing[22] while suggesting that foods like yogurt and olive oil are as highly refined as a plant-based burger.[23] The Center for Consumer Freedom may not be honest, but they are not alone.

A Giant Bag of Salt

Eliminating or reducing meat consumption asks 90% of people on the planet to change an integral aspect of their lives. Plant-based meats are supposed to make that change easier. Animal welfare and environmental advocates are probably the strongest proponents of these products. But health — not environment, not welfare — remains the strongest motivating force behind the plant-based buzz. In the process of attempting to convince consumers their products are healthier, corporations — Beyond, in particular — have adopted the same tactics as other large food industry players. This became most clear in November, when Beyond Meat announced to investors a partnership with the American Cancer Society to help "build the foundation of plant-based meat and diet data collection." This is a big longitudinal study, but data on industry-funded research consistently shows a bias toward favorable results. Perhaps a market can decide on the most likely outcome for that study. For a company with a mission to "positively affect the planet, the environment, the climate and even ourselves," intellectual honesty and transparency are two ingredients that are still missing. Without them, plant-based meats may never become *good to think*.

This goes too for the Good Food Institute, whose health messaging toes the line between spin and misinformation. "No matter which way you slice it," reads their website, "plant-based meat has significantly more nutritional benefits than conventional meat. Whether it's introducing a new source of fiber to your diet or cutting down on cholesterol, plant-based products lead to better health outcomes." This is misleading at best. At its worst, it's plainly wrong: There is no definitive evidence that eating plant-based meat leads to better health outcomes. And there's no definitive evidence that it doesn't. We have only the SWAP-MEAT trial and its short-term biomarkers.

But it *does* matter which way you slice it: Plant-based meats *do* come with trade-offs. These include higher sodium,[24] lower calcium, lower vitamin D, lower-quality protein, and lower bioavailability of the nutrients that plant-based meats claim to match in conventional beef, including iron. Big Beef can and will play the reductionist game too. These trade-offs may not be likely to matter to the average consumer, but they add up in the margins. Higher intake of red meat, for instance, is associated with better iron status even in high-income populations, and substituting plant protein with animal protein is shown to lead to decreased bone health. Moreover,

22 "Processed food can be less healthy because of what is taken away. Compared to the same product made from whole grains, removing fiber and complex carbohydrates can lead to a product that is less healthy. This is what happens with conventional meat: we lose 100 percent of the fiber and complex carbohydrates originally in the soy, wheat, corn, and other crops fed to animals."

23. "Wired notes that 'virtually everything you put in your mouth is processed.' Connie Weaver, a nutrition scientist at Purdue University, observes that 'highly refined foods like yogurt, olive oil, and bread have many, many processing steps, and they don't look anything like the original product they started with.'" Under NOVA classification, yogurt without added sugars is considered a minimally processed food (Level 1). Olive oil is a processed culinary ingredient (Level 2). Beyond Meat and Impossible Foods, as industrial products formed from industrial ingredients, are considered ultra-processed food (Level 4).

24. The evidence on sodium intake and health outcomes is also equivocal.

it's not at all clear that villainizing beef on fat and cholesterol makes plant-based meat look better than poultry, the consumption of which is rising much faster than beef is falling. And let's not forget that eliminating beef does not require substituting plant-based meats. This is not a zero-sum game.

Up to now, industry entities aligned against plant-based meat have been relatively quiet, seemingly content with the Center for Consumer Freedom's ultra-processed campaign and some scattered studies showing some benefits for beef. Should industry players choose to enter the academic fray and run their own experimental studies, it shouldn't be surprising if deep pockets and some cleverly designed trials demonstrate evidence in support of conventional meat over plant-based meats: anemia, child growth, blood pressure, and bone health are obvious areas to target. If plant-based meat companies want to retain any competitive edge in public perception, it will help to avoid being grouped with Big Food or Big Tobacco. That halo won't last long if their approach to scientific research is the same.

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But at the moment, these companies should be more worried about scoring own goals. In January, *Bloomberg*'s Deena Shanker published a piece that described plant-based meat as a flop. Impossible responded by taking out a full-page ad in *The New York Times:* a screenshot of three anonymous Reddit comments reacting to Shanker's article. "I suspect it's coming from a news outlet paid money to write a article by people who make money from meat sales," said one. "It's Bloomberg so i would take it with a giant bag of salt," replied another. It was a strange look to publicize, at a cost of something like $250,000, an unsubstantiated claim about *Bloomberg*. More so still given that Impossible criticized the article — in a letter on their website — for failing to report the facts. To say nothing of the fact that one of the main critiques of the product is that it contains, roughly, a giant bag of salt.

Nutrition science is messy and hard. Given how difficult it is to arrive at definitive conclusions, this fight is not likely to end soon. Over time, financial influence from both sides may give us more evidence, but one result may be to make the conclusions less clear. The zone is flooded with shit, and more is coming. The campaign to replace conventional meat with plant-based products should not underestimate what, in the public's eye, is a 2-million-year incumbency in the human diet. The backlash to plant-based meat intuits this.

But we don't even need to go that far back. Faced with sloppy, conflicting, and at times disingenuous messaging over a product that still costs more and tastes worse, it seems only rational if consumers continue to fall back on a simple heuristic: What would your grandmother eat?

64 *America Doesn't Know Tofu*

George Stiffman

China has spent millenia exploring the culinary possibilities of soybean curds. The West has barely scratched the surface.

ILLUSTRATION BY
David Huang

Guiyang didn't have many *restaurants*, per se. The metropolis was more of a city-wide night market. Even in the pre-COVID days, streets like Qingyun Road were only half-filled with cars, to leave room for tents and tables that stretched to the horizon, and for smoke and steam that rose into the clouds. Eateries didn't burden you with 14-page menus, common at Shanghainese or Northeastern restaurants. No — a làoguō 烙锅 shop sold laoguo (think Korean BBQ with more vegetables, cooked over a clay pot dome). A sīwáwa 丝娃娃 shop sold siwawa (shreds of 20-plus varieties of fresh and pickled vegetables that you roll into a thin, rice cake-like taco). And tofu stands sold tofu. But probably not the tofu you're thinking of.

Pale slabs of bean curd shivered over a sputtering steel grill box. As their tops bathed in the cool summer air, their bottoms tensed and colored. When Auntie flipped over a piece, the tofu's underside was purplish like a black eye, its thick skin waxy and crackly like a fried egg bottom. And then it started expanding.

The tofu began puffing up, convulsing like a pot of water that couldn't quite boil. For a minute or two it grew, and grew, and grew, until the tofu had ballooned to double its original size. Finally a ray of hot steam broke through the taut, leathery skin. Out trickled a lazy stream of creamy, off-white liquid.

Auntie furrowed a small hole on one end of the tofu and spooned in her signature sauce: ground fire-roasted chiles, soy sauce, ginger, mint, and a medicinal root prized for its grassy, fishy scent (鱼腥草 yúxīngcǎo). She passed over her creation: liàn'ài dòufuguǒ 恋爱豆腐果. *The tofu dumpling of love*.

I bit in. Out seeped a viscous, sulfurous liquid, rich as an egg yolk custard but clean as freshly ground soymilk. Firm tofu had sacrificed itself, melting into juice. My tongue refused to believe it. This was tofu?

I had found it painful going vegan in college, giving up most of the foods that I loved. But after spending a summer in China, all that changed. I was now here on the pretense of "study abroad," but really just crisscrossing the country to find foods that would excite me and other would-be vegans back in Los Angeles. I had to learn about the tofu dumpling of love.

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Guiyang's streetside tofu vendors are part of the ancient history of Chinese vegetarian cuisine. The oldest and best-known school is Buddhist and Daoist temple food, or zhāicài 斋菜. Both traditions discourage the killing of animals, or even the desiring of animal flesh, and over centuries have nurtured plants into satiating meat-free meals. Temple food has many quirks. Alliums are banned for being aphrodisiacs. Coriander seeds, originally prohibited to distinguish Chinese Buddhists from Hindus opposite the Himalayas, are also a no go. As is usually the case, constraints in one area have led to innovations elsewhere, like a closer

relationship to mushrooms and herbs like xiāngchūn 香椿, or Chinese toon. Adherents don't evangelize via protest or paid advertising; they open restaurants, from Michelin-starred eateries in Shanghai and Beijing to $3 all-you-can-eat buffets ubiquitous in the Southeast.

Austere temple food is a far cry from the lavish feasts of China's emperors, or gōngtíng sùshí 宫廷素食, imperial vegetarianism. The Qing Dynasty's Kāngxī 康熙, a devout Buddhist, commanded legions of chefs to recreate the flavors and textures of meat from plants: pork ribs made from bamboo; goose made from marinated, coiled tofu skin; and crab meat from potato and carrot. Over time, these foods have bled into more mainstream Jiangsu and Zhejiang cooking, eaten by tens of millions in the regions surrounding Shanghai. Restaurants like Shanghai's famed Gōng Dé Lín 功德林 offer a taste into history, allowing guests to eat like an emperor.

While temple and imperial vegetarianism are more overt, China's final plant-based cuisine is far more pervasive. It's not moral, religious, or even intentional. It's economic. Historically, meat was expensive. The default diet, therefore, has always been mínjiān sùshí 民间素食, or common vegetarianism. Because the cuisine is so diffuse, however, it's harder to pin it down. The unbelievable diversity of vegan foods in China is difficult to capture in words. A visit to Chinatown won't cut it. These are the foods of the Chinese poor, those who aren't able to leave.

Yet these origins have led to a paradox: Even though there are oceans of common vegetarian foods in China, Chinese people find them less desirable. They taste like poverty.

This is especially true for the king of it all — tofu.

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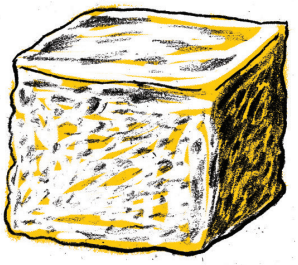
Why in the world would you study tofu making? my Airbnb neighbors would interrogate me. *It's the career for those who have no other options!*

Five months after my first taste of melting tofu, summer break arrived, and I was back in Guiyang. It took two weeks of meandering produce markets, buying and tasting different tofus, asking shop owner after shop owner, to find a teacher. Finally, one agreed. The next day, I woke in the dead of night, crawled out of bed, and wandered over. I had apparently undershot my wake-up call. At 4 a.m., the only thing for sale was sex, and my teacher was nowhere to be seen. I sat down on the curb outside his boarded-up shop, across from three women huddling in the shadows. I had nothing to do, so I pulled out my journal and began jotting down tofu goals. Learn best practices for coagulating soy milk. Measure their water's mineral content. Figure out the specific roles of acid and alkaline…

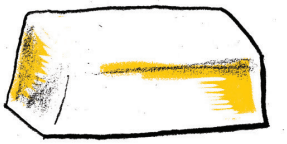
When I looked up, a skeleton of a man was approaching. Tattoo sleeves covered his bony arms, and his chiseled glare screamed out to me, *Run!* He came to a stop just one yard behind my body and stood in silence. I broke the ice because I didn't want to die — *Nice weather, bro. Are summers always this mild?* He was stupefied. One of the women came over. *What are you writing?* She laughed at this foreign idiot, journaling in a dark alley outside the brothels at 4 a.m. I half-stammered, half-shouted back, *I'm just trying to study tofu!* And she was stupefied as well. I kept my head down, writing until my teacher came 45 minutes later, with the bony pimp and bosomed woman never moving an inch. The next day, I decided to go over at 5 a.m.

Despite the early-morning wakeups and close calls, my new teacher turned out to be a double-talker. For two days, I sat in the corner of his car garage-turned-tofu shop, bathing in unventilated coal fumes and watching for hours and hours as he and his brother went through the process of making their tofu. They wouldn't talk



Frozen Tofu
凍豆腐

Tofu Sheets
千張

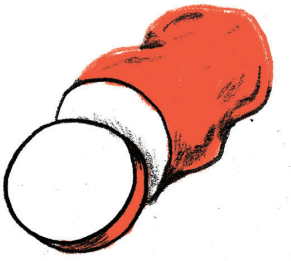


Silken Tofu
內酯豆腐

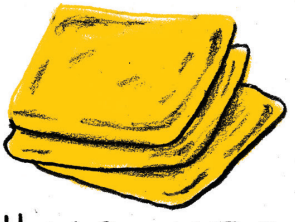
Stir fried Mung bean Okara (Beijing)
麻豆腐

Fresh Tofu Pudding
豆花

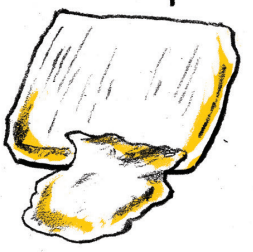
Stinky Tofu (Changsha Style)
長沙臭豆腐



Shanghai Tofu
素雞



Hand Ripped Tofu (Dafang County, Guizhou)
大方手撕豆腐



Jianshui Juicy Tofu (Jianshui County, Yunnan)
建水包漿豆腐

Anhui Smoked and Salted Tofu
臘八豆腐

Fermented Tofu
豆腐乳

to me, or allow me to ask any questions, and on the third day demanded payment: 10,000 yuan in tuition. I didn't blame the brothers — after all, they were making tofu because they had no choice. I told them I'd think about it and left to find another teacher.

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Leave soy curds to be, and they will coalesce into silken tofu. Spoon them into a mold, press out some water, and they become soft, firm, pressed, or thin tofu sheets. Smoke, dehydrate, ferment, or alkali-treat these tofus and you arrive at several new varieties. Throw them in the freezer and their inner structures will become porous like a sponge.

There are also tofus made without soy curds. Cook soy protein with fat, starch, and seasonings and you'll have a smooth, dense, fishcake-like tofu. Or warm soymilk and enjoy the rich, high-protein film that forms on top, either as thin sheets or rolled into delicious tofu sticks, fresh or dried. All in all, there are more than 20 types of tofu.

A common misconception outside of Asian communities is that tofu is just an ingredient. In fact, it's an entire category of proteins. Just as a chef would never cook chicken breast like chicken feet, so too are these tofus completely different from one another. They have different strengths and weaknesses. They have different flavors. They have different mouthfeels. It's not like substituting a black bean for a kidney bean. Because these tofus are so different from one another, and from meat, each one opens up its own world of culinary possibilities. These are the most versatile plant-based proteins in existence.

There are some foods that weave their way across China, like the legendary tofu pudding — dòufunǎo 豆腐脑, dòuhuā 豆花, lǎodòufu 老豆腐. Sichuan and Guizhou people prefer firmer tofu, eaten atop rice or alkaline noodles with burnt chile oil to dip. Those in the Jiangsu-Shanghai region eat a soft pudding and top it à la carte: pickles, soy sauce, vinegar, salt, sugar, chile oil, sesame oil. Guangdong and Fujian tofu pudding is exceptionally watery, almost drinkable, drizzled with a refreshing touch of sugar or ginger syrup. Tianjin and Northeastern pudding is rich and full-bodied, doused with a hearty gravy of star anise, dried daylily, and shiitake. Each variant adapts to the local tastes. Almost all are vegetarian or vegan.

Or variants of pressed tofu with garlic chives. Almost every region of China serves something similar — sometimes just garlic chives, tofu, and soy sauce; some with fresh chiles; others with pickled chiles; others with chile bean pastes; some with soybean oil; others with fragrant Chinese rapeseed oil or lard.

Others are regional specialties, like the Huaiyang (Jiangsu-Shanghai area) hóngshāo sùjī 红烧素鸡, red braised vegetarian chicken. Or the Dongbei (Northeast) staple jiānjiāo gāndòufu 尖椒干豆腐, tofu sheets with green chiles. Or Guizhou's tofu dumplings of love.

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It took me another week, but I finally found a tofu teacher — a wholesale producer of Dafang and bàojiāng 爆浆 "exploding-juice" tofus, two varieties that until recently had never been made outside a remote village near Bijie, Guizhou. Master Luo (罗师傅 Luó Shīfu) and his wife were waiting for me at the base of their factory, a crumbling three-story brick home atop a hill. To their left were two massive wood furnaces, which at 2 a.m. lit up the darkness with dancing flames. To their right was an outhouse. We entered the factory, and an ocean of soy milk fumes blocked the firelight, and it was once again nighttime. In the first production room, a brawny assistant perched atop a sputtering cauldron, stirring with

a pole as tall as he was. Two other production rooms sputtered away. Master Luo guided us up a back stairwell to the living quarters.

A plate of fried tofu awaited. *Eat*, Master Luo directed. I dunked a thin slice in chile powder and took a bite. A delicate burst of juice and sulfury umami danced across my tongue. I tasted another piece, letting it glide through my mouth, gentle as creamy dark chocolate but supple as sashimi. I couldn't take it. Master Luo's eyes shone, and I started to wonder whether he had ever seen a foreigner in person. *I wouldn't teach our craft to just anyone, but I see you as an American friend,* he began. *My family's been making tofu for five generations. If you choose, I will teach you too.*

A common misconception outside of Asian communities is that tofu is just an ingredient. In fact, it's an entire category of proteins.

We got to work immediately. Joining Master Luo's assistant in the boiler room, we fed pail after pail of soaked soybeans through a wet mill, through which their milk cascaded down into a stone-set cauldron as large as a bathtub. The white slurry bubbled away, occasionally crawling up the walls of the cauldron. Our wood furnace had no thermostat; we simply stirred the soy milk harder, letting cool air soothe its fever. Our soy milk took a pass through fine muslin cloth, and we folded in a redolent, green-tinged liquid. Suāntāng 酸汤, sour soup. The soy milk was perturbed. It began collapsing in on itself, its proteins coalescing into little spaetzles, then magnificent, pillowy curds, which floated up to the surface. The soy-milk had started cloudy; now it was clear.

These delicate curds warranted caution. We dared not stir. Scooping them up in rounded, plastic buckets, we lay them down into shallow wooden crates, which were then fitted snugly with a lid, stacked on top of a rickety, rusted workbench, and flattened under the weight of a hand-cranked hydraulic press. Twenty minutes later, we unloaded the molds. The beautiful curds were gone, and in their place was a 5 mm-thick slab of tofu. Master Luo dusted his creation with a sprinkle of salt, MSG, and baked baking soda (baking transforms the soda into more alkaline sodium carbonate). Upon contact, the white skin darkened, taking on a tinge of yellow. The tofu was stacked, carved, and bagged. But it wouldn't be eaten yet — it needed several hours for the seasonings to permeate. It couldn't be eaten anyways. It was still just 3 a.m., the markets weren't yet open, and we still had three more batches to go.

