Every year, nearly $100 billion is invested in biomedical research in the US, all of it aimed at teasing apart the invisible bits of the body.

Photo: Mauricio Alejo
On November 30, 2006, executives at Pfizer—the largest pharmaceutical company in the world—held a meeting with investors at the firm’s research center in Groton, Connecticut. Jeff Kindler, then CEO of Pfizer, began the presentation with an upbeat assessment of the company’s efforts to bring new drugs to market. He cited “exciting approaches” to the treatment of Alzheimer’s disease, fibromyalgia, and arthritis. But that news was just a warm-up. Kindler was most excited about a new drug called torcetrapib, which had recently entered Phase III clinical trials, the last step before filing for FDA approval. He confidently declared that torcetrapib would be “one of the most important compounds of our generation.”

Kindler’s enthusiasm was understandable: The potential market for the drug was enormous. Like Pfizer’s blockbuster medication, Lipitor—the most widely prescribed branded pharmaceutical in America—torcetrapib was designed to tweak the cholesterol pathway. Although cholesterol is an essential component of cellular membranes, high levels of the compound have been consistently associated with heart disease. The accumulation of the pale yellow substance in arterial walls leads to inflammation. Clusters of white blood cells then gather around these “plaques,” which leads to even more inflammation. The end result is a blood vessel clogged with clumps of fat.

Lipitor works by inhibiting an enzyme that plays a key role in the production of cholesterol in the liver. In particular, the drug lowers the level of low-density lipoprotein (LDL), or so-called bad cholesterol. In recent years, however, scientists have begun to focus on a separate part of the cholesterol pathway, the one that produces high-density lipoproteins. One function of HDL is to transport excess LDL back to the liver, where it is broken down. In essence, HDL is a janitor of fat, cleaning up the greasy mess of the modern diet, which is why it’s often referred to as “good cholesterol.”

And this returns us to torcetrapib. It was designed to block a protein that converts HDL cholesterol into its more sinister sibling, LDL. In theory, this would cure our cholesterol problems, creating a surplus of the good stuff and a shortage of the bad. In his presentation, Kindler noted that torcetrapib had the potential to “redefine cardiovascular treatment.”

There was a vast amount of research behind Kindler’s bold proclamations. The cholesterol pathway is one of the best-understood biological feedback systems in the human body. Since 1913, when Russian pathologist Nikolai Anichkov first experimentally linked cholesterol to the buildup of plaque in arteries, scientists have mapped out the metabolism and transport of these compounds in exquisite detail. They’ve documented the interactions of nearly every molecule, the way hydroxymethylglutaryl-coenzyme A reductase catalyzes the production of mevalonate, which gets phosphorylated and condensed before undergoing a sequence of electron shifts until it becomes lanosterol and then, after another 19 chemical reactions, finally morphs into cholesterol.

Furthermore, torcetrapib had already undergone a small clinical trial, which showed that the drug could increase HDL and decrease LDL. Kindler told his investors that, by the second half of 2007, Pfizer would begin applying for approval from the FDA. The success of the drug seemed like a sure thing.

And then, just two days later, on December 2, 2006, Pfizer issued a stunning announcement: The torcetrapib Phase III clinical trial was being terminated. Although the compound was supposed to prevent heart disease, it was actually triggering higher rates of chest pain and heart failure and a 60 percent increase in overall mortality. The drug appeared to be killing people. That week, Pfizer’s value plummeted by $21 billion.

The story of torcetrapib is a tale of mistaken causation. Pfizer was operating on the assumption that raising levels of HDL cholesterol and lowering LDL would lead to a predictable outcome: Improved cardiovascular health. Less arterial plaque. Cleaner pipes. But that didn’t happen. Such failures occur all the time in the drug industry. (According to one recent analysis, more than 40 percent of drugs fail Phase III clinical trials.) And yet there is something particularly disturbing
about the failure of torcetrapib. After all, a bet on this compound wasn’t supposed to be risky. For Pfizer, torcetrapib was the payoff for decades of research. Little wonder that the company was so confident about its clinical trials, which involved a total of 25,000 volunteers. Pfizer invested more than $1 billion in the development of the drug and $90 million to expand the factory that would manufacture the compound. Because scientists understood the individual steps of the cholesterol pathway at such a precise level, they assumed they also understood how it worked as a whole. This assumption—that understanding a system’s constituent parts means we also understand the causes within the system—is not limited to the pharmaceutical industry or even to biology. It defines modern science. In general, we believe that the so-called problem of causation can be cured by more information, by our ceaseless accumulation of facts. Scientists refer to this process as reductionism. By breaking down a process, we can see how everything fits together; the complex mystery is distilled into a list of ingredients. And so the question of cholesterol—what is its relationship to heart disease?—becomes a predictable loop of proteins tweaking proteins, acronyms altering one another. Modern medicine is particularly reliant on this approach. Every year, nearly $100 billion is invested in biomedical research in the US, all of it aimed at teasing apart the invisible bits of the body. We assume that these new details will finally reveal the causes of illness, pinning our maladies on small molecules and errant snippets of DNA. Once we find the cause, of course, we can begin working on a cure.

The problem with this assumption, however, is that causes are a strange kind of knowledge. This was first pointed out by David Hume, the 18th-century Scottish philosopher. Hume realized that, although people talk about causes as if they are real facts—tangible things that can be discovered—they’re actually not at all factual. Instead, Hume said, every cause is just a slippery story, a catchy conjecture, a “lively conception produced by habit.” When an apple falls from a tree, the cause is
obvious: gravity. Hume’s skeptical insight was that we don’t see gravity—we see only an object tugged toward the earth. We look at X and then at Y, and invent a story about what happened in between. We can measure facts, but a cause is not a fact—it’s a fiction that helps us make sense of facts.

The truth is, our stories about causation are shadowed by all sorts of mental shortcuts. Most of the time, these shortcuts work well enough. They allow us to hit fastballs, discover the law of gravity, and design wondrous technologies. However, when it comes to reasoning about complex systems—say, the human body—these shortcuts go from being slickly efficient to outright misleading.

Consider a set of classic experiments designed by Belgian psychologist Albert Michotte, first conducted in the 1940s. The research featured a series of short films about a blue ball and a red ball. In the first film, the red ball races across the screen, touches the blue ball, and then stops. The blue ball, meanwhile, begins moving in the same basic direction as the red ball. When Michotte asked people to describe the film, they automatically lapsed into the language of causation. The red ball hit the blue ball, which caused it to move.

This is known as the launching effect, and it’s a universal property of visual perception. Although there was nothing about causation in the two-second film—it was just a montage of animated images—people couldn’t help but tell a story about what had happened. They translated their perceptions into causal beliefs.

Michotte then began subtly manipulating the films, asking the subjects how the new footage changed their description of events. For instance, when he introduced a one-second pause between the movement of the balls, the impression of causality disappeared. The red ball no longer appeared to trigger the movement of the blue ball. Rather, the two balls were moving for inexplicable reasons. Michotte would go on to conduct more than 100 of these studies. Sometimes he would have a small blue ball move in front of a big red ball. When he asked subjects what was going on, they insisted that the red ball was “chasing” the blue ball. However, if a big red ball was moving in front of a little blue ball, the opposite occurred: The blue ball was “following” the red ball.

There are two lessons to be learned from these experiments. The first is that our theories about a particular cause and effect are inherently perceptual, infected by all the sensory cheats of vision. (Michotte compared causal beliefs to color perception: We apprehend what we perceive as a cause as automatically as we identify that a ball is red.) While Hume was right that causes are never seen, only inferred, the blunt truth is that we can’t tell the difference. And so we look at moving balls and automatically see causes, a melodrama of taps and collisions, chasing and fleeing.

