

A MASSIVE HEALTH STUDY ON BOOZE, BROUGHT TO YOU BY BIG ALCOHOL



Miriam Shuchman Science 10.26.17 07:00AM

A LITTLE BIT of booze, the conventional wisdom goes, can be good for you. But the evidence for that claim—beyond anecdotal accounts that a nip of whiskey can nip a cold in the bud—is surprisingly thin. [Alcohol](#) studies usually look backwards, comparing participants' historical drinking habits with their health problems. But it's [hard to prove](#) that alcohol caused those problems. The best alcohol study would randomly require people to either drink or abstain—but for many public health researchers, that's always seemed like a bridge too far. Today, though, the National Institutes of Health is planning just such an experiment. The Moderate Alcohol and Cardiovascular Health study, now in progress on four continents, is poised to be a breakthrough in public health: the first time that researchers have followed a group of people randomized to receive a daily drink or nothing at all. But it's also the first time the NIH has offered the \$1

trillion-plus alcoholic beverage industry a chance to sponsor a project. That exchange of money, along with the study leaders' failure to guard against outside influence, are jeopardizing the study's credibility before it has even enrolled its first participant.

The study has its origin, strangely enough, in tea. Back in 2006, researchers thought tea drinkers might have fewer heart attacks. So Kenneth Mukamal, an epidemiologist at the Harvard-affiliated Beth Israel Deaconess Medical Center in Boston, recruited at-risk adults and told them to drink either three cups of black tea a day or three cups of water. Getting participants to stick to the program is notoriously difficult, so to make sure they were drinking their tea, Mukamal tested urine samples from a subgroup of participants for gallic acid, a tea breakdown product. After six months, they ran the numbers: Tea had virtually no effect on a person's cardiovascular risk.

The results from the tea study may have been moot, but that gallic acid-measuring test was the proof of concept Mukamal needed for a different study. In 2008, Mukamal began giving participants an alcoholic drink—a mix of ethanol with Crystal Light or a Kraft lemonade mix—comparing their health markers to a control group that got lemonade without the booze. But people wouldn't drink the ethanol. Like in the tea study, Mukamal was tracking whether his participants stuck to the program, and a blood test that rises with alcohol intake was actually higher in the non-alcoholic group than the alcohol group. A randomized trial to test alcohol's benefits, Mukamal concluded, would have to let the participants choose a drink they actually liked.

Enter the National Institute on Alcohol Abuse and Alcoholism. In 2014, the institute solicited Mukamal to plan a six-year study of 7,000 subjects at risk of heart disease, pitting a daily alcoholic drink against total abstinence. They'd track heart attacks, strokes, heart-related chest pain, and death—the most comprehensive study of the heart impacts of daily drinking ever done, focusing on adults 50 and over. Instead of giving subjects a mix prepared by research pharmacists, though, the study would reimburse them for the drink of their choice.

Paying for more than 3,500 daily drinks for six years, it turns out, is expensive. The NIH would need more funding—and soon, a team stepped up to the plate. The Foundation of the NIH, a little-known 20-year-old non-profit that calls on donors to support NIH science, was talking to alcohol corporations. By the fall of 2014, the study was relying on the industry for “separate contributions to the Foundation of the NIH beyond what the NIAAA could afford,” as Mukamal put it in an e-mail to a prospective collaborator. Later that year, Congress encouraged the NIH to

sponsor the study, but lawmakers didn't provide any money. Five corporations—Anheuser-Busch InBev, Diageo, Pernod Ricard, Heineken, and Carlsberg—have since provided a total of \$67 million. The foundation is seeking another \$23 million, according to its director of development, Julie Wolf-Rodda.

The NIH has run into similar ethical problems before. In 2012, the National Football League made a \$30 million donation to support research on sports-related medical problems. Later, when the NIH funded an expert on football-related brain injury whom the League disapproved of, NFL representatives contacted senior NIH officers about it. A 2016 Congressional investigation faulted the NFL for attempting to use its donation “as leverage to steer [research] funding away from one of its critics.” But the investigation also concluded that the Foundation didn't do enough to protect the NIH from its NFL funders.

To protect the alcohol study from the influence of its funders, the Foundation uses detailed letters of agreement: Companies are obliged to accept NIH control of the project's scientific and administrative aspects and barred from attempting to influence its design or conduct, and from trying to access non-public project results. Those agreements were in place during the NFL deal, and Wolf-Rodda says the organization has since “tightened” the language in its agreements, making the rules “now a little bit clearer and harder for people to overlook.” Both Mukamal and Peggy Murray, a senior leader at NIAAA and the NIH staff scientist on the trial, say they haven't spoken to anyone from the alcohol industry about the project, another important wall to prevent any influence, intentional or not, from the companies.

But for some scholars, there is no right way to involve the industry in investigating alcohol's benefits. “It's a clear conflict of interest if the industry that's going to profit from the findings of the research is funding it,” says David Jernigan, head of the Center on Alcohol Marketing and Youth at the Johns Hopkins Bloomberg School of Public Health in Baltimore. Richard Saitz of Boston University's School of Public Health compares the situation to the tobacco industry's support of research that raised doubts about the risks of smoking. In some circumstances, he says, “a firewall is just not quite enough.”

And although the study has not yet begun recruiting subjects, the medical community has already found reason to validate those concerns.