The previous batch of exploding-juice tofu went quickly because we could press it using ordinary box molds. Not so for the Dafang variety. Master Luo ladled a heavy spoonful of curds onto a muslin cloth. The curds jiggled precariously inside his palm. Corner by corner, he lifted the edges of the cloth, allowing the curds to settle against each other into one cohesive lump. Pinching the sides inwards, he rolled a chunky, square burrito, then set it to the side. *We're richer than ever before, eating more meat and less tofu. But we still demand the same quality.* Master Luo seemed both proud and tired. *There is no substitute for hand-wrapped tofu.* A barrel of curds, half my size, stood awaiting.

I had come to Master Luo to learn about the tofu dumpling of love, and it turned

out that his exploding-juice tofu was not much different. Both were playing a game of pH. When we added sour soup to hot soy milk, the pH dropped, causing the proteins to clump into curds. Adding baked baking soda after pressing raised its pH, partially reversing the reaction. The resulting tofu wasn't like soy milk, though, but rather sludgier, creamier, more sulfury. Notably, while we added alkali to both Dafang and exploding-juice tofus, only the latter melted. Tofu needed to pass a certain threshold to liquefy. Any lower, as for the Dafang tofu, and alkali merely seasoned and tenderized.

Occasionally, Shiniang had too many scraps for her pan, so she would throw them on the balcony to dry. A couple days later, the tofu would be brown and shriveled. She would fry them until they puffed like popcorn, and we would eat them with a sprinkle of salt and MSG.

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These hyperlocal dishes are the heart of common vegetarianism, and their counterparts are found all over China. Even in the places you'd least suspect. The northern city of Yinchuan — famous for its whole roast lamb, not its vegan cooking — still had plenty for me to eat.

Chinese people don't reject common vegetarian foods because there is something fundamentally more valuable about meat. They do so because of perceived value — associations of plants with poverty and meat with prosperity.

Master Luo's wife, whom we called Shīniáng 师娘, didn't speak any Mandarin, so we were never able to communicate except through her cooking. Off a lone burner set against the far ashen walls of the living quarters, she would cook us family meals. Potato coins were fried in mustardy rapeseed oil and tossed with a miso-like wheat seasoning. (The seasoning, made by extended family in their village, had no Mandarin name.) Soy milk was siphoned from the production line for fresh tofu pudding, which Shiniang served with cíbā làjiāo 糍粑辣椒 — a fiery and salty fried chile paste. Unwanted edge pieces of exploding-juice tofu, thick like pizza crust, were stir-fried with chiles and green garlic. As I bit into my first bite, I almost spit it back out. The plump, slippery bite couldn't have been anything but poached chicken thigh. But it wasn't!

Corn spaghetti (玉米面 yùmǐmiàn) in a pickled vegetable soup? The noodles, plumper than their wheat counterparts, ferried a smoky, acidic broth made with wok-charred, lacto-fermented mustard greens (酸菜 suāncài). Succulent baby bok choy (上海青 Shànghǎi qīng) floated lazily through the broth; blanched, the greens gave up their own water content and reabsorbed the soup. Incredible.

Peanut tofu with hemp bran (麻麸拌花生豆腐 máfū bàn huāshēngdòufu)? The tofu had a gelatinous quality, nearer to hard-boiled egg whites than bean curd, and the hemp alluded playfully to white pepper. *It's a local specialty*, my server disclosed. *We refine hemp into oil, or boil and crumble it onto food. The taste is smoother and more balanced than peppercorn.*

Tucked behind an elementary school, a small shop advertised four types of oat noodles. The one I tried was like a toothy, ribbed linguini. Dressed with a light chile broth and carrot dice, cucumber sticks, and red and green Thai chiles, it tasted rough and substantial.

In three days in Yinchuan, I tried a dozen vegan foods that you simply couldn't find in China's big cities. And the same thing happened in every place I visited. Wuyuan, a countryside renowned for its canola fields that flower in the springtime, situated near the central-east Jiangnan region, had a breakfast cuisine that was almost entirely vegetarian. Their miniature bāo 包, loaded with chile oil-drenched potatoes, radishes, or tofu, pleated, and steamed, were juicier than a Shanghai soup dumpling. Guiyang, where I worked with Master Luo, had at least eight unique tofu varieties you couldn't find anywhere else. The city of Jinan in Shandong Province, around 250 miles south of Beijing, served a one-of-a-kind seitan called ǒumiànjīn 藕面筋, or lotus wheat gluten. The texture can only be compared to osteoporosis: Silky, gelatinous shells contained what once was whole tissue but now was just holey. These vessels were filled to the brim with spicy raw garlic, Chinese sesame paste, and cilantro, and they cleared your nose like a hearty helping of wasabi.

City by city, village by village, my astonishment gave way to wonder. How were people not talking about these foods?

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Summer waned, and the impending fall term taunted me from across the ocean. It was time to say goodbye. Master Luo sent me off with a bag of popped tofu and one wish: *Don't forget us*.

As the years passed, demand for Master Luo's tofus continued falling. Eventually, during the pandemic, sales flatlined, and his fifth-generation family business could no longer stay afloat. *We're moving to Shanghai*, he told me over WeChat. *Going to sell electronics*.

The ability of Chinese craftspeople and chefs to turn humble plant-based ingredients into dazzling culinary experiences is on par with the highest gastronomy in the West. But to the creators, these foods are rarely seen as "art." They are subsistence. To consumers, these foods are not pride and treasure. They are relics of poverty, discardable afterthoughts en route to modernization.

This trend might appear to affirm a doctrine of economic development: that rising income increases demand for meat. But I wonder if this is the wrong lesson to draw. Chinese people don't reject common vegetarian foods because there is something fundamentally more valuable about meat. They do so because of perceived value — associations of plants with poverty and meat with prosperity.

I think this fact is lost on many animal advocates in the West. Over the last few decades, investors have poured billions of dollars into companies attempting to replicate the experience of eating meat, dairy, and eggs. These products won't succeed, however, on cost, taste, and convenience; they need to win on perceived value.

But there are many ways to arrive at perceived value. There are incredible plant-based foods, with storied histories, all around the world. And there are countless foodies, elsewhere, who might enjoy them. Some of us may crave meat until our dying breath. But some of us have long since forgotten it. We're so immersed in other worlds of flavor that animal flesh is but an afterthought.

72

Read This, Not That: The Hidden Cost of Nutrition Misinformation

Stephan Guyenet

Our daily lives are inundated with misleading claims about nutrition. That's not just distracting—it's harming our health.

ILLUSTRATION BY
Adrian Forrow

"Things all came crashing down when I got a blister on the bottom of my foot that didn't heal," David explained.[1] "It put me in the hospital in danger of losing my foot."

David had spent the last nine years treating his Type 2 diabetes with a low-fat vegan diet, on the advice of a doctor who authored a popular diet book. As part of this doctor's program, David was told that diet is the best treatment for his condition, that the medical system is designed to keep us sick, and that he should stop taking his diabetes medications. Despite the doctor's confident assurances, the diet failed to control David's diabetes. Years of extreme blood sugar levels left him with nerve damage in his feet and eyes, and a reduced ability to heal.

In the hours after I asked my Twitter audience to share how they've been harmed by nutrition misinformation, a steady trickle of stories like David's began appearing in my inbox. One woman was hospitalized for oxalate kidney stones caused by a very-high-vegetable diet she had designed based on paleo and vegetarian sources online. One man lost excessive weight and had to be hospitalized for fecal impaction after following the carnivore diet. Another carnivore dieter had already gone public with his story of requiring a triple coronary bypass after years of believing the claim — common in the carnivore and low-carb diet communities — that the very high LDL cholesterol sometimes caused by these diets isn't harmful.

Reading these accounts, I wondered how many people had been harmed by nutrition misinformation in less extreme ways that are harder to detect. Investigating further, two things occurred to me. First, the public health burden of nutrition misinformation is probably larger than most of us realize. Second, we know very little about it.

1. Name changed for anonymity at David's request.

What Is Nutrition Misinformation?

Any discussion of nutrition misinformation must start by answering a deceptively simple question: What is it? *Misinformation* has been defined in various ways, but here I use it to mean information that is incorrect or misleading. Misleading information can be factually accurate, but lead us to incorrect conclusions. For example, the terms "multigrain" and "wheat" on bread packaging are technically accurate, but may lead shoppers to think they're buying whole-grain bread when in reality it's closer to white. Misleading claims also include those that are supported by some amount of evidence but exaggerate its effect size or level of certainty.

Yet this leads immediately to a thornier question: How do we decide what information is incorrect or misleading? The uncomfortable truth is that there's no bright line that separates accurate claims from misinformation. Sometimes a simple citation check reveals a clear-cut case of

misinformation; for example, a passage cites a study that directly contradicts it. More often, the judgment call is murkier. If a book accurately cites a study but doesn't mention an important limitation that weakens its findings, is that misinformation? What if a book makes an argument that one or two researchers believe, but the rest of the field thinks is hogwash?

Further complicating matters, nutrition is notoriously slippery compared to most other biological or physical sciences. There are many vigorous debates in nutrition in which neither side's arguments are misinformation.

As the director of Red Pen Reviews, a nonprofit that grades the information quality of popular nutrition books, I grapple with these problems often. Despite the challenges, we think it's possible to make useful judgments — with subject-specific knowledge, a formalized scoring system, and the right mindset.

I'll use the term "nutrition misinformation" in this piece with the understanding that it's often hard to judge and it's a flawed proxy for information quality. While it can be hard to define, it's not hard to find, and it shows up in many forms from the obvious to the insidious.

The Water We Swim In

Consider the case of Brian Wansink, former director of the Cornell Food and Brand Lab. Until 2018, Wansink was a prolific and influential researcher who wrote the popular book *Mindless Eating* and helped develop the 2010 Dietary Guidelines for Americans. In 2006, he published a position paper on nutrition misinformation for the Academy of Nutrition and Dietetics, the largest organization of nutrition professionals in the world, admonishing members to "provide consumers with sound, science-based nutrition information and help them to recognize misinformation."

In 2017, a small group of academics called the "data thugs" revealed a number of troubling irregularities in Wansink's papers. Subsequent investigation by the data thugs and others revealed a smorgasbord of scientific shenanigans ranging from sloppiness to possible data manipulation. Wansink eventually resigned his position after Cornell determined he had committed scientific misconduct, and at least 18 of his papers have been retracted. In retrospect, much of his work appears to be sophisticated misinformation.

Although this is an extreme and unusual situation, it shows that misinformation can come from anywhere, including the scientific community — and it can be hard to detect. Misinformation from the scientific community is especially corrosive precisely because scientific research provides the gold standard of information quality.

Yet I believe that people like Wansink are only a small part of the problem. Most of the misinformation that comes from the scientific community isn't due to outright misconduct, but rather suboptimal research practices by presumably well-intentioned people. Failure to follow best practices in study design, analysis, and reporting can, and often does, lead to misleading results.

This is a problem that afflicts all fields of science, but nutrition research faces several key challenges that make it an especially slippery science. First, since it lies at the intersection of countless food properties and many facets of human physiology, nutrition is incredibly complicated. Second, some of the most important nutrition-related conditions, like heart disease, emerge over many years. This makes them hard to study in tightly controlled trials, meaning that much of the evidence in nutrition science comes from

observational studies that have a harder time teasing out cause-and-effect relationships. Third, it's difficult to accurately measure what people eat in their usual lives, including by asking them, as most observational studies do. Randomized controlled trials, in which people are randomly assigned to different diets and compared over time, are a partial solution, but it's hard to get people to stick to the assigned diet unless they're locked inside a research facility (which happens in some studies).[2]

Collectively, these limitations are so serious that some researchers want to relax the standards of evidence for nutrition relative to other areas of science.[3] Others (ahem, perhaps including me) dismiss this as "grading nutrition research on a curve."[4] Even under ideal conditions, nutrition research is hard — and conditions are not always ideal.

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Although public misinformation can come directly from published research, more often it arises as the information passes through the bullhorn of academic press releases and popular media. To illustrate this, let's follow the path of a research finding as it winds its way from a scientific journal article to the public. In September 2022, the *European Journal of Preventive Cardiology* published a study reporting that British adults who drink two to three cups of coffee per day are at a lower risk of developing cardiovascular disease and dying than those who don't drink coffee. Although it's tempting to conclude that coffee is good for the heart and keeps us from dying, this is an observational study and it's not clear that the association is due to the coffee itself, rather than some other difference between people who drink a lot of coffee versus people who don't.

The authors of the paper are fairly cautious in their interpretation; they describe the finding as an association and only obliquely imply that drinking coffee reduces health risks.[5] The academic press release is similarly judicious, although it puts more emphasis on the less cautious statements in the paper. By the time we get to the CNN Health article, the shackles of restraint have been cast off. "Coffee lowers risk of heart problems and early death," the headline proclaims. The article spends two sentences acknowledging that the findings don't necessarily imply cause and effect, then proceeds as if they do.

Although in this example the CNN Health article is the main culprit, research suggests that academic press releases are

2. This is not an exhaustive list of the special challenges that face nutrition science. The inability to use placebo controls, and the fact that one food usually has to replace another, are two other reasons why interpreting the findings of nutrition studies can be difficult.

3. GRADE is a widely used system for judging and communicating the strength of conclusions in systematic evidence reviews. A group of nutrition researchers published an alternative system called NutriGrade that applies a more lenient metric to nutrition studies.

4. Peter Lurie, president of the Center for Science in the Public Interest, described it in this way when we spoke. Researchers from the GRADE working group made a similar argument in their response to the NutriGrade paper that advocates more lenient standards of evidence for nutrition: "lack of blinded randomized controlled trials and the resulting sparse bodies of randomized evidence is not a methodologic shortcoming of the GRADE approach but a limitation of the evidence base."

5. "In concert with the findings from the present study, non-caffeinated compounds are likely responsible for the beneficial effects of coffee consumption on CVD and survival. … Mild–moderate coffee intake of all types should not be discouraged but rather considered part of a healthy lifestyle." See: David Chieng et al., "The Impact of Coffee Subtypes on Incident Cardiovascular Disease, Arrhythmias, and Mortality: Long-Term Outcomes from the UK Biobank," *European Journal of Preventive Cardiology* 29, no. 17 (Nov. 2022): 2240-2249.

a major part of the problem. When press releases exaggerate research findings or provide unwarranted health advice based on them, it tends to be repeated in the news. Carried away by enthusiasm for their own work, researchers themselves are often complicit. "The problems that a lot of scientists complain about are driven by their own choices to approve press release material that is in fact exaggerated," says Chris Chambers, who led research on the media's role in scientific communication. The problem is then amplified as the information passes to journalists and popular nutrition writers, because they often have limited science literacy and a strong incentive to write articles that get clicks.

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Do you know that the scent of vanilla increases blood flow to the penis?[6] That only people with Type B blood can eat all types of dairy and remain in good health?[7] That eating too little salt as a child increases a person's risk of drug addiction later in life?[8] Questionable claims like these abound in popular nutrition books. While these particular claims may be chuckle-worthy, what's less amusing is that Americans buy about 5 million diet books per year, many of them saturated with misinformation.

What is the information quality of the average popular nutrition book? Red Pen Reviews has published 18 reviews of these books, which we score using a structured method that yields percentage scores for scientific accuracy, reference accuracy, and healthfulness. Among these books, scientific accuracy scores range from 20% to 95%, with an average of 48%.[9] Reference accuracy and healthfulness do somewhat better with average scores of 65% and 67%.[10] This suggests that the information quality of popular nutrition books is highly variable, low to medium on average, and particularly poor in scientific accuracy.

Of course, nutrition books are only a fraction of the nutrition media environment. How common is nutrition misinformation in other media? Very little research has been done on this to date, and the few studies that have been published cover only narrow slices of the nutrition media environment. A 2019 review on health-related misinformation shared on social media identified only three studies on nutrition misinformation; across very different contexts (Italian social media, YouTube videos on anorexia, and Arabic Twitter), misinformation was common. An additional study searched the scientific literature and popular media for "myths and presumptions" about obesity — mostly related to nutrition — and concluded that "false and scientifically unsupported beliefs about obesity are pervasive in both scientific literature and the popular press."

Although the problem hasn't been

6. *The Bulletproof Diet*, p. 208.

7. *Eat Right 4 Your Type*, p. 174.

8. *The Salt Fix,* pp. 100, 107.

9. For reference, we define scores of 0%-49%, 50%-74%, and 75%-100% as indicating low (red), medium (yellow), and high (green) information quality. A scientific accuracy score of 48% means that a book's claims are weakly supported by evidence, on average. Before converting to a percentage score, we use a 0-4 semi-quantitative scoring system. Forty-eight percent corresponds to a score of 2, which for scientific accuracy criterion 1.1 is defined as "Overall, relevant evidence is intrinsically weakly convincing but is consistent with the author's claim. Or, relevant evidence is intrinsically convincing but only weakly supports the author's claim."

10. Reference accuracy scores how well a citation supports the passage it's associated with. Healthfulness is a composite of scores for how well an intervention would address the target condition in the target population, how it would impact general health, and whether it would supply all essential nutrients and important nonessential nutrients like fiber.

quantified well, anyone who has used the Internet will recognize that fishy nutrition claims are common there. Take for example the ancestral lifestyle advocate Brian "Liver King" Johnson, who likes to throw spears and pose shirtless with enormous raw beef livers. With nearly 6 million followers across social media, Liver King is an influential source of diet and lifestyle advice. Until recently, he insisted that his "all-natural" bodybuilder physique was entirely due to his "ancestral" diet, exercise, and lifestyle. Late in 2022, he was forced to come clean after a video exposed his extensive use of bodybuilding drugs. Now consider that Liver King is just one of thousands of diet influencers across the Internet.

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It may not shock you to learn that a man who looks like a professional bodybuilder and wears animal pelts on his head owes his physique more to drugs than to beef liver. But nutrition misinformation isn't always so obvious. At times, it's so subtle and pervasive that it's simply the water we swim in. Walking through the grocery store, you may have noticed that many foods and supplements make health claims of one kind or another. Since explicit claims about the impact of a food on specific health conditions are regulated in the U.S. and Europe, health claims are usually more indirect. They're typically statements about a food's nutrient content like "low fat" or vague structure/function claims like "supports brain health," which are only lightly regulated.

To explain how these health claims could be harmful, consider Tang, a drink that is little more than flavored sugar water. The citrus-adjacent beverage advertises that it provides 100% of a person's daily requirement for vitamin C. Although vitamin C is not a nutrient of concern for the U.S. public and therefore likely has no nutritional benefit for most people, this may give consumers the impression that Tang is healthier than it is, increasing the likelihood that people will buy it and drink it. As we saw previously, breads labeled "multigrain" and "wheat" often confuse consumers into thinking they're buying healthier whole-grain bread, when it's actually closer to refined white bread. Studies tend to suggest that health claims on product packaging increase the likelihood that people will buy and consume those foods and beverages.