The second lesson is that causal explanations are oversimplifications. This is what makes them useful—they help us grasp the world at a glance. For instance, after watching the short films, people immediately settled on the most straightforward explanation for the ricocheting objects. Although this account felt true, the brain wasn’t seeking the literal truth—it just wanted a plausible story that didn’t contradict observation.

This mental approach to causality is often effective, which is why it’s so deeply embedded in the brain. However, those same shortcuts get us into serious trouble in the modern world when we use our perceptual habits to explain events that we can’t perceive or easily understand. Rather than accept the complexity of a situation—say, that snarl of causal interactions in the cholesterol pathway—we persist in pretending that we’re staring at a blue ball and a red ball bouncing off each other.

There’s a fundamental mismatch between how the world works and how we think about the world. The good news is that, in the centuries since Hume, scientists have mostly managed to work around this mismatch as they’ve continued to discover new cause-and-effect relationships at a blistering pace. This success is largely a tribute to the power of statistical correlation, which has allowed researchers to pirouette around the problem of causation. Though scientists constantly remind themselves that mere correlation is not causation, if a correlation is clear and consistent, then they
typically assume a cause has been found—that there really is some invisible association between the measurements.

Researchers have developed an impressive system for testing these correlations. For the most part, they rely on an abstract measure known as statistical significance, invented by English mathematician Ronald Fisher in the 1920s. This test defines a “significant” result as any data point that would be produced by chance less than 5 percent of the time. While a significant result is no guarantee of truth, it’s widely seen as an important indicator of good data, a clue that the correlation is not a coincidence.

But here’s the bad news: The reliance on correlations has entered an age of diminishing returns. At least two major factors contribute to this trend. First, all of the easy causes have been found, which means that scientists are now forced to search for ever-subtler correlations, mining that mountain of facts for the tiniest of associations. Is that a new cause? Or just a statistical mistake? The line is getting finer; science is getting harder. Second—and this is the biggy—searching for correlations is a terrible way of dealing with the primary subject of much modern research: those complex networks at the center of life. While correlations help us track the relationship between independent measurements, such as the link between smoking and cancer, they are much less effective at making sense of systems in which the variables cannot be isolated. Such situations require that we understand every interaction before we can reliably understand any of them. Given the byzantine nature of biology, this can often be a daunting hurdle, requiring that researchers map not only the complete cholesterol pathway but also the ways in which it is plugged into other pathways. (The neglect of these secondary and even tertiary interactions begins to explain the failure of torcetrapib,
which had unintended effects on blood pressure. It also helps explain the success of Lipitor, which seems to have a secondary effect of reducing inflammation.) Unfortunately, we often shrug off this dizzying intricacy, searching instead for the simplest of correlations. It’s the cognitive equivalent of bringing a knife to a gunfight.

These troubling trends play out most vividly in the drug industry. Although modern pharmaceuticals are supposed to represent the practical payoff of basic research, the R&D to discover a promising new compound now costs about 100 times more (in inflation-adjusted dollars) than it did in 1950. (It also takes nearly three times as long.) This trend shows no sign of letting up: Industry forecasts suggest that once failures are taken into account, the average cost per approved molecule will top $3.8 billion by 2015. What’s worse, even these “successful” compounds don’t seem to be worth the investment. According to one internal estimate, approximately 85 percent of new prescription drugs approved by European regulators provide little to no new benefit. We are witnessing Moore’s law in reverse.

This returns us to cholesterol, a compound whose scientific history reflects our tortured relationship with causes. At first, cholesterol was entirely bad; the correlations linked high levels of the substance with plaque. Years later, we realized that there were multiple kinds and that only LDL was bad. Then it became clear that HDL was more important than LDL, at least according to correlational studies and animal models. And now we don’t really know what matters, since raising HDL levels with torcetrapib doesn’t seem to help. Although we’ve mapped every known part of the chemical pathway, the causes that matter are still nowhere to be found. If this is progress, it’s a peculiar kind.

**Back pain is** an epidemic. The numbers are sobering: There’s an 80 percent chance that, at some point in your life, you’ll suffer from it. At any given time, about 10 percent of Americans are completely incapacitated by their lumbar regions, which is why back pain is the second most frequent reason people seek medical care, after general checkups. And all this treatment is expensive: According to a recent study in *The Journal of the American Medical Association*, Americans spend nearly $90 billion every year treating back pain, which is roughly equivalent to what we spend on cancer.

When doctors began encountering a surge in patients with lower back pain in the mid-20th century, as I reported for my 2009 book *How We Decide*, they had few explanations. The lower back is an exquisitely complicated area of the body, full of small bones, ligaments, spinal discs, and minor muscles. Then there’s the spinal cord itself, a thick cable of nerves that can be easily disturbed. There are so many moving parts in the back that doctors had difficulty figuring out what, exactly, was causing a person’s pain. As a result, patients were typically sent home with a prescription for bed rest.

This treatment plan, though simple, was still extremely effective. Even when nothing was done to the lower back, about 90 percent of people with back pain got better within six weeks. The body healed itself, the inflammation subsided, the nerve relaxed.

Over the next few decades, this hands-off approach to back pain remained the standard medical treatment. That all changed, however, with the introduction of magnetic resonance imaging in the late 1970s. These diagnostic machines use powerful magnets to generate stunningly detailed images of the body’s interior. Within a few years, the MRI machine became a crucial diagnostic tool. The view afforded by MRI led to a new causal story: Back pain was the result of abnormalities in the spinal discs, those supple buffers between the vertebrae. The MRIs certainly supplied bleak evidence: Back pain was strongly correlated with seriously degenerated discs, which were in turn thought to cause inflammation of the local nerves. Consequently, doctors began administering epidurals to quiet the pain, and if it persisted they would surgically remove the damaged disc tissue. But the vivid images were misleading. It turns out that disc abnormalities are typically not the cause of chronic back pain. The presence of such abnormalities is just as likely to be correlated with the
absence of back problems, as a 1994 study published in *The New England Journal of Medicine* showed. The researchers imaged the spinal regions of 98 people with no back pain. The results were shocking: Two-thirds of normal patients exhibited “serious problems” like bulging or protruding tissue. In 38 percent of these patients, the MRI revealed multiple damaged discs. Nevertheless, none of these people were in pain. The study concluded that, in most cases, “the discovery of a bulge or protrusion on an MRI scan in a patient with low back pain may frequently be coincidental.”

Similar patterns appear in a new study by James Andrews, a sports medicine orthopedist. He scanned the shoulders of 31 professional baseball pitchers. Their MRIs showed that 90 percent of them had abnormal cartilage, a sign of damage that would typically lead to surgery. Yet they were all in perfect health.

This is not the way things are supposed to work. We assume that more information will make it easier to find the cause, that seeing the soft tissue of the back will reveal the source of the pain, or at least some useful correlations. Unfortunately, that often doesn’t happen. Our habits of visual conclusion-jumping take over. All those extra details end up confusing us; the more we know, the less we seem to understand.

The only solution for this mental flaw is to deliberately ignore a wealth of facts, even when the facts seem relevant. This is what’s happening with the treatment of back pain: Doctors are now encouraged to not order MRIs when making diagnoses. The latest clinical guidelines issued by the American College of Physicians and the American Pain Society strongly recommended that doctors “not routinely obtain imaging or other diagnostic tests in patients with nonspecific low back pain.”

And it’s not just MRIs that appear to be counterproductive. Earlier this year, John Ioannidis, a professor of medicine at Stanford, conducted an in-depth review of biomarkers in the scientific literature. Biomarkers are molecules whose presence, once detected, are used to infer illness and measure the effect of treatment. They have become a defining feature of modern medicine. (If you’ve ever had your blood drawn for lab tests, you’ve undergone a biomarker check. Cholesterol is a classic biomarker.) Needless to say, these tests depend entirely on our ability to perceive causation via correlation, to link the fluctuations of a substance to the health of the patient.