JIMMY VOLMINK, DEAN of the medical school at Stellenbosch University near Cape Town, South Africa, first heard about the alcohol trial in the fall of 2014. To recruit a diverse set of participants, Mukamal was assembling a global

team of research partners; Volmink, a black South African physician who did his medical training under the apartheid regime, was considering signing on. Volmink holds a public health degree from Harvard and a doctorate in cardiovascular medicine from Oxford, and his claim to fame in academia is his leadership role with Cochrane, an organization that reviews clinical trial results for doctors. After a few exchanges with Mukamal, Volmink met with two colleagues to talk about the study. The Stellenbosch medical campus is in a Cape Town suburb near stylish outdoor malls rivaling those of Florida or California, but the group's discussion focused on the impoverished townships that dot the Cape Flats, only about 20 km away. The threesome worried the study could be unethical for their center, given the region's soaring rates of fetal alcohol syndrome—among the highest in the world. South Africa is also burdened by alcohol-fueled accidents and violence, a lasting reminder of the apartheid era's 'dop' system, when farm workers received part of their pay in drink instead of money. Celeste Naude, a nutrition researcher, said she also wondered about the project's funding, since the food industry often sponsors nutrition research.

When Volmink talked with Mukamal a few weeks later, he followed up on Naude's funding question. Mukamal said the project had a commitment from the NIAAA, and NIAAA would also receive alcohol industry monies. "There's no direct funding by the alcohol industry," Volmink recalls him saying.

In an interview later, Volmink said the discussion had made him uncomfortable—he hadn't heard about the industry's role before, and he was troubled by the lack of transparency. Quantitative analyses of drug and medical device studies have found that they are about 30 percent more likely to reach positive conclusions when the research is industry-sponsored.

So in mid-October 2014, Volmink e-mailed Mukamal to say Stellenbosch would not participate, citing problems they expected to have in recruiting participants, South Africa's high levels of harmful drinking, and "funding from the alcohol industry, albeit channeled through the NIAAA." But he closed with gratitude: "Thank you for inviting us to collaborate. We look forward to future opportunities to do so."

Mukamal sent a stinging reply. "Thanks Jimmy. It sounded earlier like you lack the strong trial infrastructure and experience and appropriate population we would need for this to be carried out safely and effectively, which may not exist in many places in [South Africa] and beyond."

He added, “I doubt we’ll have similar opportunities to study questions as central to nutrition as this again, as few are as prominent, but if we do, we’ll let you know.”

Two years later, when the NIAAA awarded Mukamal the grant to lead the study they’d already funded him to design, the moderate alcohol trial included sites in Nigeria, Argentina, Europe and the US. The Foundation also had established formal agreements with the five alcohol corporations for the NIAAA’s \$67 million.

Yet when I spoke to Mukamal in February 2017, he said he didn’t know about the Foundation’s negotiation for industry contributions “until relatively recently.” And a New York Times reporter who wrote about the trial in July, documenting how many of its global collaborators have received alcohol industry funding, quoted Mukamal as saying “he was not aware that alcohol companies were supporting the trial financially.” Mukamal later told me the Times’ quote was “completely wrong.” And he explained in an e-mail that his knowledge of the alcohol industry’s support is limited since he is not privy to the Foundation’s contracts with funders.

“We have no contact with funders other than NIAAA itself whatsoever,” he wrote. “To me, the whole point of having FNIH involved is exactly that—so that if industry wants to see truly rigorous science, they get no say in what happens whatsoever.” Typically, when studies supported by the Foundation of the NIH are published, scientists simply list FNIH as a funder. No information is provided about how the Foundation raised money.

But the relationship between the NIAAA and its foundation funders is less murky. Murray, who heads global alcohol research for the NIAAA appeared with NIAAA director George Koob in a promotional video for Anheuser-Busch InBev—one of the study funders—about company-sponsored research. NIH is strict about outside interests, prohibiting its employees from advising any “substantially affected organizations” <https://ethics.od.nih.gov/topics/COI-Fact-Sheet.pdf>, but Murray and Koob got permission from the US Department of Health & Human Services to attend an Anheuser-Busch meeting in New York, where the company filmed them. In an interview, Murray said the alcohol trial likely already had the industry’s commitments at the time of the filming, but she and Koob hadn’t been thinking about it. Instead they’d been focused on the reason they were invited to the meeting, an Anheuser-Busch plan to study interventions to reduce ‘harmful drinking’ in cities around the world. In the video, Murray says she “really likes” the company’s research plan, comments she said she stands by today (<http://www.ab-inbev.com/better-world/a-healthier-world/global-smart-drinking-goals.html>).

“It always surprises me when people are critical of us even talking to industry,” she says. “It is a legal industry and they are a constituency as much as anybody.” But if they had it to do again, she and Koob agree they probably would say no. Seeing NIAAA leaders in an industry promotional video was “disconcerting” for James Sargent of Dartmouth’s Geisel School of Medicine in New Hampshire, while for Michael Siegel of Boston University, the video showed the NIAAA was “corrupted by the alcohol industry.”

Without the industry’s scores of millions, the NIAAA alcohol trial wouldn’t be happening, according to Murray. The study’s cost relates to its size and breadth, key to producing findings that can withstand statistical scrutiny. But several scientists worry this is not the right tradeoff between robust research and industry influence, statistical power and ethics. Given the size and specifications of the corporate donations, there’s a real possibility of the trial being influenced, said alcohol researcher Jürgen Rehm, of Toronto’s Centre for Addiction and Mental Health. What if scientific investigators discovered the study was too risky, or too risky in certain countries, he asked. “You would stop, but because you have this funding and it’s project-specific, you won’t want to stop.”

The NIAAA trial is still undergoing ethical review by institutional review boards, the ethics panels charged with protecting subjects from study-related harms. But Mukamal is promising a game-changer—“a truly definitive experiment that will settle this once and for all,” as he wrote in an editorial last May. Others in the field don’t see it that way. “The way this is set up, it smells,” says Rehm. “I’m sorry.”