Health claims on food packaging can be informative and may lead to healthier choices in some cases. Nonetheless, *some* of these claims are harmful because — despite being technically accurate — they mislead consumers into buying food that isn't as healthy as they think it is. Although the impact of this misdirection is probably subtle, it has the potential to happen each time we buy food, so it could add up to a substantial public health burden. Yet its impact remains largely unknown.

It seems likely that nutrition misinformation is pervasive. Why is there so much of it, and why do people fall for it?

We Are What We Eat

My father once told me that the three topics people are the most irrational about are religion, politics, and nutrition. While you may or may not agree with this, these topics have two things in common that favor misinformation: They relate strongly to our identities, and they're hard to get definitive answers about.

The foods we eat, and how we eat them, are tightly intertwined with our identities. We're attached to the foods that represent our cultures and our families. We're

People who are suffering want relief, and if none is available from their doctor or other conventional sources, they may turn to alternative sources that offer sympathy, community, and extraordinary claims. And there are plenty of people ready to make them.

attached to our personal eating habits. We display our values and discernment to others through the foods we select. And as something we put into our bodies several times a day, food has a personal intimacy that most areas of science don't.

The internet has also facilitated our atomization into various diet tribes. Some even describe themselves in these terms, like the World Carnivore Tribe on Facebook. On Twitter, users form communities and announce their affiliations using icons and emojis: steak emojis for carnivores and "V" icons for vegans.

Adopting a set of tribal beliefs, whether accurate or not, may play an important social role by signaling and reinforcing group affiliation. Once a person has identified with a tribe, they tend to adopt tribal beliefs, minimize the downsides of those beliefs,[11] and defend the tribe against perceived attacks from alternative ideas. This dynamic can favor misinformation and cause people to resist corrective evidence.

To understand why this happens, we have to understand the appeal of popular diets and the communities that surround them: they offer solutions to peoples' problems. "A lot of people are just desperate to not be in pain," explains Alan Levinovitz, associate professor of religion at James Madison University. Levinovitz is the author of the book *Natural: How Faith in Nature's Goodness Leads to Harmful Fads, Unjust Laws, and Flawed Science*, which draws parallels between religion and diet cultures. "Nutrition misinformation is part of every single magico-religious tradition and is part of a broader area of misinformation, which is misinformation around healing." In addition to providing community, Levinovitz argues, diets can provide a sense of hope for people who suffer from health conditions or worry about developing them. Diets give us a feeling of control over our vulnerable human lives. They also offer simple rules to navigate life's thicket of daily decisions more easily. In these ways, diets can fill a similar psychological niche as religion (this is not to deny that diets can have physical health benefits as well). From this perspective, diets are more than just food, and believing misinformation is more than just a cognitive error.

People who are suffering want relief, and if none is available from their doctor or other conventional sources, they may turn to alternative sources that offer sympathy, community, and extraordinary claims. And there are plenty of people ready to make such claims.

Consider two books, both written in an accessible style for a general audience. One, *Why Calories Count*, argues that century-old

11. For example, the carnivore diet and to a lesser extent low-carbohydrate diets in general, appear to increase LDL cholesterol in some people. A common belief in the carnivore diet community is that high LDL cholesterol is harmless and possibly even beneficial. This is contrary to a large and convincing body of scientific evidence. The vegan diet, on the other hand, tends to lower LDL cholesterol.

findings showing that calorie intake impacts body weight are still true. Another, *The Calorie Myth*, argues that experts have been wrong about calories all along. Which do you think sold more copies? If you guessed the second, you're correct.

Research suggests that misinformation often spreads more readily than accurate information and this is correlated with its greater novelty. Novel and exaggerated claims command more attention and sell more books, so authors have a strong incentive to make them and publishers have a strong incentive to print them. Compounding the problem, there is little disincentive against publishing misinformation because the general public usually doesn't have the resources to critically evaluate it. Inaccurate or misleading nutrition claims rarely come back to bite the author. In fact, when delivered skillfully, the dividends of these types of claims are attention, respect, and money. Yet their impact on the audience is often not as beneficial.

Dying for Health

Sifting through the academic literature on nutrition misinformation, I was struck by the absence of answers to obvious questions. In particular, I wasn't able to find a single estimate of the total public health burden of nutrition misinformation. So I built a model.[12] It estimates the number of premature deaths caused by nutrition misinformation each year in the U.S.

It's not hard to understand why no one has done this before. Since we don't have estimates of the total impact of nutrition misinformation on eating behavior, we can't hope to infer a precise estimate of its impact on health. Academic researchers probably aren't excited about publishing a model whose output relies on guesses and has a 30-fold uncertainty range. So why do it?

First, it allows us to place plausible bounds around our estimate. Second, it identifies our main sources of uncertainty and helps us think about how those might be addressed in the future. Third, it provides a foundation on which more precise models can be built.

Conceptually, the model is very simple. It multiplies together three parameters:

1. How many people die each year in the U.S.?
2. What percentage of all deaths are premature and caused by suboptimal nutrition?
3. What percentage of suboptimal nutrition is caused by nutrition misinformation?

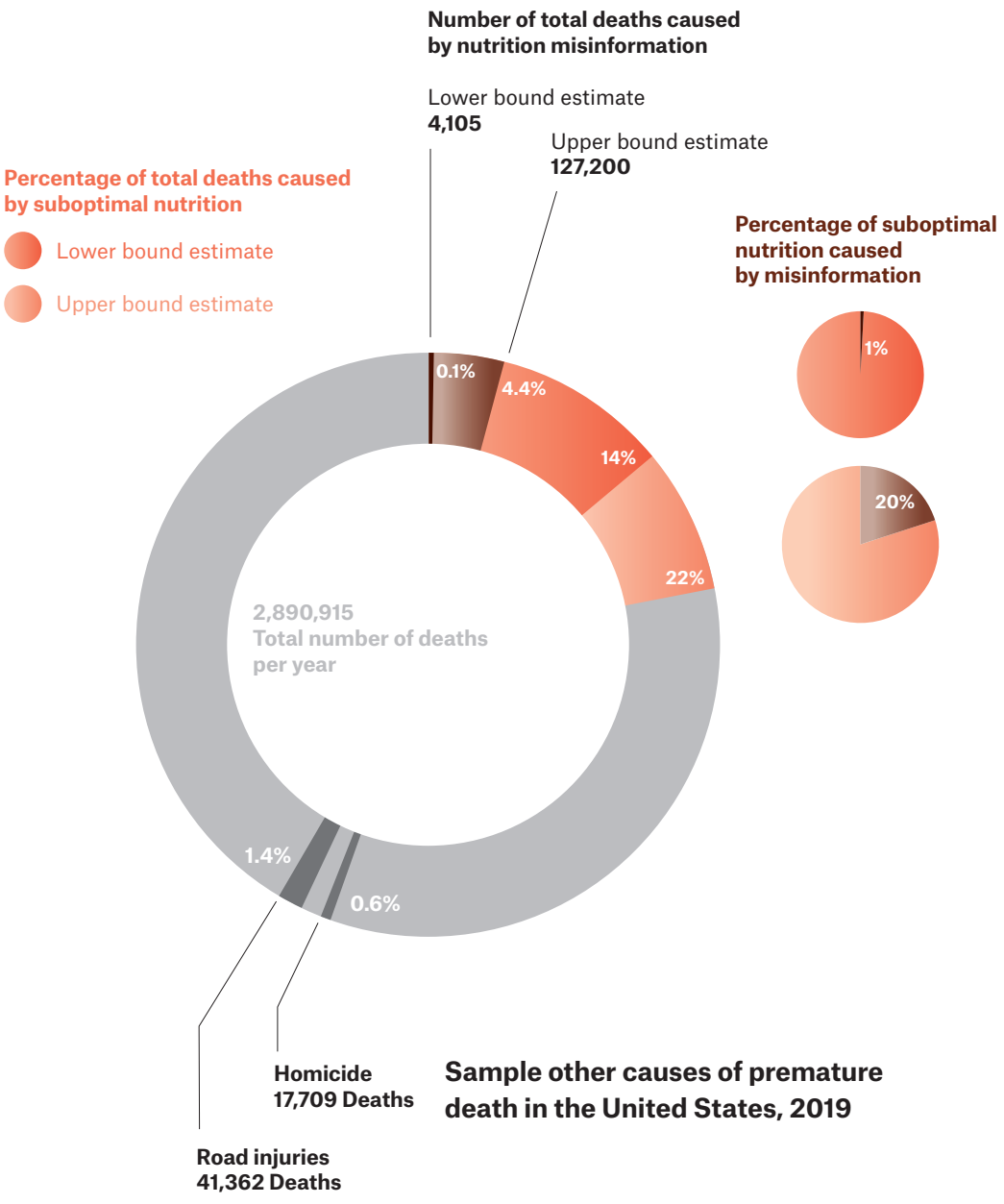
About 2.9 million people die each year in the U.S. What percentage of these are premature deaths caused by suboptimal nutrition? The published estimates I found range from 14% to 22%. This implies that about 400,000 to 600,000 people die from suboptimal nutrition in the U.S. each year. Although it's fair to be skeptical of these figures, I don't think this is the model's main source of uncertainty so I take them at face value.

The model's main source of uncertainty is the percentage of suboptimal nutrition that is caused by nutrition misinformation. I reached out to several experts, and my Twitter audience, to brainstorm ways to estimate this parameter, but I didn't come up with anything workable. So this is where we enter the world of plausible guesses. I think nutrition misinformation impacts average eating habits to some degree, but I don't think it's one of the main reasons most people eat a suboptimal diet. Obvious factors like cost, convenience, taste, habits, and culture are probably more important for most people. Therefore, I take 1% as my lower bound and 20% as my upper bound.[13] I also use corresponding lower-bound and

12. Link to the full model available at asteriskmag.com.

13. This is my 80% confidence range.

Premature deaths caused by nutrition misinformation in the United States, 2019



Sources: Institute for Health Metrics and Evaluation; Renata Mischa et al., "Association Between Dietary Factors and Mortality From Heart Disease, Stroke, and Type 2 Diabetes in the United States," *JAMA* 317, no. 9 (2017):912-924; Fanny Petermann-Rocha et al., "Nonlinear Associations Between Cumulative Dietary Risk Factors and Cardiovascular Diseases, Cancer, and All-Cause Mortality: A Prospective Cohort Study From UK Biobank," *Mayo Clinic Proceedings* 96, no. 9 (2021):2418-2431; Lukas Schwingshackl et al., "Diet Quality as Assessed by the Healthy Eating Index, Alternate Healthy Eating Index, Dietary Approaches to Stop Hypertension Score, and Health Outcomes: An Updated Systematic Review and Meta-Analysis of Cohort Studies," *Journal of the Academy of Nutrition and Dietetics* 118, no. 1 (2018):74-100.

upper-bound estimates for the percentage of all deaths that are caused by suboptimal nutrition.

Using these inputs, the model estimates that between 4,000 and 127,000 Americans are killed by nutrition misinformation yearly. If you don't like my guesses, you can make your own: As a rule of thumb, for each 1% divergence from an optimal diet that is caused by nutrition misinformation, 5,000 Americans die each year.

I think it's plausible that nutrition misinformation could kill more Americans each year than gun homicides and motor vehicle accidents combined.

For context, the U.S. Department of Transportation estimates that about 43,000 Americans were killed in motor vehicle accidents in 2021 — an unusually deadly year. The Centers for Disease Control and Prevention (CDC) estimate that about 19,000 Americans were killed in gun homicides in 2020. Both statistics have triggered urgent national conversations about public safety. For the death count from nutrition misinformation to exceed each of these individually, it would only have to account for about 9% of our suboptimal diet choices. I think it's plausible that nutrition misinformation could kill more Americans each year than both combined.[14]

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Dying is bad, but so is wasting money, and in the U.S. we waste a lot of money on ineffective dietary supplements and health foods. In 2020, Americans spent about $50 billion on dietary supplements, or $194 per adult on average. A subset of these supplements are well supported by evidence, but most are probably ineffective. For example, Americans spend about $2.1 billion per year on weight loss supplements, and despite grandiose claims from the likes of Dr. Oz, not one of these has been shown to cause clinically meaningful weight loss.[15] The ineffectiveness of weight loss supplements is particularly striking when compared with the new generation of weight loss drugs like Wegovy, which causes 15%-18% loss of body weight in people with obesity when paired with diet and exercise advice.

Nutrition misinformation can also harm us by leading us to forgo effective medical treatment. When Steve Jobs was diagnosed with a typically treatable form of pancreatic cancer in 2003, he initially declined surgery, instead trying to treat it with a vegan diet and other alternative treatments. This was ineffective, and nine months later he had the surgery. While it's impossible to say whether Jobs' flirtation with alternative remedies is the reason why he eventually succumbed to

14. This is more of a stretch if we think about it in terms of years of life lost rather than number of deaths. The reason is that nutrition-related premature deaths tend to kill people who are middle-aged and older (mostly from heart attacks and strokes), whereas motor vehicle crashes and firearm homicides tend to kill younger people.

15. Defined as at least 5% average loss of body weight sustained over at least one year, which is a common threshold for clinically meaningful weight loss.

his cancer, we do know that, on average, cancer patients who choose alternative treatments (which may include nutritional supplements and/or special diets) instead of conventional cancer treatment are about 2.5 times as likely to die during follow-up as patients who receive conventional treatment.

Nutrition misinformation can also foster an irrational fear of ordinary foods. According to the popular book *The Carnivore Code*, most plant foods are riddled with toxins, meat that isn't pasture-raised is suboptimal, and even tap water is a questionable "fluoride, chlorine, and pharmaceutical-enriched liquid." The way to avoid obesity, disease, depression, and low libido is a strict diet of pasture-raised meats and organs like liver and testicles. While it's normal and healthy to have rules around what we eat, when rules become irrationally rigid and enforced by fear they can cross the line into disordered eating. The archetype of this is orthorexia nervosa, an eating disorder in which people excessively restrict the types of foods they eat, as opposed to the total amount of food as in anorexia nervosa. This can cause serious psychological distress and disconnect people from their culture, friends, and family. People who follow *The Carnivore Code* and other strict diets don't necessarily have an eating disorder, but it's not hard to see how the arguments might incline some of them in that direction. And while a strict carnivorous diet is an extreme example, less extreme diets like gluten-free, plant-based, and low-carb diets can have a similar impact in susceptible people.[16]

Trust in institutions is a fundamental building block of a well-functioning society. I believe nutrition misinformation has a subtly corrosive effect on society by reducing public trust in scientists, nutrition professionals, doctors, and the government. A common theme in popular nutrition books is a contrarian narrative that paints these groups as incompetent, biased, and/or corrupt.[17] Delegitimizing conventional nutrition authorities lets authors fill the void with their own arguments, which in my experience are usually weaker than those they seek to dismiss. That said, conventional nutrition authorities do make mistakes, and sometimes big ones.[18] Nutrition science is hard, most people are naturally overconfident in their beliefs, and some people have real conflicts of interest. For these reasons, we should be somewhat skeptical of conventional nutrition authorities! But probably not as skeptical as certain nutrition contrarians would like us to be.

Setting the Table

How can we address nutrition misinformation? The first challenge is that we don't know much about it. How much does it guide our eating behavior? What are its main sources? What is its public health

16. To be clear, I'm not arguing that these diets are bad overall, simply that some of the information associated with these diet communities can foster irrational fears and disordered eating in susceptible people.

17. Science journalist Gary Taubes makes this argument a centerpiece of his influential nutrition books. For example, a scathing passage from page 451 in *Good Calories, Bad Calories* argues that researchers in the fields of "nutrition, chronic disease, and obesity" are not real scientists, and what they do is not real science. Much of the rest of the book details alleged incompetence in research and government nutrition policy. Similar arguments have been repeated in a number of other popular nutrition books, including Nina Teicholz's book *The Big Fat Surprise: Why Butter, Meat and Cheese Belong in a Healthy Diet*.

18. The biggest one that comes to mind for me is the idea, most prevalent in the 1980s to 2000s in the U.S., that low-carbohydrate diets are dangerous. The idea was gradually slain by a steady trickle of randomized controlled trials and observational studies.

impact? And, fundamentally, what even counts as nutrition misinformation?

It's easy to pen a concise definition of nutrition misinformation, but the devil is in the details. As we've seen, nutrition is a complex and uncertain science, and there's no bright line between accurate information and misinformation.

However, I believe it's nevertheless possible to judge the information quality of nutrition claims in a useful, if imperfect way. This topic is too complex to fully address here, but I think the following principles are important. First, due to the uncertainty involved, we shouldn't necessarily try to identify nutrition misinformation per se. A better approach is to judge the information quality of claims using a semiquantitative scale, like the zero-to-four scale we use at Red Pen Reviews.[19] Second, scoring should be done according to a well-defined method that's designed to maximize informativeness and consistency and minimize human bias. Third, reviewers need both nutrition-specific expertise and a more general ability to think critically about the strength of different evidence types.

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Once we've identified low-quality nutrition information, what do we do about it? It's important to point out that we're already addressing this problem to some extent. In the U.S. and the European Union, health claims on foods and supplements are regulated, and watchdog organizations like the Center for Science in the Public Interest help enforce this regulation through regulatory letters and in the courts. Foods and supplements cannot make direct claims about treating or preventing specific health conditions without convincing evidence. Although largely invisible to the public, and not completely effective, government regulation of health claims on foods and supplements is a vast dam holding back a churning sea of nonsense.

Yet across most nutrition media, there is very little protecting the public from misinformation. Health claims in diet books aren't regulated, publishers rarely fact-check them, and authors and publishers have little incentive to maintain high information quality because the public doesn't have the resources to critically evaluate most of their claims.

An analysis of the books we've reviewed so far at Red Pen Reviews reveals that there is no correlation between our overall information quality score for a book and its Amazon.com rating. While book reviews in respected media outlets like *The New York Times* and *The Atlantic* may appear more informative, most aren't written by experts and don't fact-check even a single citation in the book they're reviewing. One-off reviews by experts can be informative but they aren't available for most books and they may not be easily accessible to the public. The public simply does not have a reliable way to gauge the information quality of most popular nutrition books, and I would argue, nutrition media in general.

This is why we need organizations that assess and communicate the information quality of popular nutrition media in a rigorous and accessible way. Not only does this give the public a much-needed resource for judging the information quality of nutrition media, it provides a long-term incentive for authors to publish better information in the first place. I'd

19. The Fact Checker column in The Washington Post uses a similar scale to judge the factuality of political rhetoric — from one to four pinocchios.