In his resulting paper, published in *JAMA*, Ioannidis looked at only the most highly cited biomarkers, restricting his search to those with more than 400 citations in the highest impact journals. He identified biomarkers associated with cardiovascular problems, infectious diseases, and the genetic risk of cancer. Although these causal stories had initially triggered a flurry of interest—several of the biomarkers had already been turned into popular medical tests—Ioannidis found that the claims often fell apart over time. In fact, 83 percent of supposed correlations became significantly weaker in subsequent studies.

Consider the story of homocysteine, an amino acid that for several decades appeared to be linked to heart disease. The original paper detecting this association has been cited 1,800 times and has led doctors to prescribe various B vitamins to reduce homocysteine. However, a study published in 2010—involving 12,064 volunteers over seven years—showed that the treatment had no effect on the risk of heart attack or stroke, despite the fact that homocysteine levels were lowered by nearly 30 percent.

The larger point is that we’ve constructed our $2.5 trillion health care system around the belief that we can find the underlying causes of illness, the invisible triggers of pain and disease. That’s why we herald the arrival of new biomarkers and get so excited by the latest imaging technologies. If only we knew more and could see further, the causes of our problems would reveal themselves. But what if they don’t?

The failure of this drug in particular has not ended the development of new cholesterol medications. The potential market for them is simply too huge.
The failure of torcetrapib has not ended the development of new cholesterol medications—the potential market is simply too huge. Although the compound is a sobering reminder that our causal beliefs are defined by their oversimplifications, that even the best-understood systems are still full of surprises, scientists continue to search for the magic pill that will make cardiovascular disease disappear. Ironically, the latest hyped treatment, a drug developed by Merck called anacetrapib, inhibits the exact same protein as torcetrapib. The initial results of the clinical trial, which were made public in November 2010, look promising. Unlike its chemical cousin, this compound doesn’t appear to raise systolic blood pressure or cause heart attacks. (A much larger clinical trial is under way to see whether the drug saves lives.) Nobody can conclusively explain why these two closely related compounds trigger such different outcomes or why, according to a 2010 analysis, high HDL levels might actually be dangerous for some people. We know so much about the cholesterol pathway, but we never seem to know what matters.

Chronic back pain also remains a mystery. While doctors have long assumed that there’s a valid correlation between pain and physical artifacts—a herniated disc, a sheared muscle, a pinched nerve—there’s a growing body of evidence suggesting the role of seemingly unrelated factors. For instance, a recent study published in the journal *Spine* concluded that minor physical trauma had virtually no relationship with disabling pain. Instead, the researchers found that a small subset of “nonspinal factors,” such as depression and smoking, were most closely associated with episodes of serious pain. We keep trying to fix the back, but perhaps the back isn’t what needs fixing. Perhaps we’re searching for causes in the wrong place.

The same confusion afflicts so many of our most advanced causal stories. Hormone replacement therapy was supposed to reduce the risk of heart attack in postmenopausal women—estrogen prevents inflammation in blood vessels—but a series of recent clinical trials found that it did the opposite, at least among older women. (Estrogen therapy was also supposed to ward off Alzheimer’s, but that doesn’t seem to work, either.) We were told that vitamin D supplements prevented bone loss in people with multiple sclerosis and that vitamin E supplements reduced cardiovascular disease—neither turns out to be true.

It would be easy to dismiss these studies as the inevitable push and pull of scientific progress; some papers are bound to get contradicted. What’s remarkable, however, is just how common such papers are. One study, for instance, analyzed 432 different claims of genetic links for various health risks that vary between men and women. Only one of these claims proved to be consistently replicable. Another meta review, meanwhile, looked at the 49 most-cited clinical research studies published between 1990 and 2003. Most of these were the culmination of years of careful work. Nevertheless, more than 40 percent of them were later shown to be either totally wrong or significantly incorrect. The details always change, but the story remains the same: We think we understand how something works, how all those shards of fact fit together. But we don’t.

Given the increasing difficulty of identifying and treating the causes of illness, it’s not surprising that some companies have responded by abandoning entire fields of research. Most recently, two leading drug firms, AstraZeneca and GlaxoSmithKline, announced that they were scaling back research into the brain. The organ is simply too complicated, too full of networks we don’t comprehend.

David Hume referred to causality as “the cement of the universe.” He was being ironic, since he knew that this so-called cement was a hallucination, a tale we tell ourselves to make sense of events and observations. No matter how precisely we knew a given system, Hume realized, its underlying causes would always remain mysterious, shadowed by error bars and uncertainty. Although the scientific process tries to makes sense of problems by isolating every variable—imagining a blood vessel, say, if HDL alone were raised—reality doesn’t work like that. Instead, we live in a world in which everything is knotted together, an impregnable tangle of causes and effects. Even when a
system is dissected into its basic parts, those parts are still influenced by a whirligig of forces we can’t understand or haven’t considered or don’t think matter. Hamlet was right: There really are more things in heaven and Earth than are dreamt of in our philosophy.

This doesn’t mean that nothing can be known or that every causal story is equally problematic. Some explanations clearly work better than others, which is why, thanks largely to improvements in public health, the average lifespan in the developed world continues to increase. (According to the Centers for Disease Control and Prevention, things like clean water and improved sanitation—and not necessarily advances in medical technology—accounted for at least 25 of the more than 30 years added to the lifespan of Americans during the 20th century.) Although our reliance on statistical correlations has strict constraints—which limit modern research—those correlations have still managed to identify many essential risk factors, such as smoking and bad diets.

And yet, we must never forget that our causal beliefs are defined by their limitations. For too long, we’ve pretended that the old problem of causality can be cured by our shiny new knowledge. If only we devote more resources to research or dissect the system at a more fundamental level or search for ever more subtle correlations, we can discover how it all works. But a cause is not a fact, and it never will be; the things we can see will always be bracketed by what we cannot. And this is why, even when we know everything about everything, we’ll still be telling stories about why it happened. It’s mystery all the way down.


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**Tags:** back pain, causation, drugs, health, pharmaceuticals, Science
My only complaint with this article is the title. This is NOT a failure of science. This is exactly what science is supposed to do. This is a failure of our understanding: scientific research doesn't guarantee absolute answers. It doesn't guarantee that we'll understand any specific thing at the end of the research. It's not a way to make money. It's simply an attempt to show that a given guess is or isn't right. "Science," in every case mentioned in the article, is doing exactly what it is supposed to: proving an incorrect hypothesis to be incorrect.

2 months ago   171 Likes   Like

But it is an indictment of "sciencism", the belief that science does provide absolute answers, that all systems are reducible, and a number of other fallacies. Granted the title is a bit misleading but the content is spot on.

2 months ago   in reply to Andy McKenzie   13 Likes   Like

this is not any kind of scientific failure but a failure of business. Pfizer is not looking to cure or relive anything but are looking for the next billion dollar pill. From that point of
view of course you would stop at the assumption that this pill could be a major seller and look no further.

2 months ago  in reply to Andy McKenzie  13 Likes

Michael Shaw

A thumbs up isn't enough--this is exactly what I was thinking through the whole article.

2 months ago  in reply to Andy McKenzie  12 Likes

Dr. David Briggs

Agreed. Hypothesis shown to be false. The fact that it was a very very expensive one is neither here nor there.

Next hypothesis please.

2 months ago  in reply to Michael Shaw  22 Likes

tchernik

I think the author may be -albeit slightly- trolling for replies.

2 months ago  in reply to Andy McKenzie  5 Likes

Jasper Janssen

The Title "Trials and Errors : Why Science Is Failing Us". I read it more as that its the belief that the scientific method will solve everything is failing us. We need to rely more on Trial and error.

2 months ago  in reply to Andy McKenzie  3 Likes

Schtupph

The scientific method is directed trial and error.