20. Credit to Alan Levinovitz for getting me to think about this.

like to see these types of efforts expand into other media classes like social media and news media, and other domains of health and performance like medicine and athletics, but they will need more attention and resources to realize their potential.

***

Social media is a major conduit for misinformation, so voluntary or legislated anti-misinformation measures could potentially apply some portion control to the public's nutrition misinformation diet. Research suggests that a combination of modest anti-misinformation measures could reduce the spread of viral political misinformation on social media by more than half. For example, platforms could curtail the algorithmic amplification of misinformation topics, reducing their impact without having to remove them outright. Or they could "nudge" users to consider information accuracy before sharing content more likely to contain misinformation, which reduces the spread of misinformation. However, studies like this haven't yet been done on nutrition misinformation specifically. In addition, curtailing nutrition misinformation on social media requires being able to identify it in the first place, which can be challenging.

Another strategy for combating misinformation is to give the public stronger signals of the quality of online information sources. One project along these lines is NewsGuard, a browser extension that uses a green-red signal and a zero-to-100 "trust score" to indicate whether a news website meets basic standards of credibility and transparency. Nothing like this currently exists for nutrition media.

We should also work toward addressing misinformation in scientific research and its translation through university press releases and news media. There are many possibilities for addressing this problem, including emphasizing best research practices in scientific training and journal requirements, identifying and addressing the countless "predatory journals" that don't meet scientific standards, supporting watchdogs like the "data thugs" and Retraction Watch, improving how researchers communicate their findings to journalists, and training journalists to communicate science more accurately. Since we know that many studies don't replicate, public communication about science should focus on bodies of evidence rather than the unreliable churn of the latest nutrition studies.

Ultimately, we may also need to ask a deeper question: How do we address the suffering and alienation that drive some people toward nutrition misinformation? If we're going to pull the rug out from under beliefs that give people hope and a sense of control over their lives, can we offer them a better alternative?[20] I don't have answers to these questions, but perhaps we should consider how society might meet these needs in a more constructive way.

Given its apparent importance, I think we should be investing more resources in studying and addressing nutrition misinformation. I hope to see a world where people like David don't have to face amputation before figuring out that the diet they're on isn't as infallible as they were told.

86

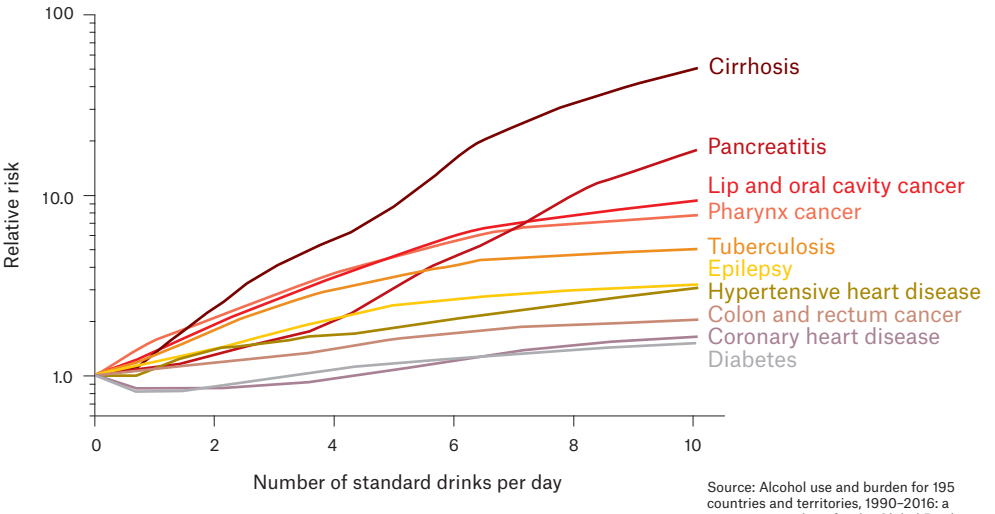
My Primal Scream of Rage: The Big Alcohol Study That Didn't Happen

Dynomight

Five years ago, the National Institutes for Health cancelled the largest study on alcohol ever planned. Here's what happened—and why you should be mad too.

An earlier version of this text appeared at dynomight.net

Health risks of alcohol consumption



Source: Alcohol use and burden for 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016.

What does drinking do to your health? We can say two things with confidence:

1. Drinking is associated with lots of health problems.

2. Heavy drinking is bad for you.

Above is a graph of some associations.

Someone who averages 10 drinks per day is 50 times more likely to get cirrhosis than someone who doesn't drink at all (controlling for age, sex, and drinking history).

This looks bad, but there are two caveats. First, it doesn't establish causality. It *could* be — if all you had was this figure — that cirrhosis causes hormonal changes that in turn create the urge to drink more.

But we *do* know that heavy drinking is bad. That's partly because we know *how* alcohol causes problems. It causes cirrhosis by destroying liver cells. It causes cancer by getting converted to acetaldehyde and then damaging DNA. There are also randomized controlled trials (RCTs) that take heavy drinkers and get them to drink less. These inevitably show improved health (either health outcomes or biomarkers like blood pressure).

The second caveat is the little dip in relative risk for diabetes and heart disease around 1-2 drinks. Some people think alcohol is causing this dip. Lots of mechanisms have been proposed: Maybe it reduces inflammation. Or maybe it impairs the cells that build up plaques in arteries. Or maybe it creates a hormonal imbalance that changes blood pressure regulation. Or maybe it increases HDL cholesterol or insulin sensitivity or adiponectin levels.

Or, maybe alcohol doesn't help diabetes and heart disease at all. Mathews et al. (2015)[1] tried to model how alcohol affects the heart, ending up with a terrifyingly tangled figure.

Alcohol does a *lot* of different things and interacts with a *lot* of other factors. It's great to try to unravel all this, but I don't trust anyone who says they understand everything with confidence.

If alcohol doesn't improve heart health, then why the dip? Well, it could just be that the

1. M.J. Mathews, L. Liebenberg, & E. H. Mathews, "The mechanism by which moderate alcohol consumption influences coronary heart disease," *Nutrition Journal* 14, no. 33 (2015).

same people who drink moderately are also more likely to exercise and eat well.

So we don't know if moderate drinking is bad for you. It almost certainly causes harms like cancer, but it might help heart disease enough to offset those harms. In the US, around 20% of adults drink 1-2 drinks per day. Even if the effects are modest, the collective impact is huge. Second perhaps to caffeine, alcohol is humanity's favorite drug. We need to know what it does.

This is the story of a trial that came close to answering this question and then exploded. At first, this looks like a simple story of corruption, but when you look closely it's a very *complicated* story of corruption.

We Need an RCT

You might be thinking, "What we need to do is compare the health of people who drink different amounts, while controlling for income, diet, education, exercise, et cetera." The problem is that "controlling" for things is a dangerous business. It requires tons of different assumptions, like what you control for, how you code stuff, and how you model everything. For example, if you "control for exercise," do you measure the number of hours people exercise each week? Should you distinguish different kinds of exercise? Reasonable people can disagree about these choices. For alcohol, reasonable people do disagree. Some, like Ronksley et al. (2011)[2] find a strong association between moderate alcohol consumption and improved cardiovascular health, and argue that the association is likely causal. But others, like Goel et al. (2018)[3] are unconvinced and suggest there could still be confounding variables, while Wood et al. (2018)[4] do a meta-analysis of observational studies that suggests even small amounts of alcohol hurt cardiovascular health.

There's also some recent research using Mendelian randomization, which suggests alcohol could be *bad* for cardiovascular health. The idea is that a variant of the ADH1B gene makes it hard to metabolize alcohol. People who have it drink less. If you assume that the gene is random in the population and that it's *causing* reduced drinking, then you can treat it like a random assignment to drink less. Holmes et al. (2014)[5] did this and found that carriers of ADH1B had better cardiovascular health by every measure. This suggests alcohol makes cardiovascular disease worse, not better.

So what do we do? We take the long, slow, hard path:

1. Get a large group of people.
2. Tell some of them to drink moderately, tell the others not to drink at all.
3. Wait years, monitoring people to make sure they are actually drinking (or not) like they're supposed to.
4. Follow up and see which group is healthier.

Lots of things make this difficult. Because the expected effects aren't huge, you need a *large* group of people. Because culture and genetics vary, you need people from around the world. Because diseases take a long time to show up, you need to wait years. And imagine the challenge of telling people how much to drink and then making sure they follow instructions.

An international effort monitoring thousands of people around the world for years — does that sound expensive?

2. P. E. Ronksley, S. E. Brien, B. J. Turner, K. J. Mukamal, W. A. Ghali "Association of alcohol consumption with selected cardiovascular disease outcomes: a systematic review and meta-analysis" *British Medical Journal* 342:d671 (2011).

3. S. Goel, A. Sharma, & A. Garg, "Effect of Alcohol Consumption on Cardiovascular Health," *Current Cardiology Reports* 20, no. 19 (2018).

4. Angela M Wood, Stephen Kaptoge, Adam S Butterworth, Peter Willeit, Samantha Warnakula, Thomas Bolton, et al., "Risk thresholds for alcohol consumption: combined analysis of individual-participant data for 599 912 current drinkers in 83 prospective studies" *The Lancet*, 391, no. 10129 (2018).

5. M. V. Holmes, C. E. Dale, L. Zuccolo, R. J. Silverwood, Y. Guo, Z. Ye, et al, "Association between alcohol and cardiovascular disease: Mendelian randomisation analysis based on individual participant data," *British Medical Journal* 349:g4164 (2014).

A Solution

Back in 2013, the NIH's National Institute on Alcohol Abuse and Alcoholism (NIAAA) got interested in funding this. They figured it would cost on the order of $100 million for the full trial. This doesn't seem crazy given the NIAAA's $500 million annual budget, but the NIAAA has lots of other priorities and didn't feel they had the money.

You know who has a lot of money, though? The alcohol industry. Worldwide, $85 million of booze is sold every 30 minutes. In principle, the industry could directly fund a study, but who would trust it?

In 2016, it looked like the NIAAA had found an elegant solution:

- Five alcohol companies would donate money for a trial.
- The NIH would ask researchers to send proposals for how they'd run a trial.
- The NIH would choose the scientifically best proposal, just like they do with any government-funded grant. The donors would have no influence on the process.
- To make the results trustworthy, there would be a "firewall", with no communication between the industry and the research team.

Sounds promising. But if we go forward a couple of years, everything suddenly blows up.

June 15, 2018

NIH cancels $100 million study of moderate drinking as inescapably compromised

What happened? You might imagine banal corruption, with cocaine and overseas bank accounts, but it's nothing like that.

The real story is a much more interesting cocktail of science, academia, bureaucratic maneuvering, ambition, politics, capitalism, the "deep state," secret emails, and slippery ethical slopes. It's a huge stroke of luck that we know about any of this. You have to ask how often similar things happen and *don't* blow up.

Timeline

If you're brave, you can read the 165-page report the NIH prepared before canceling the program. But I warn you: it's mostly out-of-order redacted emails written by people who wanted to conceal what was happening. There's an executive summary, but it's written in a frustratingly bureaucratic style. There are also newspaper stories, but they don't try to give the full timeline.

After way too much time reconstructing things, here's the full story as best as I can tell.

2001-2013. Kenneth Mukamal, a physician at Beth Israel Deaconess Medical Center and faculty member at Harvard Medical School, published many papers that argue that moderate alcohol consumption has health benefits, usually for heart disease or diabetes. During the same period, John Krystal, a psychiatrist and professor at Yale, also published many papers on alcohol, mostly focusing on addiction and mental health. (Many other researchers were involved in this study, but these two were most prominent.)

Here's a characteristic sample of Mukamal's 189 papers on alcohol:

> In summary, all of this evidence implicates alcohol consumption rather than lifestyle factors ... as the primary factor in the lower rates of cardiovascular disease found among moderate drinkers. (2001)

> In this large cohort study of older adults, there was a lower risk of congestive heart failure associated with moderate drinking compared with abstention. (2006)

> There is convincing evidence that light-moderate, non-binge alcohol intake reduces the risk of coronary heart disease. (2009)

> In 9 nationally representative samples of U.S. adults, light and moderate alcohol consumption were inversely associated with cardiovascular disease mortality, even when compared with lifetime abstainers. (2010)

> Long-term moderate alcohol consumption is inversely associated with all-cause and cardiovascular mortality among men who survived a first myocardial infarction. (2012)

You may notice that all of them find that moderate drinking has health benefits.

Early 2013. Some NIAAA staff were convinced that moderate drinking is good for you, and an RCT could prove it conclusively enough that doctors might recommend it to patients like they do with aspirin now. They had the idea of getting the alcohol industry to fund the study, but faced two problems. First, the alcohol industry wants lots of details before forking over any cash. Second, the NIAAA isn't allowed to solicit from industry. They tried to get around these problems by having outside researchers (including Mukamal and Krystal) meet with industry to give details on how such a trial might work. This created a dynamic where everyone (the NIAAA, the alcohol industry, Mukamal) wanted to coordinate with each other, but maintain a pretense of being isolated. There was lots of scheming about how information should flow to maintain this pretense.*

They settled on the strategy of having the industry make a "gift" to FNIH, the not-for-profit arm of the NIH that was set up to take industry money and then do NIH-stuff with it.**

At the same time, they decided that they could get rid of the appearance of soliciting by getting an external researcher to make the case. They settled on Kenneth Mukamal. The record is silent on exactly why they chose Mukamal. My guess is that it was partly because of Mukamal's pro-alcohol research record, and partly because it helped to overcome some apparent issues regarding collaborations between Harvard and Beth Israel (BI).***

The NIAAA wanted someone else to present the idea of the study to overcome their prohibition of solicitation, even though they'd obviously set this whole thing in motion. The alcohol industry was excited about what they heard directly from the researcher, but wanted the plan to come "from NIAAA."

July 12, 2013. The NIAAA published NOT-AA-13-004. This was a "planning grant," which basically means that the NIH would give you some money to do some work that would allow you to successfully submit a much larger grant soon. By NIH rules, this was a public opportunity, meaning any researcher could submit and win the grant if they had the best science. Yet they obviously wanted "their" PI to win:

> I would be fine with a one-year term; I think the PI can easily meet that, given that we have gone over in a lot of detail what the ultimate RCT should look like; plus that tight a timeframe would discourage other applicants who have not even begun to think about this idea yet!

They stacked the deck in three ways. First, they asked for an extra-short deadline, and said that applications would need to get preapproval before submitting a grant. Both of these tricks were overruled by NIH central, though "prior consultation" was still "strongly encouraged." Second, rather than a typical open-ended call for research, they asked for a specific trial to be done — coincidentally exactly the trial Mukamal wanted to do. Third, NIAAA staff decided to physically travel to Boston to help Mukamal write the grant. Since this was totally forbidden, they went another way.

> I am going to Boston for a brief "vacation". It would be entirely coincidental if I happened to spend a day with some friends who might be in the process of writing a U34 grant application, and if we also just happened to have some "hypothetical" discussions about details of such a study. This is a purely personal, i.e., NOT NIAAA-funded or authorized, trip.

All the scheming from the NIAAA worked. Ultimately, they received exactly one application: from Mukamal.

November 21, 2013. There is a meeting at the Distilled Spirits Council in Washington, DC between the alcohol industry, the NIAAA, and three researchers, including Mukamal and Krystal. Someone from industry later reported to NIAAA staff that "he was tremendously enthused about the project" and that they would need similar meetings with other companies. He specifically wanted to hear more from "the guy from Harvard and the guy from Yale" — in other words, Mukamal and Krystal.****

According to *The New York Times*, representatives of beverage conglomerates Anheuser-Busch InBev, Heineken, and Diageo later confirmed that these meetings were

*

From: [redacted] (NIH/NIAAA) [E]
Sent: Friday, June 14, 2013 01:53 PM
To: [redacted] (NIH/NIAAA) [E]; [redacted] (NIH/NIAAA) [E]
Subject: RE: COMMENTS/EDITING, please

[redacted], as I've raised, I don't see how we can include Alternative C, at all, without the appearance that we're (A) soliciting funding, which we're not allowed to do, and (B) specifically soliciting it from industry. We just flat out can't come out and say that.

I don't know how we could partner with the FNIH to perhaps allow THEM to undertake such an effort, but I can't support that language as written. It's not just a red flag, it's a screaming red flashing neon light.

**

I really am very concerned about anything being presented to industry from NIAAA directly. That could constitute "solicitation" of a gift, which we absolutely cannot do. The best timeline for something like this would be for the gift to come to F-NIH with interest in a study in this area of research from which we would "draft a proposal" in response. If they are concerned about having NIH backing, by giving it to the Foundation, that worry should be alleviated. We have to be very careful not to be seen as driving this process.

***

From: [redacted] (NIH/NIAAA) [E]
Sent: Friday, June 14, 2013 11:57 AM Eastern Standard Time
To: [redacted] (NIH/NIAAA) [E]
Subject: URGENT - Can I do this?

[redacted]

When we discussed this briefly after the senior staff meeting this week, you said the best way to get a sense of industry's interest in this was to have an extramural researcher make the approach.

Much to my surprise (as I told you I didn't think [redacted] or [redacted] could/would, and [redacted] had seemed even more skittish than [redacted] when we were discussing writing papers in collaboration with the BI), [redacted]@ harvard (who works with [redacted], and who thus will be part of the project) has done this ! In response, industry has requested a written document (preferably from NIAAA, whom they would rather deal with, instead of directly with any of the potential actual researchers). The turnaround time for this request is apparently "immediate", as they want to discuss it at a Board Meeting next week.

Assuming I can get my "draft business plan" into a non-draft state over the weekend, can I send it to them ? And, if so, would I need to run it by [redacted] first?

****

From: [redacted] (NIH/NIAAA) [E]
To: [redacted] (NIH/NIAAA) [E] ; [redacted] (NIH/NIAAA) [E] ; [redacted]
Sent: Friday, November 22, 2013 2:54 PM
Subject: Feedback from DISCUS

[redacted], [redacted], [redacted],

I had a phone call from [redacted] a few minutes ago. He wanted to tell me that he was tremendously enthused about the project and the presentation yesterday and wanted to thank us for being willing to come and make the presentation. He was very impressed with all 3 presenters. He stated that since the meeting he has only had the opportunity to talk with one company, who he said was a very large company in the spirits field though he declined to name it (as if we didn't know that it was Diagio since [redacted] was right there in the room and was with him the rest of the day) but he did point out that this big company was very enthusiastic as well. He stated that our group will likely need to make a presentation(s) to the other companies and very much wanted specifically the same two speakers (as he put it –"the guy from Yale and the guy from Harvard"). I assured him we could get the same team together (I hope that is true!) and we would be happy to come to a Board Meeting anywhere or meet with the companies individually anywhere they want to meet.

*****

From: [redacted] (NIH/NIAAA) [E]
Sent: Monday, March 03, 2014 2:57 PM
To: [redacted] (NIH/NIAAA) [E]
Subject: RE: story in today's news

So let me see if I understand this correctly, [redacted] without input from [redacted] or [redacted] or the DMHE has initiated this process? Anything seem broken here?

[redacted]
Division of Metabolism and Health Effects
National Institute on Alcohol Abuse and Alcoholism
National Institutes of Health
Bethesda MD 20892
Office Phone: [redacted]
Cell Phone: [redacted]
email: [redacted]g@mail.nih.gov

******

From: [redacted] (NIH/NIAAA) [E]
Sent: Monday, March 03, 2014 3:56 PM
To: [redacted] (NIH/NIAAA) [E]
Subject: RE: story in today's news

[redacted]

Best not to respond right now but we can't keep him totally in the dark. I am more than happy to talk with him and convey an accurate picture of the eventual initiative we are interested in. If anything was sent now it would have to be just to emphasize that there are many inaccurate statements in the article.

****

We would like to emphasize one important point, however. Many of these issues will ultimately be decided by a combination of NIAAA (as co-leader of a U01 or similar funding mechanism at NIH) and the final set of investigators. Our responses accurately reflect our efforts to date, which have developed in conjunction with NIAAA, but some of the smaller details will necessarily need to be adjusted based upon both internal and external review at NIH, thus ensuring that the trial is viewed as scientifically valid and unbiased and receives the widest possible attention. Nonetheless, the protocol that we submit to NIH will adhere closely to our suggestions below.

important for their decision to go ahead and fund the trial.

January 2014. The preliminary planning grant was reviewed. One reviewer was concerned about the alcohol industry, but NIAAA staff were able to exclude the reviewer from voting on procedural grounds. When responding to reviewer comments, Mukamal stated that he "tried to be discrete about the industry stuff." The grant was formally awarded on March 20, 2014. There was a parallel conference grant that was also successfully steered to Mukamal at the same time.

February 26, 2014. There was a meeting in Palm Beach, Florida, including alcohol industry representatives, at least one NIAAA staffer, and outside researchers. According to *The New York Times*, Mukamal and Krystal's slides stated, "A definitive clinical trial represents a unique opportunity to show that moderate alcohol consumption is safe and lowers risk of common diseases," and suggested that the trial might make doctors recommend alcohol as part of a healthy diet.

February 28, 2014. *Wine Industry Insight* published "US Govt Asking Industry To Fund Most Of $50 Million Alcohol/Health Study":

> The federal government, along with scientists from Yale and Harvard, are asking wine, beer and spirits organizations to fund a landmark clinical study on the health effects of moderate alcohol consumption estimated to cost $36 million to $54 million....
>
> ...The prime movers from the university research sector are [John Krystal] of the Yale University School of Medicine and [Kenneth Mukamal] of the Harvard University Medical School.

This caused a lot of concern within the NIAAA. Some people had no idea what study it was talking about and sent emails asking what was going on. Someone from the NIAAA communications office was clearly annoyed:*****

In one e-mail, two senior staff in the NIAAA discussed how they could best conceal information from an NIAAA division director:******

June 21, 2014. There was a meeting in Seattle, led by Mukamal, and including NIAAA staff and the alcohol industry. Afterward, representatives from industry sent Mukamal a list of reasonable concerns about the design of the RCT like what outcomes will be measured, how to measure them, who will be eligible to enroll in the trial, how many sample sites will be used, and how to ensure compliance. Mukamal sent back a detailed response which looks sensible to me.

There is, however, a curious passage at the beginning of Mukamal's response, implying that the final investigator had not yet been decided.*******

I don't know how to judge this. Did the alcohol industry really think that other investigators would be involved? Or had the NIAAA winked at them enough that they knew it was going to be Mukamal?

December 8, 2014. A large joint conference call was coordinated between the alcohol industry, NIAAA staff, and researchers including Mukamal. Here are three topics that industry asked about:

1. Would the data be shared with other researchers? Mukamal stated that they would make "controlled data sets" available one year after the study ends.
2. Might industry funding call the study into doubt? Mukamal reassured that it's fine because there will be a "firewall" between research and industry.
3. Would results be published even if they are negative? Mukamal said yes, but they would "most certainly" see a positive impact at least for diabetes.

February 26, 2015. Mukamal and NIAAA senior staffers coordinated edits to an email that would be sent to someone in industry. This email stated that yes, they really needed $100 million, and "one of the important findings will be showing that moderate drinking is safe."

Here's the full quote to show that isn't taken out of context:

> One of the important findings will be showing that moderate drinking is safe. Small studies

> pose a serious risk of spurious results, including showing harm simply because of bad luck. As we discussed, this will be the first RCT (i.e. "gold standard") evidence of this and it is important to answer statements made by WHO and others that "no level of alcohol is safe" with certainty.

Oct 5, 2015. The NIAAA publishes the funding opportunity for the big RCT, "Multi-Site Randomized Controlled Clinical Trial Research Center on Alcohol's Health Effects." Apparently the NIAAA originally requested that this funding opportunity be a limited competition where only people who had won the preliminary planning grant — that is, Mukamal — could apply. NIH central rejected this, but the funding opportunity still "encouraged" it with language like the following:

> Applicants for the U10 Clinical Trial Implementation Cooperative Agreement must be able to begin the trial without further planning activities when the U10 is awarded. Therefore, investigators who have already completed planning activities through an NIAAA-funded U34 clinical trial planning grant are expected to apply.

Mukamal submitted his application on December 18.

March-September 2016. The proposal was reviewed by the NIH, and eventually awarded to Mukamal. Little information seems to be publicly available about these reviews. The project began on September 30.

July 3, 2017. *The New York Times* published "Is Alcohol Good for You? An Industry-Backed Study Seeks Answers." There's this quote from George Koob, director of the NIAAA:

> "This study could completely backfire on the alcoholic beverage industry, and they're going to have to live with it," Dr. Koob said. "The money from the Foundation for the N.I.H. has no strings attached. Whoever donates to that fund has no leverage whatsoever — no contribution to the study, no input to the study, no say whatsoever."

There's also this:

> Dr. Mukamal ... said he was not aware that alcohol companies were supporting the trial financially. "This isn't anything other than a good old-fashioned N.I.H. trial," he said. "We have had literally no contact with anyone in the alcohol industry in the planning of this."

The careful reader will note that in the above timeline, Mukamal just spent several years contacting the alcohol industry about this trial.

In October, Wired published their own story about the study, in which Mukamal again insists, "We have no contact with funders other than NIAAA itself whatsoever,"

February 5, 2018. The trial began enrolling patients.

March 17, 2018. *The New York Times* published "Federal Agency Courted Alcohol Industry to Fund Study on Benefits of Moderate Drinking." They interviewed former federal officials and used Freedom of Information Act requests to get emails and travel vouchers related to the grant. This story reveals that, contrary to Mukamal's claims, there were various meetings in 2013 and 2014. This includes a "working lunch" at a Beer Institute-hosted convention in Philadelphia in October 2013.

March 20, 2018. Based on the previous article, NIH director Francis Collins ordered an investigation into the trial.

April 11, 2018. Collins appeared before the House Appropriations Subcommittee on Labor, Health and Human Services to discuss the NIH's budget. When asked about the trial, Collins responded that he was very concerned and was investigating the issue as a matter of priority.

May 10, 2018. The NIH suspended enrollment in the trial.

June 8, 2018. Anheuser-Busch pulled its funding.

June 15, 2018. Based on a recommendation from an NIH working group, Collins terminated the study.

Why I'm Mad

When I talk to people about this story, I'm angry with so many different entities for so many different reasons that I have trouble putting my words in a coherent order.[6] So let's start with the basics.

People did bad stuff: The trial started out with some corner cutting and bureaucratic maneuvering. But somehow this escalated into Mukamal and the NIAAA lying to the public. They claimed that this was just like any other NIH trial, where any researcher could propose a study design, and the NIH would choose the best entirely based on scientific merit. In reality, the NIAAA intentionally steered the money to one pro-alcohol researcher. Mukamal claimed he had no idea that industry funding was even involved, despite the fact that he had just spent several years coordinating things with industry.

The incentives encouraged misconduct: When I first read about this trial blowing up in the news, I was stupefied — how could everyone have been so shameless? What were they thinking?

Of course, we can't know for sure — no one knows the heart of man. But I think that if you consider the perspectives of the different actors, it exposes deeper problems in the landscape of research funding.

So the NIAAA staff stretched the rules and misled the public. But imagine you knew a study would be valuable, except there's some bureaucratic rule that prevents you from doing it. Wouldn't you be tempted to stretch the rules?

If you've ever worked in government, you know that being able to work around bureaucratic obstacles is a key job skill. So think about the NIAAA staff who took "personal vacations" to visit Mukamal to help him write the original planning grant. I don't get the sense that these people were trying to screw over the public for their own personal gain. Rather, they were trying to work around some rules that they saw as silly and inflexible barriers that were preventing them from accomplishing something important.

Say you're a scientist and you want to send a grant to the National Science Foundation (NSF). According to The Rules, you will propose a detailed plan of *future* work. In some (more theoretical) fields this is absurd: you have to do half the work in order to write that plan! And in other (less theoretical) fields, your grant will be reviewed by other scientists who will expect to see "preliminary work" to show your idea has promise. This leads to a funny situation where people do much of the research and then "propose" it afterward.

Everyone involved knows that this is happening. The grant reviewers aren't fooled. The people at NSF aren't fooled. (Though if they've been around for a while, they might not notice the doublethink anymore.) Everyone is just trying to do the best they can inside of a system that they did not design.

At the NIAAA, The Rules say that you can't solicit grants from industry. But what exactly is "soliciting"? If you run into someone in industry, can you abstractly mention that they're allowed to donate money? What amount of detail can you go into? You might imagine there's some oracle somewhere ready to lend definitive answers, but I doubt it. Instead, what you probably see is some people doing things that are a little like soliciting, and it's fine. Eventually, someone pushes things slightly too far (or is just unlucky) and gets into trouble. The rules get clarified a bit then, but without acknowledging the institutional incentives that made everyone bend the rules in the first place. The person who got in trouble probably feels like a duck shot out of a flock.

So that's what I guess happened at the NIAAA. The staffers are used to bending the rules because that's what everyone does all the time. They think that the alcohol study would be beneficial and go for it, and over time things sort of spiral out of control.

No one thought about the impact of cancellation: When the NIH canceled the trial, they

6. My editor here has patiently confirmed that my first several attempts were, indeed, incoherent.

didn't seem to explicitly consider the information that was lost by cancellation, or the fact that there would be little cost to taxpayers. (Though Collins' letter to Senator Charles Grassley reveals the NIH did pay around $4 million out of pocket.) Could a different principal investigator be put in charge? Could the study design be modified to address the concerns? Could the monitoring bodies have been strengthened so people could trust the results? Maybe the trial was unsalvageable, but it's telling that the NIH didn't bother to make that argument.

The public health benefits of a well-designed and well-executed trial would be massive. So before jumping straight to cancellation, the NIH should have asked — if this trial goes ahead, should we trust the results?

When I first read about this trial blowing up in the news, I was stupefied — how could everyone have been so shameless? What were they thinking?

Despite the somewhat sordid history of this trial, the arguments that we shouldn't aren't as strong as you might think.

Clearly, Mukamal *thought* the trial would show a benefit, but that doesn't mean he was right. Mukamal didn't start claiming alcohol was safe as a cynical ploy to get his hands on grant money. He had been publishing on the health effects of alcohol for years. Can Mukamal be trusted? We can look at his track record. In 2002, he published observational research that showed tea drinkers were less likely to die from a heart attack than non-drinkers. In 2007, he was first author on a paper that randomly assigned patients to consume black tea or not. They looked at tons of different biomarkers and found that the tea did ... basically nothing. This is the kind of case where it would be easy to p-hack your way to force some conclusion, but they straightforwardly state they found no evidence. Anyone who's worked in science knows what it's like to confidently run an experiment, only to get smacked in the face by reality's indifference to your pet theories and career goals.

But OK, say you don't trust the research team. What do you think they are going to do, fabricate data? The study was a collaboration of a large team around the world. The data would be stored at a Data Management Center at a different university and inspected every six months by a monitoring board. The organizational structure for the study involves over a dozen boards, committees, subcommittees, and centers.

This isn't some excel spreadsheet stored on one grad student's laptop. You'd need a big conspiracy.

Or maybe you don't think they'd falsify data, but that for publication they would use some tortured data analysis to spin the results. The thing is, it's not unusual to have researchers who want to find a given result — that's every researcher everywhere! We have a system for this, which is that studies pre-register their statistical analysis. This study did that, and the plan seems fine (although, see below). There just aren't many places to hide the bodies.

Even without a conspiracy, there are two concerns about the study design. For one, it's plausible that the biggest harms of alcohol (e.g. cancer) appear later, while cardiovascular and diabetes benefits (if they exist) happen quickly. So a five-year study might find alcohol reduces mortality while a ten-year study could show the opposite.

Fine, but what's the principle here? Should we cancel all studies where there's a much more expensive and difficult variant that would be more conclusive? We know this is an issue now, and we'd still know it when interpreting results after the study is done.

Another concern is that the study population maximizes the chances for alcohol to look good: it would only enroll people who are either ≥75 years old or at elevated risk for cardiovascular disease while excluding anyone with liver disease, a personal history of colon/liver/breast cancer, a family history of breast cancer, suicidal ideation, or dementia. If I wanted to maximize the chance that alcohol could be beneficial while minimizing the chance that alcohol could be harmful, this is the population I would choose.

If you want a final verdict on whether moderate drinking is safe, I agree this seems like stacking the deck. I'd prefer a random sample of all adults. You can call this a "bias." But you can also call it "refusing to take the sampling scheme into account when interpreting results." There's still value in knowing how alcohol affects a restricted population. And we can extrapolate — since the people in this study were exceptionally likely to benefit from alcohol, a neutral result in this study population would suggest alcohol is harmful to the average person.

You might also argue that it's ethically *required* to exclude people who are at higher risk for being harmed by alcohol. I don't really agree, but I'd imagine many people would.

The final NIH report notes that the researchers do not have "the requisite equipoise." You could interpret this in two ways. One, you might say the whole thing seems rotten and damn the logic of it. The other is that it looks bad *for the NIH* — that, even if useful, it needs to be canceled to preserve trust in the institution. I understand this. But if that's the reason to cancel, it makes me sad — in an ideal world, the best way for the NIH to preserve trust would be to ruthlessly pursue knowledge to benefit the public interest.

The problems could have been fixed — but not by these people: The study *might* have been fine. I've tried to argue above that there are lots of structural factors that make the behavior of everyone here much easier to understand, and which mitigate some of the risk of bias. But despite that, I think this story also shows why it's important to have personal principles.

I'm open to industry-funded research. I don't necessarily mind a lead researcher who was chosen because they believe something that happens to support industry. I can even live with industry having influence on the study design. I stubbornly hold all this even when the study has a goal of proving it's safe to use humanity's most harmful drug.

But my (possibly delusional) open-mindedness is based on the idea that it's possible to compensate for the biases these issues create. That's not possible if we don't know about them.

So I can accept that the NIAAA staff might have thought that this study might have had value, despite all the obvious issues. But if they had tried to rescue the study, they would have needed to make that argument openly, not pretend the issues don't exist.

Many people are also complicit in silence. Maybe the alcohol industry really didn't think anything underhanded was happening. Well, they knew on July 7, 2017, when the first New York Times story came out, including untrue or misleading statements from Mukamal and the NIAAA. They had months to correct the record, but they did nothing. The same is true for many of the other researchers involved.

Because of the scandal, the idea of industry funding with a firewall — which could be tremendously valuable — was tarnished. If we interpret the NIAAA and Mukamal charitably, what they seem to be suggesting is that there was a "late firewall" with lots of contact with industry early on, but no influence after the trial started. But that didn't happen! How do I know? Well, did you notice the part where Anheuser-Busch pulled its funding? Having the power to shut down the entire trial whenever you want qualifies as *influence*.

Media coverage didn't help either. Take that *New York Times* article again. Remember that when this was written, the firewall still held, as far as anyone knew. Besides mentioning that the study exists and is funded by industry (which is totally legit) it's largely a collection of whatever random connections they could

dig up between anyone connected to the study and the alcohol industry. (One investigator "has conducted research at institutions that received industry support," another was paid to speak at an industry conference nine years earlier). There are also quotes about how industry funding skews research, but it doesn't address that that's why there was supposed to be a firewall.

Obviously, I'm glad *The New York Times* followed up on this story and revealed holes in the firewall. I just wish there was a more nuanced tone that engaged with the premise that the problems with industry funding are, in principle, possible to overcome.

The trial didn't happen: Yes, I'm mad the trial didn't happen. Despite people doing bad stuff, despite the industry influence, despite the imperfect study design, this trial would have provided unparalleled ability to answer some really important questions. Globally, the average person apparently drinks around 6.18 liters of alcohol per year, or around 1.5 standard drinks per day. What impact is this having? Should doctors encourage moderate drinkers to stop? Should they encourage abstainers to start? Currently, we just don't know. This trial was a chance for us to get some kind of an answer, and we didn't get one. Instead of imperfect data (which is all data), we got none.

What did we get instead? Collins says that "three individuals are no longer employed" at the NIH, and they made process changes to avoid similar problems in the future.

That's something, but what about the researchers? To their credit, Harvard and Beth Israel did do an investigation of Mukamal, which led to him formally apologizing and both institutions creating safeguards to make sure no future employees would do anything similar.

Hahahaha, no. Here's what actually happened:

1. Mukamal stated, "We stand fully and forcefully behind the scientific integrity," and "Every design consideration was carefully and deliberately vetted with no input or direction whatsoever from private sponsors." (Yes, these are real quotes from *after* the study was canceled.)

2. As far as we know, there were no investigations by Harvard, Beth Israel, or any of the other researchers' institutions. No one faced any penalty of any kind.