2 months ago  in reply to Jasper Janssen  2 Likes

Tom Helios
I've come across few scientists in my career, academic or industry-based, who believe deeply in the infallibility of reductionism. On the contrary, most of us are pleasantly surprised when the results fit our quaint models at a single level, let alone at every level from cell to whole animal. It's still the go-to method for reasons that underlie the lack of an alternative proposed in this article.

I doubt the investigators behind Torcetrapib thought any differently. Nobody, least of all a veteran of industry, watches a drug enter Phase III truly convinced of its success. Being human, it's usually quite the opposite feeling. Of course, this doesn't get played out when the company is trying to reassure shareholders and encourage investors, for obvious reasons. Similarly, in academia, scientists are not known for expressing their more cautious sides when plying for funding, or angling for a glamour pub.

Torcetrapib was put out there, and found to have undesirable effects. It happens. All the time. And not necessarily because there was something explicitly wrong with the cholesterol model, either. Drug trials could just as easily be rephrased as Drug Trial and Errors, because that's ultimately what they are and, importantly, what they are for. We haven't sufficient data by a long shot to model animal physiology in its entirety, so the only way we can gauge the final usefulness of a medication is to pump it into some poor mammal and hope for the best. At that stage, reductionism doesn't have a whole lot to do with it so much as luck and hope.

The author goes on to say the following:
"It would be easy to dismiss these studies as the inevitable push and
pull of scientific progress; some papers are bound to get contradicted. What's remarkable, however, is just how common such papers are."

No, actually it isn't remarkable, and for reasons the author actually explains in the article. Science is hard. The easy stuff has largely been resolved. The nature of publishing has also changed such that scientists are encouraged to publish piecemeal rather than wait for Ultimate Certainty before submitting a study for publication. On the plus side this keeps a good flow of information rolling, but on the minus side it means the likelihood of being inaccurate, or downright wrong, proportionately increases.

"Nevertheless, more than 40 percent of them were later shown to be either totally wrong or significantly incorrect."

Jings, only half were bollocks, eh? That's not bad going.

"The details always change, but the story remains the same: We think we understand how something works, how all those shards of fact fit together. But we don't."

No. We hope we understand how something works, and we do our best to identify the bits and how they fit together. Few scientists who aren't merely trying to dazzle a study section, keep the company bean-counters from pulling the project, or satisfy the public relations folk with a few choice quotes to the media, actually believe that their latest model is definitive and final.

(Edited by author 3 months ago)

3 months ago 93 Likes

Arden White

I agree-- nicely expressed. "Scientism" is a phenomenon, but I've always had trouble distinguishing whether scientists themselves fall prey to it as often as non-scientists; my impression is that they don't. They are grappling too closely with the complexities of the problems at hand.

2 months ago in reply to dsks 1 Like

Guest

Well put.
This piece of science journalism strikes me as excessively postmodern and, dare I say, anti-science. What agenda are you pushing Jonah?

You're essentially saying "Look! Scientists were wrong several times, and they were only able to figure out that they were wrong by doing large, well-controlled scientific experiments! Therefore causality is broken and we need to rethink the scientific enterprise!"

I understand your premises, but your argument doesn’t follow. If anything your examples only reinforce the point that sufficiently powered, double-blind studies are the only check we have against our frequently incorrect assumptions and intuitions about causality.

That is certainly an interesting interpretation. I found the article to be remarkably even-handed. The argument seems to me simply to be: we've made many mistakes, we should be more careful in future, and by the way, our knowledge-gathering methods might be able to be improved. I certainly don't detect any corporate agenda, and the author certainly isn't pushing any kind of neo-ludditism, what kind of agenda do you detect?

My impression was that this article's perspective could be supporting a holistic, alternative medicine type view. It seems to be throwing up its hands at the idea of trying to understand the intricacies of biology.

I think that conclusion is pure projection. The author makes no such claim and based on his other writings, I would find no reason to rest on such an assumption. Someone inclined to alternative medicine might draw your
conclusion, however. But an author can hardly be expected to qualify his writings for every possible interpretation. I think it was pretty clear overall.

Let's not forget to also hide results and withdraw funding of any research that could - in your authoritative opinion - be supporting a holistic, alternative medicine type view. And shoot all such researchers, to avoid any future bias.

Finally, a conclusion that I agree with totally.

I fail to detect signs of awareness of the sarcasm in my post... shall I look better?

Or when doing holistic medicine research, to not publish negative results; the "file drawer" effect.

Just an FYI, 'negative results' are not published in journals in any area of science.
"My impression was that this article's perspective could be supporting a holistic, alternative medicine type view."

And that is exactly the problem with it.

There's nothing wrong with "holistic" medicine as an abstract concept. The problem is that, without fail, practitioners of holistic medicine don't actually have a view of the whole, they're just looking at a different set of variables.

I never understood this line of thinking. Arguing that a problem exists within a system is not the same as desiring its destruction. Also of note, you assumed a causal relationship about an article about the fallibility of causation.

Trevor, your second paragraph is exactly what I thought upon getting about a third of the way through the article. I decided to skip through to the comments to see if anyone concurred...and voila, there was your comment.

No need to read the rest of the article, thank you.
You're missing a good explanation for the reversal of initial studies, Jonah, particularly drug studies.

Drug research conducted by Big Pharma is typically not peer-reviewed, nor published in peer-reviewed journals. Instead, the studies are submitted directly to the FDA or other nations' regulatory bodies to persuade regulators to unleash new patented drugs on the public.

To say Big Pharma has a vested interest in study outcomes is like saying ants are interested in picnics. Which is not to say that no objectivity ever exists in corporate-sponsored studies. But too often, it's in short supply.

Many drugs admitted to the market will eventually be removed because they are either unsafe for the intended purpose or they are ineffective. The idea that they were safe and effective was derived from industry-sponsored research and approved without either peer review or independent replication of results. When independent researchers - who do not have anything like the research budgets of Big Pharma - get around to examining the actual performance envelopes of these drugs, the drugs often fare poorly in safety, efficacy or both, contradicting original industry research.

You'd be amazed at the variety of methods drug company researchers have at their disposal to cleverly slant studies to the outcome which supports their bottom line. Many of the drug companies have been caught red-handed doing it, too. But enforcement by regulators is lax; there's little downside to cheating and the upside can yield billions in profits.

Enforcement is lax because regulators have been captured by the industries they regulate.

[Then why, you might ask, would a drug company itself pull the plug on a drug that was faring poorly in Stage III clinical trials? Wouldn't they just plow ahead and make a few billion dollars in the gap between approval and independent nullification of a drug company's initial claims? Not if it's obvious that selling the drug will create liabilities for the drug company. The mortality uptick for torcetrapib was severe enough to impress a hypothetical jury; which in turn made it severe enough to impress company lawyers. It didn't make the cut.]

None of this is to disagree with the thrust of the article. Human physiology is horribly complex; a human being is a shambling collection of millions of variables in rapid motion. Causation isn't a dead principle, and reductionism hasn't ended its useful life in science, but it's a sure bet that sorting out causation in a biological equation as complex as the human
organism is a tough nut.

Still, if you're looking for why initial drug studies are so often being overturned by later studies, part of the explanation has nothing to do with complexity and everything to do with corruption. That explanation should not be overlooked; it's integral to our system.

In addition to all the perverse incentives in this line of research though, the author is ultimately missing the point of a "linear" versus "nonlinear/complex" view of systems. The "I'll adjust this one dial and that operates independently of everything else to control the system" is the definition of the linear approximation point of view. Now, linear approximation of systems has worked GREAT for a long time giving us fundamental knowledge about the world, but when you get past that low hanging fruit and into the world of complex nonlinear systems (e.g. the human body...) you just CAN'T use those approaches anymore and hope for much success.