3. In 2020, in what a brazen display of academic shamelessness, the researchers published a paper on how awesome the study would have been.[7]

Here's a quote from that paper's "sponsorship" section:

> The Foundation for the National Institutes of Health (FNIH) supported the trial financially and managed contact between public and private organizations on behalf of NIH. The funds provided by FNIH for this project were contributed to FNIH by the brewing and distilling industries following contract negotiations that established an intellectual and financial firewall between MACH15 investigators and private contributors. **The corporations providing support agreed to have, and had, no contact with trial investigators about any aspect of the study after their commitment of funding**, and they agreed to receive no data or updates until they became publicly available. Ultimately, however, the most important safeguard for impartiality lies in the execution of a rigorous, transparent protocol following independent, expert peer review, and in the conduct of the statistical analyses as described in the protocol.

Emphasis mine. You can't make this stuff up.

7. Diederick E. Grobbee, Pablo E. Gulayin, Vilma Irazola, John H. Krystal, Mariana Lazo, Margaret M. Murray, Eric B. Rimm, Ilse C. Schrieks, Jeff D. Williamson, Kenneth J. Mukamal, "The Moderate Alcohol and Cardiovascular Health Trial (MACH15): Design and methods for a randomized trial of moderate alcohol consumption and cardiometabolic risk," *European Journal of Preventive Cardiology* 27, no. 18, (2020): 1967–1982.

98

Salt, Sugar, Water, Zinc: How Scientists Learned to Treat the 20th Century's Biggest Killer of Children

Matt Reynolds

Oral rehydration therapy is now the standard treatment for dehydration. It's saved millions of lives, and can be prepared at home in minutes. So why did it take so long to discover?

In June 1832 *The Lancet* published a remarkable letter written by a Scottish physician named Thomas Latta.[1] Europe was in the grip of the second cholera pandemic — the first outbreak to reach Europe — and the medical journal's pages were filled with speculation about how to treat the disease that seemed to kill half of all the people it infected.[2] One surgeon wrote in to recommend a concoction of wine, vinegar, camphor, mustard, pepper, garlic, and crushed beetle to be rubbed into the patient's feet and hands while they sweated under their bedclothes.[3] Others suggested that laughing gas or bleeding might correct the tar-like blood that ran through victims' veins[4] — a consequence of the ceaseless diarrhea that dries out cholera victims until their organs are at the point of failure.

Latta knew cholera patients' blood lacked water and salt, so he'd tried pumping a briny solution into their intestines. It only made the vomiting and diarrhea worse. Undeterred, he decided to inject the solution directly into the veins of an elderly patient at Drummond-Street Hospital in Edinburgh. The woman was so ill Latta feared she'd die before he had a chance to piece together his syringe and tubing. He inserted a tube into a vein in the woman's upper arm and slowly pumped the solution into her body. At first there was no response, but then the woman started to grow stronger. "Soon the sharpened features and sunken eye, and fallen jaw, pale and cold, bearing the manifest impress of death's signet, began to glow with returning animation," he wrote in the letter published in *The Lancet*.[5] Six pints of fluid later, the woman declared in a firm voice that she was feeling fine and only needed a little sleep. The transformation astounded the young doctor: It had been like seeing a corpse reanimated right before his eyes.

The woman's luck did not last long. Shortly after Latta left her bedside, she began to vomit and experience diarrhea again. Five and a half hours later she was dead. But the experiment was enough to convince Latta that the key to treating desperately ill cholera patients was to keep them hydrated long enough for the disease to run its course. He kept experimenting with his intravenous injections, later reporting that three out of nine gravely ill patients injected with his saline solution went on to recover. For a time, the pages of *The Lancet* buzzed with dispatches from other doctors reporting their own experiments with intravenous therapy.[6]

1. Thomas Latta, "Malignant Cholera," *The Lancet* 18, no. 457 (June 1832): 274.

2. The real case fatality rate of cholera was lower, but this is what contemporaries thought it was. This is because they were unaware of the large numbers of asymptomatic infections. See: Romala Jane Davenport et al., "Cholera as a 'sanitary test' of British Cities, 1831–1866," *The History of the Family* 24, no. 2 (November 2018): 404–38.

3. E.T. Complin, "The Cholera," *The Lancet* 17, no. 428 (November 1831): 216.

4. W.B. O'Shaughnessy, "Proposal of a New Method of Treating the Blue Epidemic Cholera," *The Lancet* 17, no. 432 (December 1831): 366.

5. Latta, "Malignant Cholera," 275.

6. See, for example, *The Lancet* 18, no. 469 (August 1832); and no. 471 (September 1832).

This page and page 103: Stamps produced to increase public awareness and improve education about oral rehydration therapy.

This enthusiasm turned out to be short-lived. By the end of 1833, the cholera pandemic in Great Britain was waning and Latta was dead of tuberculosis. The brief vogue for saline injections died with him. Since most of the experiments had been reserved for the patients who were nearest to death, survival rates under intravenous therapy weren't exactly encouraging. And without a knowledge of germ theory, doctors risked giving their patients septicemia every time they slid their tubing into a vein. When cholera returned in 1848, doctors in Latta's old hospital on Drummond Street reached for their blood-letting scalpels.[7] It would be over a century before intravenous rehydration was established as the main treatment for severely dehydrated cholera patients.

The history of cholera treatment is full of these scientific cul-de-sacs: moments where a breakthrough therapy seemed inevitable but failed to materialize. Yet nearly 140 years after Latta's experiments, work on the disease would lead to one of the 20th century's most consequential medical discoveries: oral rehydration solution (ORS). This cheap, simple solution of sugar, salts, and water mixed in the right proportions and delivered orally has saved the lives of more than 70 million, mostly children, since its introduction in the 1970s.[8] It has helped slash the number of children under five dying of diarrhoeal diseases from around 4.8 million in 1980 to about 500,000 today. All of this from a drink that in its most basic form can be made by anyone with access to kitchen salt, sugar, and water.[9] But why did it take until 1968 to develop such a simple life-saving solution?

False Starts

The ingredients in ORS are so ubiquitous that its discovery feels unavoidable. Sugar, salt, and water have been mixed in broths and drinks for millenia. Surely someone must have stumbled across the fact that in the right concentrations, these ingredients could rehydrate diarrhea victims? History is dotted with early versions of ORS-like treatments. The ancient Ayurvedic text *Sushruta Samhita* recommends that people with diarrhea drink tepid water in which rock salt, treacle, and medicinal herbs have been dissolved.[10] In the 1950s a Swedish doctor recommended carrot soup, while doctors in the U.S. reported good results from an oral treatment made from carob flour and dehydrated bananas.[11]

Why did none of these treatments lead to ORS sooner? One reason is that until the mid-1960s, scientists didn't have a good understanding of how well cholera victims were able to absorb nutrients through their gut. They knew that intravenous therapy could rehydrate patients; the standard therapy was to put water and electrolytes directly to where they were needed, in the blood. But it wasn't clear that cholera victims were even capable of absorbing food or water through their gut; medical wisdom in the mid-1950s held that the patient should be starved for a while before they attempted to eat or drink, particularly for children with diarrheal diseases.

Perhaps because of these biological blind spots, promising early experiments with ORS generated surprisingly little momentum. In 1952–3, an Indian doctor from West Bengal named Hemendra Chatterjee tried an oral

7. Gnanandan Janakan and Harold Ellis, "Dr Thomas Aitchison Latta (c1796–1833): Pioneer of Intravenous Fluid Replacement in the Treatment of Cholera," *Journal of Medical Biography* 21, no. 2 (May 2013).

8. Bernadeta Dadonaite, "Oral Rehydration Therapy: A Low-Tech Solution That Has Saved Millions," *Our World in Data*, August 27, 2019.

9. David Nalin and Richard Cash, "50 Years of Oral Rehydration Therapy: The Solution Is Still Simple," *The Lancet* 392, no. 10147 (August 2018): 536–538.

10. Kaviraj Bhishagratna, *An English Translation of The Sushruta Samhita,* Vol. III (Calcutta: 1916), 354.

11. Joshua Ruxin, "Magic Bullet: The History of Oral Rehydration Therapy," *Medical History* 38, no.4 (1994): 366.Ruxin, Joshua Nalibow. "Magic Bullet: The History of Oral Rehydration Therapy." *Medical History* 38, no. 4.

glucose-sodium treatment similar to the solutions that would prove successful in the late 1960s. Chatterjee treated 186 patients with an oral solution, 33 of whom took fluid alone and a further 153 who also required an enema.[12] All survived. Although Chatterjee's work was published in *The Lancet*, it failed to inspire similar follow-up studies. That may have been partly because Western scientists were unimpressed with Chatterjee's approach — he used herbs to try and stop his patients' diarrhea and the study was mostly focused on stopping vomiting. Most of Chatterjee's patients were too dehydrated for him to even attempt giving them an oral solution. And there was another reason to overlook Chatterjee's work: Scientists didn't have a good physiological explanation for why his patients got better. At the time they didn't know that the presence of glucose increases the uptake of water and salt — the key biological mechanism behind the success of ORS.[13] "Because there was no scientific underpinning for [the Chatterjee study], it just got tossed to the side," says Richard Cash, one of the doctors who would later help develop the first practical ORS treatment.

Without a solid biological underpinning, scientific advances can be overlooked or forgotten altogether. Today we know that scurvy is caused by a lack of vitamin C — a nutrient found in fresh food, particularly lemons and oranges. Medics in the Royal Navy during the 19th century had never heard of vitamin C, but they did know that sailors who drank a regular ration of lemon juice never seemed to fall ill with the disease, so that's exactly what they supplied on long voyages.[14] In 1860 the Royal Navy switched from lemons and Mediterranean sweet limes to the West Indian sour lime, not realizing that the West Indian limes contained a fraction of the vitamin C. For a while the error went undiscovered because the advent of steamships meant that sailors were no longer going months without access to fresh food. But in the late 19th century, polar explorers on longer voyages started to fall ill with scurvy — a disease that they thought they'd seen the back of decades earlier. Without a knowledge of the underlying biology behind scurvy, a cure had been discovered and then promptly forgotten. In the mid-20th century, work on oral rehydration for cholera was also in desperate need of a firmer biological basis.[15]

While work on oral rehydration was stalling, using intravenous saline to replace the water and salt lost during diarrheal dehydration had caught on in the West. In the early 20th century, scientists working on cholera refined Latta's approach to intravenous therapy and developed relatively safe and effective rehydration formulas that could be given by drip. By the mid-20th century, it had become common to treat children with severe diarrhea by initially starving them and keeping them hydrated through intravenous fluid.[16] Rehydration by drip was seen as a high-tech and precise treatment for countries that had plentiful access to sterile needles and saline solution. "Cholera had become a condition of low- and middle-income countries," says Cash.

But with the end of World War II, American scientists started to take a renewed interest in cholera. Wary that their soldiers might be exposed to new diseases in far-flung locations and with an eye on increasing America's influence abroad, the military had set up new institutions where scientists could study

12. Hemendra Chatterjee, "Control of Vomiting in Cholera and Oral Replacement of Fluid," *The Lancet* 262, no. 6795 (November 1953).

13. David R. Nalin, "The History of Intravenous and Oral Rehydration and Maintenance Therapy of Cholera and Non-Cholera Dehydrating Diarrheas: A Deconstruction of Translational Medicine: From Bench to Bedside?" *Tropical Medicine and Infectious Disease* 7, no. 3 (Mar. 12, 2022): 50.

14. Earlier voyages carried supplies of sauerkraut, which is also rich in vitamin C, but this was later replaced by lemon juice.

15. Tim Harford, "South Pole Race: When the Limeys Get Scurvy," *Cautionary Tales,* August 2022.

16. Nalin, "The History of Intravenous and Oral Rehydration."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diseases that mainly affected the developing world.

One such scientist was Robert Allan Phillips. An industrious researcher, Phillips had a habit of designing quick experiments that he would iterate on the fly, noting down his results on small index cards.[17] Early in World War II he had developed a blood test for measuring dehydration that could be used on the battlefield, making it easier for medics to treat burned or bleeding soldiers where they lay.[18] In May 1945, Phillips was briefly assigned to the newly liberated concentration camp at Dachau, where he set up a laboratory to help treat a typhus outbreak that had killed thousands of the camp's former prisoners. His first brush with cholera would come two years later, shortly after he was appointed the commander of NAMRU-3: a medical research facility run by the U.S. Navy in Cairo.

In September 1947, Cairo was experiencing its first cholera outbreak in a generation. Phillips had a knack for turning lab research into new clinical treatments, so he started using his knowledge of blood analysis to improve the intravenous saline solutions widely used for dehydration in the west. Of the 40 patients infused with Phillips' solution, just three of them died.[19] It was a remarkable result in an epidemic where the fatality rate outside the hospital was 50%. Over the next decade Phillips would refine the treatment to a precise science. Patients were started on a drip until the water content in their blood had reached a normal level. Then the drip was slowed down so the patients received about as much fluid as they lost in diarrhea. (Measuring diarrhea accurately was a crucial — if unpleasant — part of treatment. One of Phillips' colleagues designed a bed with a hole cut just below the patient's buttocks. Diarrhea would flow through this hole, down a plastic sleeve and into a bucket where a doctor or nurse could measure the volume with a dipstick.)

More than 99% of patients treated in this way survived.[20] From a purely mechanical standpoint, the problem of cholera was solved; doctors knew exactly how to treat the disease. "If he has no other complex diseases, any patient who can get treatment will survive," Phillips declared at a 1960 conference in Dacca,[21] then East Pakistan.[22] In other words, the difficulty of treating cholera wasn't about a lack of effective treatments — it was a problem of getting people access to the 60-plus bottles of intravenous saline they might need to stave off deadly dehydration.

"The facilities in rural areas simply didn't exist or were so limited that you could not count on having the materials or supplies they needed," says Nathaniel Pierce, an American doctor who worked on oral rehydration therapy in Calcutta in the mid-1960s. When a cholera outbreak exploded in a rural area, half of all patients would die until a mobile team arrived with sufficient supplies of sterile needles, tubing, and distilled water.[23] Even patients relatively close to big cities might struggle to access intravenous therapy. In the Dacca cholera hospital where Cash worked in the 1960s, patients sometimes arrived only after long, tortuous journeys by bicycle rickshaw. And for every patient who made it to the clinic, Cash knew there were others who would never survive the long trip. In the West, doctors weren't coming up with new treatments for dehydration because they already had easy access to intravenous drips. For doctors like

17. From my interview with Nalin.

18. Stephen Savarino, "A Legacy in 20th-Century Medicine: Robert Allan Phillips and the Taming of Cholera," *Clinical Infectious Diseases* 35, no. 6 (September 2002): 713–20; and R.A. Phillips, "Water and Electrolyte Losses in Cholera," *Federation Proceedings* 23, no. 3 (1962): 705-12.

19. Phillips, "Water and Electrolyte Losses."

20. W. E. van Heyningen and John R Seal, *Cholera: The American Scientific Experience*, 1947–1980 (Boulder, CO: Westview Press, 1983), 83.

21. Now spelled Dhaka, but I've stuck to the contemporaneous spelling.

22. Van Heyningen, *Cholera*, 83.

23. *WHO Expert Committee on Cholera: Second Report* (Geneva: WHO Technical Report Series, 1967), 20.

Cash, Pierce, and Phillips, however, it was clear there was a pressing need for a much simpler way of treating dehydration.

By the summer of 1962 Phillips and his colleagues had started experimenting with oral treatments at a cholera hospital in Manila. Phillips knew that cholera killed patients by causing them to lose vast amounts of water and electrolytes — mostly vital salts — from the body through watery diarrhea. He thought that an oral solution given while a patient was on a drip might help minimize the amount of saline solution needed to be given through the veins. In one of his characteristic quick, iterative experiments, Phillips tested different oral solutions on cholera patients. He tried a saline solution, but that only seemed to make the patients lose more water and electrolytes. He then switched to a solution that contained salt and glucose. The results from this experiment were much more promising. Phillips was stunned to observe that when he added glucose, the patients were able to absorb it and the loss of electrolytes from the body slowed down.

This wasn't what Phillips had been expecting. He had only reached for the glucose as a way to see what happened in the intestine when he increased the concentration of his solution without adding more electrolytes. According to some accounts, glucose just happened to be the closest non-electrolyte Phillips had at hand. Whatever the reason, the scientist had inadvertently demonstrated that adding glucose to a saline solution could help cholera patients absorb glucose *and* retain vital salts, and he immediately saw the implications of his work. It was a tiny study — just two patients — but it was also evidence that an oral treatment for cholera dehydration might actually work.[24]

In the West, doctors weren't coming up with new treatments for dehydration because they already had easy access to intravenous drips. For doctors like Cash, Pierce, and Phillips, however, it was clear there was a pressing need for a much simpler method.

Enthused by his findings, Phillips instructed his colleague Craig Wallace to lead a larger study of oral "sugar-electrolyte cocktails." In September 1962, Phillips asked the doctors to run a trial where 30 patients would receive intravenous treatment until they had been partially rehydrated, and then given a new version of the oral solution. In order to mimic conditions in treatment centers, the trial scientists wouldn't have access to laboratory tests that could tell them what was happening in the blood of their patients. Still, Phillips felt confident that he was on the verge of a breakthrough. Shortly before he left his colleagues behind in Manila, Phillips held a press conference where he reportedly stated that an oral cure for cholera was close at hand.[25]

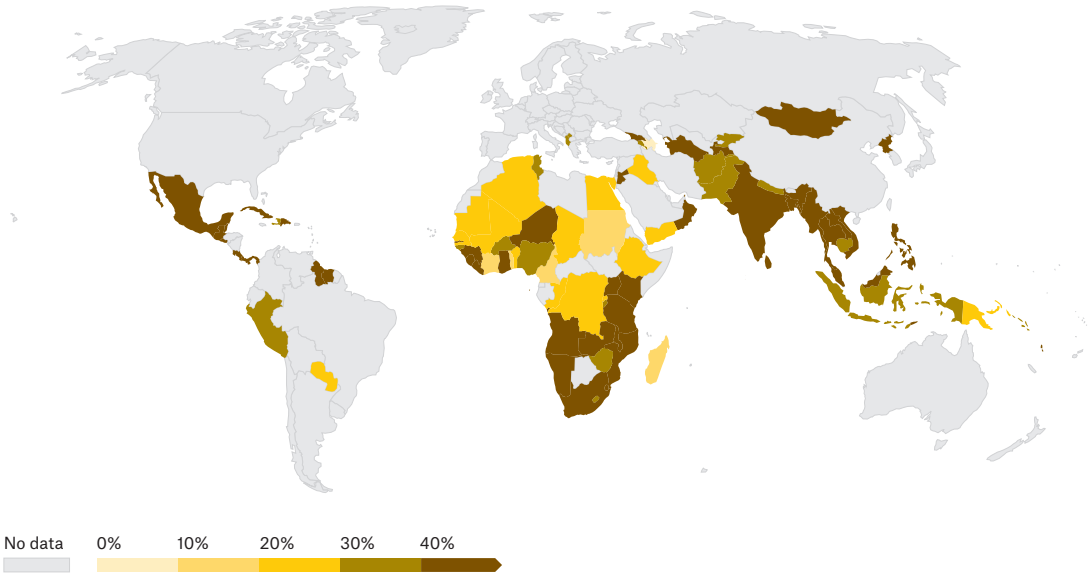
The trial was a disaster. When Phillips returned to Manila a week later he was told that five of his 30 trial participants had died. It's not clear exactly what went wrong with

24. Ruxin, "Magic Bullet"; and Phillips, "Water and Electrolyte Losses."

25. Van Heyningen, *Cholera*, 231; and Ruxin, "Magic Bullet," 372.

Share of children with diarrhea receiving treatment, 2020

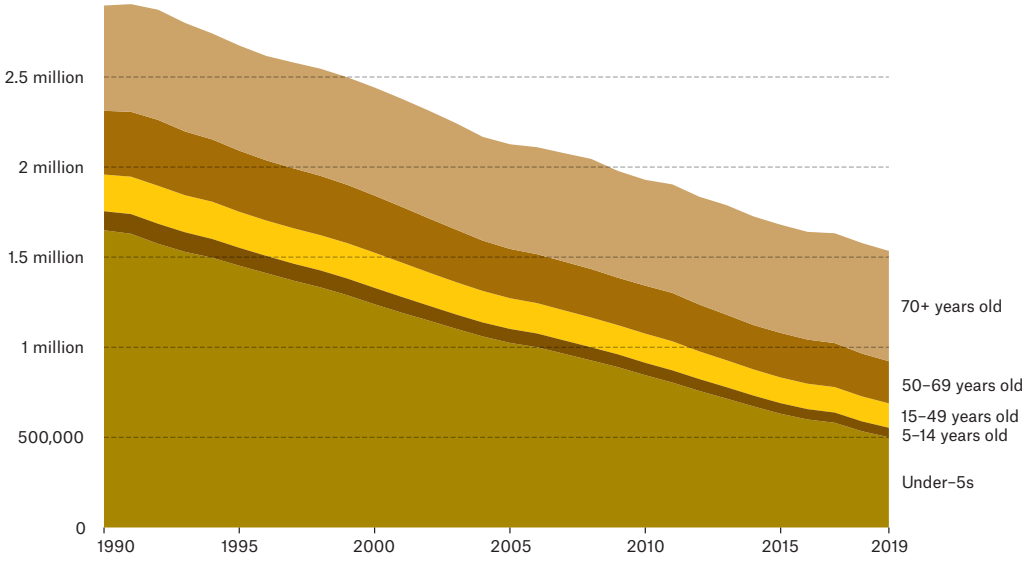
The share of children under five years old with diarrhea who received either oral rehydration therapy or increased fluids, whilst feeding continues.



Source: Demographic and Health Surveys (DHS) and UNICEF (via World Bank) / Our World in Data

Deaths from diarrheal diseases, by age, World, 1990 to 2019

Annual deaths from diarrheal diseases, differentiated by age categories.



Source: IHME, Global Burden of Disease (2019) / Our World in Data

Phillips' experiment, but we do know that the oral solution he put together had far too much glucose and salt. This made the solution extremely hypertonic — it drew water out of the patients' cells and exacerbated their dehydration. Faced with deteriorating patients and without laboratory tests to know exactly what was going on in their bodies, it's possible that the doctors panicked and gave the patients too much intravenous fluid. This excess fluid would have collected in their lungs, leading to their deaths.

The trial was called off and a shocked Phillips concealed the results of his research, including his promising work on a glucose and electrolyte solution. Years later Pierce would meet Phillips in Calcutta and tell him that he wanted to work on oral rehydration. The elder researcher told Pierce not to bother wasting his time. "We've tried that. It didn't work."

Why did Phillips' attempt at oral rehydration fail? It seems that the scientist didn't yet know some of the fundamental biology of how glucose and sodium was absorbed in the body. Work in the late 1950s and early 1960s had established that sugar and sodium ions are absorbed together in the gut through a sodium-glucose cotransport protein. In turn, this sodium and glucose pulls water from the gut into the body. It's possible that Phillips, who was based in Taipei at the time, wasn't up-to-date with the journals that would arrive on his desk many months after they'd been published. Even if he had seen these early studies, the scientist might have thought them irrelevant because they were mostly in vitro or animal models. Phillips was treating cholera patients, and no one knew exactly what was going on inside their guts while they were sick.

Phillips was working on the assumption that cholera somehow prevented sodium from being absorbed in the gut — something he called the "poisoned pump" hypothesis. He thought that glucose might fix this problem by stopping the diarrhea and allowing the patient to reabsorb water. When Phillips opted for a highly concentrated oral solution, he was hoping that the extra glucose would act like a medicine that would stop his patients' diarrhea. But Phillips' premise was badly mistaken, and — just like with scurvy in the previous century — a promising treatment receded from the foreground.[26]

The First Success

The physiological groundwork for oral rehydration solution was finally laid in the summer of 1966 at the Cholera Research Laboratory (CRL) in Dacca. Inaugurated in December 1960, the CRL was set up under the auspices of the Southeast Asia Treaty Organization and consisted of a 20-bed cholera ward on the first floor with libraries, office space, and laboratories on the floors above. A sign outside the CRL read: "In this hospital we treat free of charge all patients with diarrhea and study how to better treat and prevent cholera. All patients will take part in these studies for their own and their countrymen's benefit."[27] Later the CRL would become the International Centre for Diarrhoeal Disease Research, Bangladesh, commonly known as icddr,b — one of Bangladesh's leading research institutions and the center of major breakthroughs in diarrheal disease research.

The CRL was an unusual place to do research. One American epidemiologist who arrived in 1963 described it as a place where people took a "do-it, build-it, fix-it, sail-it-yourself" mentality.[28] It was staffed by a mix of local doctors and expatriates, mainly from the U.S., some of whom were there to avoid the Vietnam war draft. Researchers at the CRL were working on all aspects of cholera; studying vaccines, mapping transmission, and trying to figure out if nutrition played a

26. Nalin, "The History of Intravenous and Oral Rehydration," 90.

27. Van Heyningen, *Cholera*, 105.

28. Letter from Robert Oseasohn to Margaret Pittman (May 1965), Wellcome Library.

role in the severity of the disease. Amid the frenetic activity in the lab, junior researchers had to jostle for precious space to carry out their experiments. Sometimes they'd return from a trip only to find that their room had been commandeered by a colleague who had decided that their experiment was more important.

Context influences innovation. If cholera had continued to afflict wealthy Western nations in the late 19th century, then work on intravenous rehydration may not have languished for so many decades. Similarly, if the work of developing treatments for diarrhea had been left to scientists based in the West, they might not have been familiar with the constraints that led to the development of ORS. Joshua Ruxin, who wrote an academic history of ORS in 1994, has also pointed out that the background of the doctors who would go on to develop ORS was important. They had little or no experience in pediatrics — a medical discipline that favored treating diarrhea by intravenous therapy and restricting fluid intake by mouth.[29] The young doctors were less hampered by medical dogma, and more focused on the situation they could see before their eyes.

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But before they could develop a treatment, the CRL scientists needed to prove that cholera patients could be treated with an oral solution. In the summer of 1966 a scientist called David Sachar asked a cholera patient to swallow a thin plastic tube that ran all the way through his digestive system, down into his intestine. The idea was to figure out whether Phillips' "poisoned pump" hypothesis was correct. If the apparatus registered a jump in negative charge it meant that Phillips' hypothesis was mistaken and cholera patients actually were capable of absorbing sodium through the lining of their intestine.[30]

As soon as Sachar added sugar to the solution, the reading on his meter jumped. It was obvious right away that the patient was able to absorb sodium. One of Sachar's colleagues, a doctor named Norbert Hirschhorn, immediately realized what this meant for a potential oral rehydration therapy. "That means that we can actually use a glucose electrolyte solution if we can figure out how to do it safely," Hirschhorn recalls thinking at the time. "I knew instantly that was exactly right." Six years earlier biochemists had realized that glucose and sodium were transported together in healthy guts. Now Sachar had proved that the same was true of cholera patients. With the right solution, a cholera patient should be perfectly capable of absorbing glucose, sugar, and water from a solution given to them by mouth.

In order to run a trial, however, Hirschhorn would have to convince Phillips. Dacca was in the grip of a major cholera outbreak at the time and the cholera lab was in danger of running out of saline solution. "I was able to say we'd better have a backup if we run out of clean intravenous fluids," says Hirschhorn. Still, the failed Manila experiment preyed on

29. Ruxin, "Magic Bullet," 396.

30. "2019: The Frog Skin that Saved 50 Million Lives," The Golden Goose Award, accessed February 9, 2023, https://www.goldengooseaward.org/01awardees/frog-skin-cholera.

Phillips' mind. He invited Hirschhorn into his office to look at the unpublished data, locking the scientist in the room while he looked it over. Hirschhorn realized that the experiment had failed because the solution Phillips had used was much too concentrated. For his own experiment he would use an isotonic solution with the same concentration as blood.

Hirschhorn's study ran between November 1966 and March 1967. Eight cholera patients were fed fluid either directly into their stomachs or intestine at the rate of 1 liter of solution per hour.[31] When the patients were fed a glucose-sodium solution they produced less diarrhea, which wasn't the case when they were fed a solution without glucose. In Calcutta, a similar study carried out by Nathaniel Pierce backed up these findings.[32] Together, these studies effectively confirmed that a glucose-sodium solution could be the basis of an oral therapy for cholera patients but a practical therapy that could be used in outbreaks in rural settings was still a long way off. Now it was up to the CRL scientists to find a way to turn this breakthrough into a therapy that could be delivered where cholera patients were dying — in the rural areas surrounding Dacca.

Simplicity At Scale

In July 1967,Hirschhorn and Pierce presented the results of their studies at a cholera symposium in Palo Alto, California. In the audience were David Nalin and Richard Cash, two young doctors who were about to be sent out to Dacca to fulfill their military service. Hearing these presentations, Nalin thought that the work on an oral therapy for cholera was already finished, but when he looked through the literature on oral rehydration he realized that none of the scientists involved seemed to believe that they were on the verge of a therapy that could work in rural areas. Even in a WHO report on cholera published in 1967, the prospect of oral rehydration is little more than footnote.[33]

Hirschhorn remembers feeling pessimistic about the future of an oral cholera treatment even after his successful experiment. "It was clear that if you had to put that much fluid through a tube it wasn't going to be field-worthy," he says. How were they going to get this solution into patients, and who would give the treatment in rural settings? The researchers had the biological foundations for a treatment, but they couldn't quite see how to turn it into something that would save lives where it was really needed.

That would all start to change just a year later. In April 1968, Nalin and Cash enrolled their first patients in a practical trial of oral therapy. The big change here was that after stabilizing the patients using intravenous saline, the researchers hydrated their patients using a glucose-sodium solution given only by mouth — not a feeding tube. Nalin and Cash were so keen to avoid the mistakes of previous studies that they alternated 12-hour shifts in a tiny room next to the cholera ward, ready to be on hand if one of the patients unexpectedly deteriorated.

Still, it was clear during the trial that the oral solution was keeping the patients hydrated. "Each success made me more convinced that this was working and we should do this study as quickly as possible," Nalin says. The results of the study were published in *The Lancet* in August 1968, where the authors concluded that an oral glucose-sodium solution could eliminate the need for over three-quarters of the intravenous fluid in severely ill cholera patients.[34] Mild cases of cholera could be treated using oral solution alone, they suggested. But this was still in a hospital setting, overseen by medical staff who had intravenous drips on hand in case any patients deteriorated. What Cash and Nalin really needed to prove was that their approach

31. Ruxin, "Magic Bullet," 377–8.

32. Ruxin, "Magic Bullet," 379.

33. *WHO Expert Committee.*

34. David Nalin et al., "Oral Maintenance Therapy for Cholera in Adults," *The Lancet* 292, no. 7564 (August 1968).

could work in areas where other options were extremely limited.

"You have the ORT [oral rehydration therapy]and you've shown that it worked in the hospital. Now what are you going to do with it? Now you've got to take it out to where people are because if you depend on people to come to your facility lots and lots of people are going to die," says Cash. In the autumn of 1968 the researchers ran another study in a rural cholera treatment center in East Pakistan where access to intravenous solution was much more limited. There they managed to treat 350 cholera patients with oral therapy alone, and the overall amount of intravenous fluid needed to rehydrate even severely ill patients was reduced by 70%.[35] The results weren't perfect — the patients on oral treatment still had more diarrhea and vomiting than those treated with drips alone — but it was a huge vindication of the idea that cholera could be treated successfully even in rudimentary treatment centers.

"It's better to reach 80 percent of people with something that's 80 percent effective than five percent of people with something that's 100 percent effective," says Cash. Subsequent studies would show oral rehydration therapy was effective in non-cholera patients and — notably — in children too. In the six years that had passed since Phillips' failed Manila experiment, oral rehydration therapy had gone from unthinkable to a clearly revolutionary intervention with the potential to save millions of lives.

The largest demonstration of the potential of ORT happened during the Bangladesh War of Independence in 1971.[36] In June, cholera had broken out among refugees fleeing from what was then East Pakistan into India. The case fatality rate ran at 30%. An Indian pediatrician named Dilip Mahalanabis set up a cholera ward in the border city of Bongaon and soon 200 cholera patients a day were flooding the limited facilities. The situation was so crowded that often two adults or four children had to huddle together on a single bed while other patients were treated on the floor. Researchers in Calcutta put together ORS packets of table salt, baking soda, and glucose that were continuously shuttled the 50 miles to Bongaon. At the field hospital, the diluted oral solution was fed to patients by their relatives or nurses. Even in this extremely under-resourced setting, the death rate was just 3.6%, and half of those deaths occurred before the patients were started on any rehydration therapy.

The Mahalanabis study accelerated the adoption of oral rehydration therapy. In May 1978 the WHO's diarrheal disease group met in Geneva and recommended a global program for ORT. Within a couple of years nearly 200 million sachets of ORS were being produced, at a total treatment cost of less than 50 cents per patient (compared with more than $5 for intravenous therapy).[37] Countries ran radio broadcasts and printed comics to inform their citizens where to get ORS and how to use it. In Egypt, a soap actress famous for her role as a loving mother was chosen to front adverts for what became known in Arabic simply as *mahloul*: solution. In rural villages in

35. Richard Cash et al., "A Clinical Trial of Oral Therapy in a Rural Cholera-Treatment Center," *The American Journal of Tropical Medicine and Hygiene* 19, no. 4 (1970).

36. Dilip Mahalanabis et al., "Oral Fluid Therapy of Cholera Among Bangladesh Refugees," *Public Health Classic*, 1 , no. 1 (2012).

37. "The Management of Diarrhoea and Use of Oral Rehydration Therapy: A Joint WHO/UNICEF Statement. Second Edition," World Health Organization, Geneva, 1985.

38. Glen Williams, *A Simple Solution: How Oral Rehydration Is Averting Child Death from Diarrhoeal Dehydration* (UNICEF Special Report, 1987).

39. Williams, *A Simple Solution.*

Bangladesh, community health workers went door-to-door to teach mothers how to make their own at-home versions of ORT with a three-finger pinch of salt and a scoop of sugar mixed in a half-liter container. By 1987 almost a third of young children had access to ORT and the therapy was preventing half a million deaths a year.[38]

Even with the rapid ascendancy of ORT, the rollout didn't always go smoothly. In a UNICEF report from 1987, a North African doctor complained that parents were suspicious that such a low-tech treatment could be effective. "I know the views of certain pediatricians who say that ORS on its own is enough, but it's difficult. If someone comes from 50 kilometers away to see me, what am I supposed to do? Just give them some ORS and send them home again?"[39] In many places the old advice that children with diarrhea shouldn't try to eat persisted, despite WHO and UNICEF recommending that children are fed even when they're suffering with diarrhea.

Despite saving so many lives, the impact of ORT is easily overlooked. Ask someone what the biggest health innovations were in the 20th century and they're likely to think of insulin, or the discovery of penicillin. Why hasn't the development of ORT been elevated to a similar place in the history books?

One reason might be the sheer simplicity of the treatment. But the simplicity wasn't an accident — it was the whole point of ORS. Scientists like Nalin and Cash were searching for a treatment that could scale to be used anywhere on the planet, even in the most rudimentary settings. "Once the physiology was worked out and once the clinical trials were carried out, you then had to market it and get it out to where the doctors and nurses and people were going to use it," says Cash. Simplicity meant scalability.

In many ways, the challenges that ORT faced during its rollout mirrored those that may have held back its development. First, a preference toward seemingly high-tech interventions like intravenous rehydration. Second, a misunderstanding of the underlying biology of diarrhea and the uptake of nutrients in the gut. And finally, a need to develop a treatment that isn't only effective in hospital trials but works in the field too. The road around these obstacles — as was the case when ORT was being developed — is still long and circuitous. "Science in the development of these things is a progression," says Cash. "It's not a sudden moment and then everything changes. It doesn't work that way."

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112

Is Cultivated Meat For Real?

Robert Yaman

Cultivated meat faces a wall of scientific skepticism, but investors haven't been deterred. A decade in, how close are we to seeing it on our plates?

ILLUSTRATION BY
Sarah Mazzetti

A decade ago, the optimism around cultivated meat (also known as "cultured meat," or less appetizingly, "lab-grown meat") was infectious. Mark Post, a professor at Maastricht University, unveiled the first cultivated burger in 2013. It cost $325,000, was financed by Sergey Brin, and received a breathless profile in *The New York Times*. Excitement grew and investment poured in for new organizations trying to develop their own products. Commentators envisioned a world where meat would remain exactly the same, but the way it was made would change behind the scenes.

For those who care about animal welfare, cultivated meat holds tremendous promise. Instead of convincing people to stop eating meat entirely, we can give them what they want but remove animals from the equation. In 2013, it almost seemed like a cheat code to skip to a world where animals were treated with compassion, without the messiness of slow, painstaking social change.

Instead, timelines for initial market entry were repeatedly pushed back, and some experts began to voice skepticism. Year after year, cultivated meat failed to appear on grocery store shelves. The gossip was that the technology might just be vaporware.

In 2022, cultivated meat was back in the news. Believer Meats broke ground on a 200,000-square-foot commercial plant, and GOOD Meat announced massive facilities in Asia and the U.S. Another company, UPSIDE Foods, received a green light with the Food and Drug Administration's approval in December — a sign that cultivated meat might soon be available in the U.S.