The author seems to take the view that the linear approach to modeling and analysis is all that science is, and wants to say that when that simple approximation breaks down Hume the penultimate skeptic is sitting from on high laughing at our follies of attempting to know the world. That's just total BS that undergrad humanities majors throw out at the sciences to make themselves sleep better at night. The nonlinear approach to problem solving is by nature a lot more complex, therefore until researchers get beaten over the head with the fact that linear approaches in their field no longer work, that will be what they try to exploit. We are at that point in a lot of fields nowadays - complex systems theory is very "new" by scientific standards and almost never gets presented until grad school - so it shouldn't be surprising that the vast majority of researchers haven't caught up.

Failure of science my hindquarters, it's merely failing to realize you need to use something other than your favorite hammer...

My. You've hit the nail on the head, but wow, that's touchy. So the author making assumptions by the way science works _now_, and pointing to its pitfalls, and
providing an incendiary title (obvious patented journalism shock tactics), somehow discredits him as "a disgruntled humanities major."

Science is not a completely unified or consistent thing; you’ve admitted as much. Its methods and underlying principles have changed, and will again. But many scientists and their allies are just not willing to accept that the linear approach is beginning to fail-- they make the exact assumptions about causation that the author criticizes them of making.

It's really quite incredible how fascinatingly touchy people get when Science is criticized. You would think the rational thing to do would be simple: call for scientists to adopt a greater understanding of causation and the non-linear processes you’ve described. The two go hand-in-hand.

What you say about Big Pharma reveals the perversion hidden within our society by corporations out of control. Profit generated by greed and corruption, sustained by self created importance. What Jonah states so eloquently about causation perhaps is better described as cultural entitlement pretending to be science. Both of you I laud for revealing the fallacy which has become the norm, as present day medicine tries to evolve in analogous fashion much the way computers have via the microprocessor revolution.

The future of medicine is one best defined in the new science of Epigenetics. The Food and Drug Administration sits before as an impediment to all future therapeutic innovation. It is an anachronism with its outdated, politically driven structure. The tolerance of its existence now only serves to promote a system so corrupt that it is embarrassing to call oneself an American Scientist.

For those of us that call ourselves physician, the insult that we endure everyday is beyond unbearable. It is the pinnacle of greed in America, health insurance mythology. It is time for Americans to wake up and "Feel the disease". Not Big Pharma, but most evil entity of them all, the Health Insurance Corporate oligarchy. It veils itself in wholesomeness, advertising itself as the savior of all Americans so blessed by its illusion of luxury. While in reality, it steals the economic vitality of the United States, and destroys it healthcare industry. This while hiding behind its mask of altruistic lies. Perhaps its time Anonymous focus itself on the real corporate mafia? Hopefully before
we all succumb to illness that could otherwise be prevented by the money pocketed by the giants of corporate greed.

Thanks for writing this, saved me the trouble. Big Pharma is a highly flawed example of science at work, since, as you just pointed out, lawyers and profit play a bigger role in drug development than the science does.

I identify with your frustration about the FDA. Remember, however, that they are under tremendous pressure, and unfortunately no group with gatekeeper power over multi-billion industries can be expected to be left alone. The best we can do is to exert through our representatives pressure to keep them independent, free of corporate influence, and adequately funded. Corruption does NOT have to be integral to the system. But we most definitely are up against it.

One can get a taste of the pressure to deregulate by looking up one Gregory Conko of the “Competitive Enterprise Institute.” Funded by those adorable conservative names we have come to know, including Koch, Scaife, Gilder, oil companies, etc., this group has campaigned relentless for years against government regulation of, among other things, drug safety. One of this group’s more notorious campaigns of misinformation was Michelle Malkin’s claim in 1996 that natural events like forest fires produce dioxins, evidence that they were not dangerous (see “Rachel Was Wrong, Malkin and Fumento, CEI, March, 1996). But I digress.

There is a bill which like toenail fungus keeps popping up just when we thought it was cured, going by sympathetic names such as Compassionate Access Act (H. R. 4732) or its previous iteration, S. 3046 from 2008. Both iterations had some interesting language in common. Both mandated that the FDA was to make available to qualified patients experimental drugs whose efficacy was supported by “...case histories...animal and computer models...) i.e. It worked for my former roommate’s ex wife’s cousin so I want it. Both also mandated that the sponsor (pharmaceutical company) could (“...charge for a Compassionate Investigational Access drug without notifying the Secretary or seeking or obtaining prior approval of the amount charged, provided the sponsor of the drug is actively pursuing marketing approval with due diligence.”) i.e.
whatever they want. No matter that a mechanism for providing experimental drugs in the same situations was implemented in the Expanded Access provisions of the FDA Modernization Act in 1997. One problem then, however, was that the companies had to submit to oversight, including of their charges. This act, supported by Conkovich the CEI in an article in the Wall Street Journal (August 23, 2008), would essentially take the FDA out of oversight. It takes years to bring a drug to FDA approval. How easy would it be for a company to encounter a few bureaucratic obstacles to its phase two and three preapproval testing, delaying approval but providing an investigational drug to those who can pay whatever the market will bear during that time, and during that time remaining legally immune from accusations of ineffectiveness and toxicity. There is tremendous pressure for this sort of unscientific wild west approach. Although neither H. R. 4732 nor S. 3046 became law, just like the Terminator we can bet they will be back. The Prescription Drug User Fee Act, also supported by the CEI, works somewhat similarly. Almost every company pays the fee these days. When they do, the FDA is on basically the football equivalent of the two minute drill to approve a drug. Review and approval requirements can be as little as six months, which is pretty ridiculous when years are often required to assess the efficacy of drugs targeting cancers, heart disease, or AIDS. And yet, user fees are now the majority of the FDA’s operating budget. An article in the New England Journal of Medicine in 2008 by Daniel Carpenter noted that it contributed to deadly fiascoes like the now withdrawn drug Vioxx. As long as we allow ourselves to be treated like the proverbial mushrooms, we will continue to be showered with this sort of shit. We may not like the FDA’s cautious reductionism, but they, and yes scientifically designed trials of drugs, statistically valid, are Americans’ best defense against more Vioxx and thalidomide prescriptions. We have to hold Congress accountable to keeping the FDA making sure that is the only basis of the drugs we take.

2 months ago  in reply to urgelt

Like

Douglas

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2 months ago  in reply to urgelt

Edward Stevenson

All sources of research has its sources of bias. all research public and privates seeks to please its source of funding in order to get more of it. the simple desire to publish and have your toil and work meaningful to the scientific community is powerful enough to inject bias into work. The independent researchers you mention, "auditors" if you will, have a strong desire to find flaws in research and win praise as whistle-blowers, they certainly play an important role as a check on hyped research but it is because of their strong skeptical bias while reviewing research that they often find the flaws they do.

2 months ago  in reply to urgelt

urgelt

There is a difference between "researcher bias," which does indeed exist in all science and is the subject of considerable effort to reduce among peer-reviewed scientists (well, most of them), and "deliberate slant."

Bad science: not peer reviewed, deliberately slanted, with only the intention of moving a captured regulatory body to approve the means by which vast profits are unlocked, is far more sinister than ordinary researcher bias.

"Skeptical bias" is an interesting phrase, Edward; it implies that skepticism itself distorts and is bad for science. I call the phrase an absurdity. Science does not need to put aside skepticism to reduce bias; it needs skepticism to combat bias.

My original point stands. Wired failed to mention that original not-peer-reviewed studies from Big Pharma are often reversed by later, peer-reviewed studies, not because of complexity in physiology, but because the original studies were not honest science at all, were never peer-reviewed, and - frankly - they lied to secure for Big Pharma government-granted monopolies selling drugs whose
benefits are often largely fictional. It's a rather startling oversight in an article that purports to explain why studies are often reversed.

Medical and surgical diagnosis and treatment are better than anything else for true emergencies.

Health care for other conditions works 85% of the time -- Mother Nature, with no intervention, gets 90% of us well. Good care gets 95% well from the world's greatest expert on your life and health -- yourself. You know at least a million times more about yourself than anyone else could.