But while the industry releases increasingly optimistic projections, well-informed commentators remain skeptical. It's still unclear if cultivated meat can be made affordable or at large-enough scale to compete with conventional animal products. As we approach the decade anniversary of Mark Post's first burger, many are confused as to when, if ever, cultivated meat will be on their plates.

After spending a few years inside the industry, I've come to believe that the true prognosis for cultivated meat is somewhere in the middle, between that exuberant initial hopefulness and more recent cynicism. I agree with the pessimistic commentators that "The Dream" of cultivated meat — full bio-replicas, cost competitive, at scale — is not feasible in the short term. However, comparison to other technologies like solar energy suggests that cultivated meat may take decades and hundreds of billions of dollars in investment — but is ultimately possible. If we accept longer timescales, many of the seemingly intractable problems become tractable. In the meantime, companies can justify large venture capital investments by pursuing cheaper products that combine cultivated and plant-based components.

Cultivated meat is by no means inevitable. But it's still a bet worth making.

The Challenges of Cultivated Meat Are Real

In 2020, David Humbird published a techno-economic model that took a critical eye to the technology.[1] There were, he noted, some massive technical challenges. His critique was popularized in a 2021 piece in *The Counter*. The challenges he identified — which include fundamental cost barriers for input materials, challenges in scaling production processes,

difficulty maintaining sterility at large scales, and constraints set by investors — make a convincing case against The Dream of cultivated meat being feasible within the next 5 to 10 years.

The Prices of Input Materials

The manufacturing of cultivated meat requires three inputs:

- Starter cells, often stem cells of some type.
- Nutrients that the cells need to duplicate and turn into the relevant tissue types. These include sugars, fats, minerals, and amino acids.
- Signaling molecules that tell the cells how to behave, called "growth factors." Unlike many types of microbes, animal cells don't multiply by default. GFs' presence in animal cells' environment gives them the cue to multiply or turn into different tissue types.

Early economic analyses pointed to GFs as the costliest input to cultivated meat,[2] but Humbird deemphasizes this as a long-term bottleneck, and I agree. GFs are expensive now, but GF production via precision fermentation is easily scalable. Bulk purchases often yield massive drops in unit price. The supporting industries that produce the relevant GFs at massive scales don't exist yet, but they should be able to grow at least as quickly as cultivated meat itself. Companies can also modify the starter cells to require lower concentrations of GFs or to forgo them entirely.

Put another way, GFs carry *information*, which is fundamentally easier to manipulate than mass. There are unlikely to be long-term thermodynamic or biochemical limits on getting information to cells.

This same is not true for amino acids. Amino acids are the fundamental building block of the proteins in meat; cells can't be engineered to need less. In Humbird's model, amino acids alone may constitute $7 to $8 per pound of cultivated meat (although there is by no means a consensus about this). They also have to be pure enough to avoid negatively affecting the cell culture, which adds to the price. Absent new breakthroughs, it's possible that price floors on bulk amino acids could be a fundamental bottleneck on the price of cultivated meat.

Scaling Up the Manufacturing Process

Manufacturing cultivated meat happens in two stages: proliferation and differentiation. During proliferation, the starter cells continually divide to create more cells until there's a sufficient quantity of "cell slurry" — a mass of cells mixed in a liquid. During differentiation, cells in the slurry transform into the desired tissue type, like muscle or fat.

There are various types of suitable manufacturing processes for both stages. For the proliferation stage, the most common is a "stirred tank" process, where materials are mixed in a container of liquid, which is stirred to ensure a homogeneous distribution of cells, nutrients, and GFs. This type of process has a long history of use in other industries, like biopharmaceutical manufacturing. While cultivated meat would likely require substantially larger tanks in the long term, the basic procedure is well understood.

The differentiation stage is more complicated. Since large-scale cell differentiation isn't a challenge other industries face, cultivated meat companies have to design new processes. UPSIDE Foods distributes cell slurry onto a "sheet" where cells adhere to some substrate and turn into tissue. Alternatively, Mosa Meat has developed a novel culture vessel where muscle cells grow in a ring around a central pole and are then sliced off when fully formed.

Even with proven technology, scaling up to successively larger sizes of bioreactor is costly and challenging. Each process characteristic needs to be reevaluated for each level of scale. For example, going from a 1,000-liter to a 10,000-liter stirred tank reactor involves more vigorous stirring to keep cells and

1. David Humbird, *Scale-Up Economics for Cultured Meat: Techno-economic Analysis and Due Diligence* (Centennial, CO: DWH Process Consulting LLC, 2021), https://engrxiv.org/preprint/view/1438/2973.

2. Liz Specht, *An Analysis of Culture and Medium Costs and Production Volumes for Cell-Based Meat* (The Good Food Institute, 2020), https://gfi.org/resource/analyzing-cell-culture-medium-costs/.

nutrients homogeneously distributed. Cells might not thrive in this more tumultuous environment and could stop growing or break open entirely. Operationalizing these larger bioreactors might involve reworking fundamental characteristics of the input cells, and even then they may not be able to achieve the same cell densities. The number of possible problems increases with bioreactor size, as does the cost of running each experiment. Reaching the bioreactor size needed to make a substantial dent in meat demand will be a massive engineering challenge.

Maintaining Sterility at Scale

A bioreactor creates a closed environment designed to be perfect for biological growth. Unfortunately, cells aren't the only things that want to grow here: External microbes carried in by humans or present in the input materials can also thrive. Since bacteria tend to duplicate much faster than mammalian cells, a single microbe can contaminate an entire batch of product. This makes cleaning a critical aspect of the manufacturing process.

This problem gets worse as scales increase. A bigger batch means a longer, more complex process with more materials — and a higher risk of contamination. To make matters worse, a larger contamination means more material goes to waste, leading to a larger financial impact. There are well-established procedures for maintaining a sterile environment for large-scale cell culture, but they require expensive and complex facility upgrades and cleaning procedures. They've also never been tested at the relevant scales. Wasted materials from contamination will need to be priced in to the total cost of the final product, meaning that maintaining sterility will be a major engineering focus of the industry as it matures.

Massive Capital Investments

Scaling and maintaining sterility are engineering problems, meaning that they can — at least theoretically — be solved with enough persistence and innovation (although not necessarily in a cost-effective manner). However, the only way companies will truly be able to tackle these challenges is with access to massive amounts of money.

Technological development in the physical world requires substantial capital, capital flows to things that investors think will succeed, and firms demonstrate potential for success through technological development. This is what I'll call the "virtuous cycle of capital deployment." Technology firms solicit funding from investors and promise certain milestones. Whether or not the investors invest is a function of how well firms have performed in the past, the financial situation of the investors, and the vibes of the investment environment.

The virtuous cycle can break if one of its parts slows down. If technology firms don't hit their promised milestones, investors may start to lose faith. On the other hand, if there's an economic downturn that causes investors to tighten their belts, money for speculative research and development or large capital projects can dry up. But a major technological breakthrough or a new funder (say, a government with sustainability goals) can catalyze a new flurry of investments.

Different investors are more suitable for different stages in a technology's lifecycle. Right now, venture capitalists are the primary funders of cultivated meat, since their risk tolerance is high and the technology is unproven. As the technology matures and investments become less risky, investors with lower risk tolerance but much larger checkbooks — such as governments, public equity markets, and debt markets — may enter the scene.

Many milestones exist between now and The Dream of cultivated meat becoming a reality. First, companies have to develop scalable processes and demonstrate them in pilot plants. Regulatory agencies then need to certify that these processes yield products that are safe to eat. Then the long road of scaling and cost reduction begins. Companies will need to build and operationalize larger and larger facilities to increase production capacity, and invest in further R&D to lower costs, all the while demonstrating that there is consumer demand.

As each new milestone is hit, cultivated meat will seem more concrete and more possible, unlocking additional capital. However, the capital required to reach subsequent milestones will also increase. At some point, the low-hanging fruit of R&D will be plucked, and capital will begin to flow toward investing in scale to further decrease production costs.

Believer Meats' recently announced $123 million facility in North Carolina is projected to be able to produce thousands of metric tons of product. This investment is an impressive and important step for the fledgling industry, but the projected capacity would still be a sliver of conventional meat production. Plants like this one generally take two to four years to finance, design, build, and operationalize. In order for cultivated meat to compete with conventional meat, thousands of much larger facilities will be needed in the U.S. alone, and the global supply chain will need to shift to meet the demands of this new product.

As the technology progresses there may come a milestone that's too costly for investors to stomach, either because it's too hard, or because investors have lost patience with the rate of progress. The feasibility of cultivated meat therefore comes down to whether the virtuous cycle can be sustained long enough and with sufficient resources to hit the relevant milestones.

The Goals Were Overly Ambitious

Back in 2021, *The Counter* article brought attention to a number of real challenges that cultivated meat will face. It then posited that they need to be solved in the next 10 years — but that isn't true.

Cultivated meat is a capital-intensive industrial manufacturing technology that aims to produce high-volume, low-margin products. Industrial animal farming, the incumbent technology, is fully commoditized and has had decades to lower costs through scaling, optimization, consolidation, vertical integration, and R&D. However, these structural challenges are not unique. Other technologies have faced similarly daunting prospects, and some have even succeeded, albeit over many decades of slow, steady progress. Looking at how their stories played out can help us understand the path forward for cultivated meat.

Solar energy, now heralded as one of the most notable success stories of clean tech, is a particularly useful comparison. It also involves a completely novel industrial process and is capital intensive, low margin, high volume, and in a commoditized market.

The technology of photovoltaics was demonstrated at lab scales as early as the 1970s. Over the last 60 years, the virtuous

cycle of capital deployment has gone through booms and busts, with periods of heavy investment from venture capitalists, oil companies, and governments. Many decades and hundreds of billions of dollars later, solar is now the cheapest source of new energy. However, it's still a small part of global energy production, suggesting that even more time and money are needed to transition to a world run on renewable energy.

Looking back, there were periods of pessimism and missed milestones where many proclaimed the "death of clean tech." In 2011, BP exited solar, saying it couldn't "make any money," despite being one of the technology's champions in the previous decade. Around the same period, the International Energy Agency used the best data at the time to forecast future solar capacity and was consistently overly pessimistic.

How did solar and other technologies like it (e.g., electric vehicles and nuclear energy) succeed, given that investors generally look for profit within a few years? One answer is by finding intermediate business models that generate income on faster timelines, providing profits to reinvest in R&D and boosting investor confidence. For solar panels, this was getting energy to satellites and other remote locations not connected to the broader energy grid. For cultivated meat, it's creating "hybrid products" that mix plant-based and cultivated components. By using a small amount of cultivated meat as an ingredient, hybrids will have a meatier taste than purely plant-based products, but with massively lower costs than fully cultivated meat.

Hybrid products could be seen as the next evolution of those made by companies like Impossible Foods, which uses biotechnology to produce heme, a critical component of meat taste. Adding a new tool to the alternative protein toolkit may be just what the plant-based sector needs to stimulate growth after its recent slump.

Many startups like Mission Barns, New Age Eats, and SCiFi Foods are explicitly adopting a hybrid approach for their initial market entries, and other industry leaders like Believer Meats and UPSIDE Foods haven't ruled it out. While these products won't be able to boast full biosimilarity to traditional meat, they'll likely taste amazing and be reasonably priced. If they're successful with consumers, they'll validate the massive venture capital investments these companies have taken on and further stimulate the virtuous cycle of capital investment to keep advancing the core cell culture technology.

With less than a decade of R&D and only a few billion in funding, cultivated meat is still in its infancy. Companies have primarily been focused on setting up basic pilot-scale operations and acquiring regulatory approval. To my mind, only three demonstrable milestones have yet been hit: GOOD Meat's regulatory approval in Singapore, its subsequent regular sale of product at pilot scale, and UPSIDE Foods' FDA approval in the U.S. There hasn't yet been a real opportunity to truly tackle the core technical challenges discussed above. Trying to predict the future of cultivated meat now is like trying to predict the future of solar in 1990 — it's too soon to tell.

The Limits of Techno-economic Modeling

After the Humbird model was published, I argued that TEMs can show that something is possible but have a harder time showing that it isn't.[3] I used the analogy of trying to find your way through a mountain range. You try your hardest to find walkable paths, but you'll never know if you've done a truly exhaustive search. You'll also never know if there are creative options that didn't occur to you, like building a helicopter and flying over.

TEMs try to project the economics of a technology once fully implemented at scale. They take inputs like the price of various feedstocks, bioreactor size, and the metabolic rates and doubling times of cells, and use them to calculate output metrics like cost per pound of product and volume of product produced. The pessimistic TEMs in cultivated meat argued

3. Robert Yaman, "Techno-economic Models and Cultivated Meat," robertyaman.com (blog), September 13, 2020, https://www.robertyaman.com/blog/techno-economic-models-and-cultivated-meat/.

that, even under idealized conditions, cultivated meat couldn't get anywhere close to the price of conventional meat.

However, each of these assumptions can be creatively loosened, especially with a healthy dose of uncertainty appropriate when thinking on longer timescales.

In the next section, I'll suggest some ways that companies might work around the identified bottlenecks. The following list is not exhaustive — given the intellectual property sensitivities in the space, the most creative and innovative work is most likely being done confidentially.

Cell Density and Alternative Processes

Since stirred tank bioreactors are the only ones with a track record of use for large-scale mammalian cell culture, Humbird understandably limits his analysis to this type of system. Indeed, stirred tank systems are likely to be common in the near future, while the industry is far away from the idealized conditions that Humbird assumes. However, other bioreactor systems may offer better trade-offs for cultivated meat in the longer term.

In "adherent" proliferation processes, cells are secured onto a substrate so they remain stationary, and liquid is circulated through the substrate to deliver nutrients and remove waste — similar to how blood flows in an animal's body. Adherent processes can achieve massively higher cell densities than stirred tank systems, one of the core bottlenecks in Humbird's analysis. It's easy to see why: A liquid containing cells and nutrients becomes harder to mix effectively as it gets thicker and less viscous. However, if cells are kept stationary, they can be packed very tightly, as they are in natural tissue.

One reason these systems could be underexplored is that cultured meat is ultimately solving a different problem than the industries that precede it. In biopharmaceutical production, cells produce the end product, but for cultivated meat, cells are the end product. If a producer needs to extract a drug from the cell culture, it may be easier with everything loosely floating in a liquid, rather than trapped in a dense matrix of cells.

The problem with adherent systems is that it's difficult to find comparable examples. Operationalizing and scaling up a new bioreactor system is massively more challenging when nothing is known about how cells might behave in the new environment.

Cell Size

One avenue to scalability that's unique to cultivated meat is increasing the size of each cell. Even after the number of cells in a batch is set in the proliferation phase, more mass can be added during the differentiation phase. Fat cells in particular vary by orders of magnitude in volume and could likely be grown much larger than seen in nature. Fat will likely be critical to hybrid products, since fat carries many of the important flavor compounds we associate with meat.

Humbird's TEM underweights the potential impact of cell size, since it only considers the proliferation phase. His rationale is likely that if cell slurry can't be produced at comparable costs to meat, then neither can fully differentiated tissue. However, if significant mass is gained during the differentiation phase, this could be a critical aspect of the total cost competitiveness of the product. Since differentiation processes differ across companies, the possibility is difficult to model.

Genetic Engineering

Until recently, one might have thought that any sort of explicit genetic tinkering would have been a regulatory non-starter. This would make it much more difficult to achieve the metabolic efficiencies and other desirable cell traits that Humbird views as necessary (but insufficient) for cost-competitive cultivated meat. Fortunately, UPSIDE Foods' recent FDA approval included the use of genetic engineering to make cells overexpress a particularly helpful protein. This is a positive sign for the industry. It frees up companies to pursue a host of research directions to make cells more efficient and more suitable for large-scale cell culture.

Amino Acids

As I've discussed, amino acids could be a long-term cost bottleneck. Currently, cell culture media is made by combining each individual amino acid one by one. But this isn't how animals get amino acids in nature. Rather, animals eat food, and then break down proteins into the constituent amino acids via digestion.

Technologies that mimic this process could help lower the cost of cultivated meat in the long term. Humbird explicitly mentions soy hydrolysates as a potentially promising solution. With this technology, soy (the main source of protein for livestock) is broken down in a chemical reaction with water and added to media as a single composite ingredient. This is a novel technology with its own host of challenges, but with a longer time horizon for cultivated meat, it isn't out of the picture (just as our highly optimized system of growing corn and soy for animal feed developed alongside industrial animal agriculture).

Another avenue to decrease the cost of amino acids is to decrease the percentage of them in the final product by focusing on fat. Since fat cells have more lipids and fewer amino acids than muscle cells, they could be cheaper to produce at large scales. This could be an important factor in the cost competitiveness of hybrid products, which can primarily get amino acids from plant-based components.

A Bet Worth Making

When the Good Food Institute said that government support would be necessary for the success of cultivated meat, *The Counter* treated it as a "concession" from the industry. However, looking at the critical role world governments played in the development of solar, I see it differently. The Biden administration recently allocated $550 billion to clean energy and climate programs, much of which will be added to the $1.3 trillion already invested in solar energy last decade. These expenditures signal society's belief that the future of the planet is worth enormous investment.

Cultivated meat can follow a similar path, if we as a society decide that it's similarly worthwhile. This will take longer and cost more than originally thought, and in the meantime, companies will likely compromise with hybrid products. It will require buy-in from top institutions, entrepreneurs, and most importantly governments. But once one accepts longer timescales for The Dream of cultivated meat, it might seem less unreasonable to bank on massive engineering accomplishments, the concurrent development of multiple supporting industries, and a restructuring of the global agricultural supply chain. When you're talking decades, paradigm-shifting advances are possible.

A longer timescale will come as a disappointment to those who bought into the early, more optimistic projections for cultured meat. But in the fight for animal welfare, there is no silver bullet. Plant-based meat has shown tremendous promise and has the potential to undercut conventional meat on price in the longer term, but it's unclear whether consumer demand will be there. Traditional advocacy has had some major wins (a third of egg-laying hens in the U.S. are now cage-free), but social change is hard to steer and even more difficult to predict. Given how little we can truly know about how the future will play out, I believe we need to maintain a diversified portfolio of bets across cultivated, plant-based, and traditional advocacy and social change.

The eventual success of solar wasn't augured by carefully constructed models of possible future outcomes. Rather, the decision to double down during one of solar's pessimistic periods would have been an expression of determination that the future isn't set in stone, but is shaped by idealists who take bold action in the face of uncertainty. When the stakes are as high as they are with cultivated meat, I think it's worth making that bet.

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