With over a billion American health care visits a year, 5% (over 50 million) get worse and 0.1% (over a million) die from health care (over 40% of a total of 2,423,712 deaths). Death is almost always within 10 days and is the hidden #1 cause of death at all ages from all reported causes. We know this, because, in less than 10 days, deaths drop 17% to 60% -- usually about 25% -- whenever doctors go on strike. Deaths remain low until the strike ends, and in less than 10 days, deaths at all ages from all reported causes rise 20% to 120% -- back to before the strike. Israel has the most doctor strikes, and morticians there mediate a quick end or go out of business. Prescription drugs are not intended to cure illness nor prolong life, but to relieve symptoms, and make money for Big Pharma, Big Government, Big Health Care, and other monopolies. Competitive free enterprise is prevented by Food and Drug Administration demand for years and over $2 billion of tests to get approval for synthetic patent drugs. Cures make very little money. Letting more non-productive elders live increases health care costs.

Was medical director of Wisconsin Veterans Home, with 800 residents, most wives of veterans, getting prescription drugs up to 4 times a day. The #1 employer in a rural county. Cut number and dose of medications, emptied beds as they recovered and left. Nurses were laid off. False rumors were broadcast of my abuse of the residents, Was terminated without cause as if still on probation after 11 months. A doctor was hired to put them all back on their medications, filled up the beds, rehired the nurses, and deadly peace resumed.

Am retired, but still make home visits, encourage patients to list and build upon the good influences on their lives and their personal strengths, focus on their major concern, relax with closed eyes and receive internal suggestions of the most promising next step to take, select the best one, take that step, discover real life consequences, and 90% get better. The other 10%...
soon sensed they were heading in the wrong direction, suddenly knew what step they should have taken, took it, and could hardly believe the good outcome. Could not wait to take the next step -- whether pleasant or not. Could enjoy the pleasant, and the unpleasant taught them a valuable lesson that immediately brought such great good it seemed too good to be true, but time told it was true.

Always billed insurance companies for the home visit. Never got paid, until Wisconsin Blue Cross - Blue Shield sent the one and only check, with a letter saying they do not pay for what I do, but those who call me their doctor used to cost $thousands a year and now cost nothing, so this was just to say thanks. Followed patients at least 6 months. Almost never saw them again. Asked if they got help elsewhere, said they're doing this all by themselves.

3 months ago  39 Likes

Quartz

Please, could you state the source of those numbers? And how comes you equate health systems of different countries? And "forget" to mention all iatrogenic episodes and systematic issues? Very objective, indeed.

2 months ago  in reply to Dr Richard W Biek MD MPH  2 Likes

Richard Lee

"At first, cholesterol was entirely bad; the correlations linked high levels of the substance with plaque. Years later, we realized that there were multiple kinds and that only LDL was bad."

I have spent over a decade studying cholesterol, and this passage shows a complete lack of understanding of what LDL and HDL is. Lipoproteins are a complex of proteins, lipids, and cholesterol that circulate through the plasma. Lipoproteins, which include LDL and HDL, are often isolated based on density, and differ in their lipid, protein, and cholesterol composition. Decades of study have shown that Low Density Lipoproteins (LDL) is known to be taken up in arterial walls, accumulate, and eventually lead to the build up of instable arterial plaques that rupture, leading to thrombosis and coronary events. High Density Lipoproteins have also been studied, and while it is less well established, is thought to remove cholesterol from plaques back to the liver, where it is processed and removed from the body via the feces.

There is one "kind" of cholesterol, as it is a chemically defined molecule. Whether it is "good" or "bad" (words that any self-respecting scientist loathes), depends on the lipoprotein that the cholesterol is packaged in. The author statement that there are different kinds of cholesterol
is completely false. Also his assessment of the failure of torcetrapib is oversimplified at best, which he ironically cautions against throughout the article.

From a cholesterol metabolism standpoint, this is a poorly researched, irresponsible article that causes me to question the authors credibility (of course as a scientist, I may be oversimplifying it.)

(Edited by author 2 months ago)

2 months ago 30 Likes

Will Olsen

"I have spent over a decade studying cholesterol, and this passage shows a complete lack of understanding of what LDL and HDL is."

I have spent over a decade studying English, and this sentence shows a complete lack of understanding of subject-verb agreement.

2 months ago in reply to Richard Lee 8 Likes

jthias

Richard, thanks for reminding me of some basic biochem = )

2 months ago in reply to Richard Lee 1 Like

Geoffrey Brooks

These concerns about the article echo concerns I've had about a number of Lehrer's previous articles, and I've concluded that I'm better off not reading them unless I have the time to strip away the froth. I've found the same is true of Gladwell and Errol Morris.

2 months ago in reply to Richard Lee

nashvilledharma

Excellent article. And given the sadly predictable tenor of most of the responses, I'd say very brave on the part of Mr. Lehrer. Science is a tool for understanding reality. An extraordinary tool to be sure, but just one tool. The only heresy the author is committing is to effectively
suggest that perhaps a hammer is not the best tool to use to change a light bulb.

I come from a family of scientists, so I am not without grounding in this discipline. As such it seems to me that one of the most seminal aspects of the scientific mind at its best is the ability to recognize that it doesn't know something, and to then strive to methodically figure it out. Sadly though the edifice of science has become seemingly more fundamentalist and insecure in its defensiveness than the "faith" based worldviews it too often decries.

Interestingly as we get to the limits of what the tool of science can do, science is discovering (sometimes to its chagrin) that the territory it is treading is not undiscovered, but well trodden.

An open minded scientist can see the scrapes and dents of other worldview tools' attempts at getting at the same answer. In fact, if they are really willing to look at the evidence, they might notice that some worldviews have already opened the boxes at which science is still methodically clawing.

This is not a defense of some kind of "anything goes" worldview. Rather a pat on the back to a writer and a magazine willing to embrace the TRUE spirit of science, which is not hubris, but wonder.

“Imagination is more important than knowledge. For knowledge is limited to all we now know and understand, while imagination embraces the entire world, and all there ever will be to know and understand.”
~ Albert Einstein

(Edited by author 3 months ago)

3 months ago   28 Likes

TDB2011

"some worldviews have already opened the boxes at which science is still methodically clawing."

A hoary postmodern/social constructivist cliche. I'd be interested in hearing a specific example of such a box-opening breakthrough. Based on your name, I assume it's some fuzzy, feel-good, untestable notion from Buddhism?

(Edited by author 2 months ago)

2 months ago   in reply to nashvilledharma   3 Likes
Hi TDB2011,

Thanks for commenting. Yes, by the name I chose for the post, it's obvious that I do study Buddhism. But that does not mean Buddhism is all I study, or have studied.

I too am particularly allergic to "fuzzy, feel-good, untestable notions". Which is EXACTLY what drew me circuitously to Tibetan Buddhism, which has by the way one of the most rigorous systems of debate as a mechanism of checks and balances, as has ever been in any philosophical system on the planet. VERY scientific actually.

The reason I spoke in broad terms in my post and not in specifics is that the primary concept I was referring to is something usually only explained very carefully because it is so likely to be misunderstood. The principle is called Sunyata, or "Emptiness".

I've searched through countless scientific, philosophical, religious, and mystical systems and NEVER encountered anything like this idea.

My scientific studies have included such things as course work with world renowned physicists, and growing up in the tutelage of a CDC and WHO laboratory administrator and in demand lecturer. So I do value the concept of evidence. So much so, I'm willing to look wherever it seems to be found, even if it's outside the regular silos.

A real touchstone for me within my scientific studies was Bohm and Pribram's Holographic Universe theory, which is not a bad metaphor to try to model the way things work slightly better than our admirable but sadly disjointed reductionist and incomplete method so far. David Bohm was a colleague of Einstein, and as brave a man as he in his bold intellectual and scientific explorations of the cosmos. If your intellectual tastes run chiefly in scientific circles, I highly recommend sampling some of this vintage, if you are willing and able. Quite illuminating.

But then in my other studies I finally heard about Emptiness, or more accurately, I was fortunate enough to hear about it from the right person, in the right way, and for it to "Click".
Then I realized, as I was trying (perhaps badly) to convey in my previous comment, that the very thing that I and so many other vastly more qualified individuals had been trying to get at purely through the scientific method, had already been cracked, and experienced, and mapped out, and explained in detail elsewhere, LONG before.

Some might choose to ignore some kinds of knowledge because it comes from a different laboratory, and that is of course a person's own prerogative.

Science works extremely well at establishing rules and then following them. But science itself also has a history. The rules change with new information. At the risk of hauling out a cliché, the definition of "Genius" in science often refers to a person who is able to arrive at a conclusion without covering the intervening steps. I would suggest that this REQUIRES a certain amount of careful but willful breaking. Being willing to take in new information which of course could not fit previous models, because they were only designed for the old information. It seems to me that this is the very nature of science. To make these leaps, and then to test them rigorously. But I believe that rigorously testing without the occasional leap is a fallow methodology.

For my part, I'm interested in testable results. And I am interested in valid authentic sources. And purely from my own perspective, I can tell you that at least one part of the set of field research which happens to currently wear the label "Buddhism" does seem to offer something of incredible value. So I'm studying it.

I do hope this does not offend you. And I do hope that whatever course your own studies take you brings you happiness.

(Edited by author 2 months ago)

2 months ago  in reply to TDB2011

Bob Marley

"Based on your name, I assume it's some fuzzy, feel-good, untestable notion from Buddhism?"

"The principle is called Sunyata, or 'Emptiness'."

I got a good laugh.
I'm no Buddhist, but I know enough about it to know that it's anything but "feel-good" and that abstract ideas are testable in the laboratory of logic. Did you learn and test it objectively before you laughed or is your laugh a way of dismissing it without bothering to test it?

TDB2011 asked for a specific example. nashvilledharma failed to provide one. The burden of proof lies with those making a positive claim. That's true whether your laboratory is philosophic, legal, or scientific.

If you make a claim and provide evidence, I'm accepting. If you make a claim with no evidence, I'm skeptical. If someone asks you to provide evidence directly, and you fail to provide it, I'm dismissive.

Shall I test every claim someone makes that has no evidence? No, and neither do you. If I claim that I'm a prince and all you have to do for me to give you $5 million dollars is dance around the house, a reasonable person is not going to dance.

If nashvilledharma had said "Look, there's this concept of Emptiness in Buddhism, and it turns out that it has many applications in physics (or whatever, I don't) and here's a link" I would not have been dismissive.

Frankly, any other course of action would have been illogical given the assumption (which I made) that nashvilledharma is of at least average intelligence and can understand what a request for specific example means. One who works in a "laboratory of logic" should know that.
Like

2 months ago   in reply to msnIncomplete

msnIncomplete

I have yet to see a convincing proof on a comment board; they contain feelings and half-truths. On comment boards, we largely speak in the language of emotions as a kind of short-hand for the evidence we have personally collected about our world. My reprimand came as an expression of disappointment in some comments on this discussion board for an apparent lack of curiosity.

The reference was provided, the information is readily available, there is no specific study referred to, no link is needed.

$5 million dollars from a Prince for a dance round the house is mighty intriguing when the sentiment seems sincere, even if the "Prince" is clearly a pauper.

2 months ago   in reply to Bob Marley   1 Like

Andrew & Sabrina

It doesn't seem to be science that's failing us; rather it's corporately motivated research looking for that one thing you can whack in a pill that's failing. And that is being defeated not just by the complexity they're failing to take seriously, but by the structure of clinical trials and the scientific method. Science is, in fact, not failing us at all; rigorous experimental design (eg Phase III clinical trials) are defeating the poor initial research.

(Edited by author 3 months ago)

3 months ago   26 Likes

coriha

That's what I was thinking. The author is either a bit naive about the difference between real scientists and those who've sold their souls for pharma paychecks or he's backhandedly skewering them. I can't decide which.

3 months ago   in reply to Andrew & Sabrina   4 Likes
I am a practicing physician.

Loved the article perhaps because it validated much of what I have been thinking and discussing with friends over the last few years. So what do we do? Do we stop doing science? Obviously that does not make sense. One thing I would like to add to the discussion is that perhaps our methodology needs revision—we are using in a manner of speaking linear solutions to complex problems. Stable systems and the human body is a stable system—depend on the synchronous interplay of multiple ongoing (mainly negative) feedback loops. The relationships are necessarily complex. Will complex dynamic systems theory prove some solutions?

In the meanwhile, some humility in my profession may be in order.

Lately, I have taken to counselling my patients—something like this all we have are intelligent guesses as to what effects any particular intervention may have—even though many of our guesses work, there is really no good way of predicting what the actual outcome will be.

The trend in health care today is to try to systematize everything under rather inflexible protocols. I have been fighting a losing battle trying to get colleagues to understand the limits of our theories of causation.
Lehrer's, but rather the editors'. The aim is to push buttons, and in that, the title succeeds. Those who actually bother to read the article, however, will notice that nowhere in it does Lehrer state, or even imply, that science is a global failure. Lehrer merely demonstrates the obvious: That science is flawed, as its practitioners are flawed. To put the matter a little differently, science is no better than the humans who practice it.

Of course, there will always be those whose quasi-religious, purely emotional, and utterly irrational belief in Scientism will cause them to have dyspepsia, and to resort to name calling ("pomo") whenever someone suggests, however gently, that, unlike Mary Poppins, science is not "practically perfect in every way". The chasm that separates those who see science sensibly and those who see it with rose-colored glasses makes the divide between Snow's "two cultures" seem millimetric by comparison.

(Edited by author 2 months ago)

Typical straw man argument from the social constructivist crowd. Who is saying science is "perfect"? It's obviously not, but it is clearly superior to introspection, anecdotes, mystical revelation, arguments from authority, and all the other ways that humans have tried and failed to understand the objective universe throughout our history. Sorry if that makes you English majors uncomfortable.

Please define "superior" carefully. And "tried and failed." And "perfect." You won't be able to do it. That's why this English major is not uncomfortable, just sighing and muttering "ur doin it wrong."

Your notion of "perfection" -- implicit in your statement-- is a symptom the problem, whether or not science lives up to it in your estimation.

I've been doing biotech for 20 years
The problem today is the same as when I started: we don’t really know a whole lot about molecular physiology of H Sapiens.

True, we know a lot more then in 1990, and incredibly more then in, say 1970, but that is not the relevant guage.

Compared to what we need to know, to develop pharmaceuticals effectively, we know almost nothing.

As an example, when you can, in silico, predict if a new drug will cause cardiac arrythmias, for genomes representing 95% of the human population (assuming a long tail on variation, 90% of the variation in a small % of population) then your talking for all you "scientists" who are criticizing the author: go back and look at time series data on rates of epidemic diseases like yellow fever, malaria, etc, then look at time series data on clean water, sanitation and vaccines.

what I remember, the sanitation engineers saved a lot more people then the PhDs.

Isn’t that true of all complex systems? The more we learn, the more we discover how much more remains to be discovered.

Which means prevention research is far more effective in getting the desired results then anything the drug manufacturers can sling at us. Avoids expensive drug trials too.

However, it looks like the low-hanging fruit—sanitation, vaccines—has been picked when it comes to prevention, too. What is left is mostly interventions that have only incremental benefits, and the ones that most people can’t or won’t follow (keep your weight down, stop smoking, stop drinking).
All the low-hanging fruit in biomedical science has long since been picked. Scientists today, in their pursuit of grants and tenure, are reduced to teasing trivial correlations out of gigantic data sets of questionable integrity, via tortured multivariate analyses that too often seem to include every variable but the ones that really matter.

You didn't cover it, but the same is true of climate science. We hear a lot of angry shouts of "The Science is Settled!", frequently from people who have a financial interest in seeing it remains so, but there are many lessons for them to be drawn from the recent history of the life sciences.

It is certainly true that the low-hanging fruit--the reality of CO2-induced global warming--was picked many decades ago. Modern climate scientists are struggling with complex-system questions: what will happen to regional severe weather, which regions will suffer the most, what the consequences will be for agriculture.

But one lesson that the biomedical sciences teaches us is to be wary of plausible-sounding fixes when complex systems are involved. Is ameliorating the consequences of global warming like traveling to the moon? Or is it more like finding a cure for cancer?

Science does not fail us, the media does...

So very true, though not so nearly much as politicians in their abject greed and stupidity...

Mary Parlange
As usual, I think Jonah Lehrer has written an interesting, thought-provoking article. And I can't help but wonder about the commenters that jumped all over it - but in truth it's not surprising that when the story we've so carefully built up to explain the way things work (i.e. modern scientific methods) is shown to have built in weaknesses (i.e. the shortcomings of human perceptions and our considerable baggage of cognitive biases) people get defensive and upset. Particularly when their lives, efforts and belief systems revolve around those stories.

He's not trying to diss science and the careers and efforts of scientists - far from it. He's just trying to get us to think out of our little cognitively-biased boxes.

Another point - most medical research is based on mouse models. There's a whole lot to be said for mice, but they are not human. Why would we think that what holds in a strain of horrifically inbred rodents raised in unnatural conditions would apply equally to a genetically diverse population of primates like us, living in the wild world? Now there's a cognitive disconnect.

People aren't jumping all over the article because the article is bringing to light that science can be tricky and that things aren't always what they seem. We're jumping all over the article because these sorts of problems are well known, and have been well known for a very long time, but the article implies that this is a "new" development that everyone should be aware of.

No, this isn't new. Yes, everyone should be aware of it, and they should be made better aware of how the process works and why it can fail. In reality, this article is a testament to just how poor our education system really is at teaching people about what science really is and how it actually works. That's the real cognitive disconnect here, not that biological analogs may not be perfect stand-ins for the systems we really want to treat.

I stopped being at all interested in listening to the advice of any doctor after teaching chemistry to pre med students at an elite university. The varieties of people who should be encouraged to give medical advice generally go into basic research because they would prefer to use their minds to help solve problems, rather than perform endurance cram
festivals and not sleep for days during residency. Unfortunately the private sector medical industry, which is the only section with the power to 'do anything' is mostly corrupt. The only reason doctors have a somewhat positive benefit on peoples health is that they have the power to prescribe antibiotics when necessary, and can perform life saving surgeries for acute problems.

There is no better medical treatment than eating well and exercising regularly. Those who have the opportunity to do so, but choose not to, earn their ill health, and those who are prevented from doing so by coercion should be protected.

The modern western medical system is the biggest waste of life and energy going on the planet. That medical industries are one of the only growing segments of the USA's economy is what's sick.

Science can’t fail or succeed. Greed can however corrupt people of science . . . and religion and government and finance. Science has no guilt, but mankind . . . there’s yer enemy!

The problem is that we are too full of ourselves and really don’t understand complex systems. Nature has had millions of years to bring biological organisms like the human body to the state of development that exists today. The drug company scientists wanted to believe that LDL cholesterol was a primary cause of plaque problems and heart disease.

But LDL exists for some purpose and Nature has also built at least one means to control it (HDL according to the article). As Pfizer discovered, removing LDL wasn’t the right answer. Doing so obviously affected the body in unanticipated ways and caused heart pain & failure.

Have you ever actually read the warnings on a modern drug? Paragraphs upon paragraphs of possible side-effects, all illustrating that changing (blocking/enhancing) one thing in the body can have many effects. And those warnings are only the ones they think they know about!

The body, like the Earth and universe around us, is a complex balanced ecosystem where changing one thing has the potential to affect many underlying subsystems. Until we have the science to to fully understand what we are affecting when we block something in the body or
create a new virus, maybe we should stay away from creating new drugs.

3 months ago 11 Likes

chrisbrandow

I have to agree that this entire article felt premised on a strawman that scientists actually believe that everything is a neat and tidy system that has single component solutions.

I think perhaps the author was trying to say that even though scientists know better, they still act as though things were reductionist in a simple fashion, but I don't think that argument was completely fleshed out.

3 months ago 11 Likes

Chris Marrou

Next to the human body, about the most complex system any of us deals with is the federal government, and yet politicians persist in thinking that a program designed to achieve X will do so and without producing Y, Z and several X primes. They, too need to be a bit more modest about causation. The libertarian view may work simply because it allows failures to occur at a much smaller and cheaper scale, and when something does work, eventually we monkeys see and do it.

2 months ago 9 Likes

DrGamma

Very humorous. Using reductionism to attack reductionism. This type of comedy is very entertaining.

2 months ago 8 Likes

atimoshenko

Fascinating article. Got me thinking about the differences between simple and complex systems. A simple system has a few components, right? Each of only interact with one another in a small number of specific ways? So if you want to have a particular outcome, you need to set the system up exactly right.
Complex systems, on the other hand, have a large number of components, each of which influences and is influenced by at least a few of the others, no? This means that perturbing one part of the system is quite likely to influence at least something else, and that there is probably more than one set of initial conditions that can lead to the same final result.

Perhaps then, instead of looking for the one specific cause to make something happen (as we do in simple systems), in complex systems we should instead look for the things that reliably prevent things from happening (so – figure out how to predictably break the system, then try to use this predictable breaking to your advantage)? In other words, instead of looking for a very specific and analytically precise chain of events (which likely end up eventually being destabilised by at least one of the unforeseen perturbations of the complex system), we should look for broadly true heuristics?

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Rohit Patnaik

Complex systems don't have to have a lot of moving parts. Take the three-body-problem, for example. Just like it says, it only involves three bodies, each following Newton's Laws of Motion and linked by gravity. Yet, the behavior of such a system is chaotic. There is no analytic solution - the best you can do is an approximation which will diverge from the behavior of the system with time.

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Roger Kamben

This article is just crap and even contradicts itself. The last MRI example doesn't even have correlation let alone causation. Yes science is based on the scientific method and critical thinking which does prevail in the end despite human short comings. And I'm afraid science is not like living in the ideal world of making computer programs which might explain where the author is coming from.

Here is another bad analogy for you: Just because you know how a hard drive works doesn't mean you know anything about what will happen to the computer if you start messing with it.

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Tim Luther Lewis

The problem is absolutely financially motivated research, rather than the practice of science.
itself. It is vitally important that the practice of free inquiry and empirical based understanding is not blamed for the ills of the world - evil, greedy people are responsible for those.

I don't think that medical research and laissez-faire capitalism are at all a comfortable mix. Some things just aren't and it's easy to tell which, just follow the money.

The end goals of medical research should be to prevent or cure. Unfortunately, that's not profitable! So the end goal of commercial medical research would, more logically, be to create dependencies. That's not right and that should be as illegal as pushing recreational drugs.

For many things, making a profit is either amoral (as in it's orthogonal to morality, has nothing to do with it, isn't measured on the axis of 'good-bad') or it's goals can be aligned with moral goals. Medical research is not one of these areas. Much like war profiteering, it's an ugly, ugly side of the callous, money first, neo-feudalistic new world order.

So... modern science is hopeless to completely understand the machinations of the human body, but Al Gore and his army of crank scientists know *exactly* what temperature the earth should be. Excuse me if I'm a bit incredulous.

Right. Just negate both points and you obtain a perfectly reasonable pair.

Btw since when did Al Gore have an army of crank scientists, that parasite?

Here's another one who knows better than the WMO, should tell it my bartender...