

## No amount of alcohol is safe, at least for dementia risk

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For years, the common wisdom and science was that a little bit of alcohol wasn't bad — and even beneficial — for your health: a toast to moderation.

But new research published in *BMJ Evidence-Based Medicine* suggests that even light alcohol consumption can increase dementia risk.

The finding comes from data of more than 550,000 adults ages 56 to 72, as well as genetics information from 2.4 million study participants. It adds to evidence that even small amounts of alcohol can be harmful to our health, including increasing the risk of cancer or disrupting sleep.

Excessive alcohol consumption — more than 12 drinks per week — and alcohol use disorder have long been linked to dementia, an umbrella term for different types of progressive cognitive impairment, including Alzheimer's disease.

But the science on an occasional glass of wine or beer had been more rosy. One influential study published in 2003 seemed to suggest that people who had one drink a day were actually less likely to get dementia than those who didn't drink at all.

"For a long time we thought that the healthiest way to approach drinking and brain health was to take about a drink a day," said Joel Gelernter, a professor of psychiatry, genetics and neuroscience at Yale University School of Medicine and senior author of the study.

Gelernter himself would regularly have one drink a day because the data suggested that was a sweet spot for cognition.

But the accumulating new evidence has caused him to avoid alcohol more than he used to, he said.

"I think people should be aware that even a small amount of alcohol intake may have negative cognitive effects down the line," Gelernter said. "And if that's the most important thing to you, then you ought to reconsider drinking even a small amount."

However, experts say that their goal is to give people the best data possible so they can manage their own risk, not to tell them how much to drink or not drink.

“It’s okay to drink,” said Natalie Zahr, an assistant professor of psychiatry and behavioral sciences at Stanford University. “We shouldn’t have a fear of the thing itself. We should enjoy alcohol at the right time, in the right place.”

But the effect of alcohol on our brain probably depends on the dose. If you “reduce your intake, even if you’re not stopping completely, then that’ll probably benefit” you, said Anya Topiwala, a senior clinical researcher and honorary consultant psychiatrist at the University of Oxford.

## Even light drinking increases dementia risk

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Previous studies generally relied on self-reported alcohol intake and repeatedly found a slight increase in dementia risk for nondrinkers, the lowest risk for light to moderate drinkers, and a much higher and increasing risk for heavy drinkers.

When Gelernter and his colleagues looked at the self-reported drinking data for their study, they found a similar risk profile.

But relying only on self-reported data has a number of issues: People may not reliably recall their drinking, and their current drinking habits may not reflect their intake over their lifetime.

“Obviously, a [randomized controlled trial] would be the gold standard to determine causality, but that’s not practical or ethical for this research question,” Topiwala said.

Instead, the researchers employed the next best thing: They used a treasure trove of genomics data culled from 2.4 million people to predict how much people are likely to drink over their lifetime, which allowed them to infer causation.

They found that increasing alcohol intake invariably increased dementia risk: Every threefold increase in drinking prevalence upped lifetime dementia risk by 15 percent. That is, increasing intake from one drink to three drinks per week or from three drinks to nine drinks per week was associated with a 15 percent increased risk of dementia.

The study also countered previous research that found that alcohol was “protective” or that light to moderate drinkers had the lowest dementia risk, even when compared with nondrinkers.

Those who didn’t drink may have had a higher dementia risk because that cohort included people who may have been past drinkers who stopped drinking because of health problems such as cognitive decline.

The study found that people who developed dementia reduced their drinking faster than those who didn’t, suggesting that cognitive decline could be causing people to drink less.

That is, alcohol consumption affects dementia but the reverse is also true: Dementia affects alcohol consumption.

“If you drink habitually, and you want to take a drink per day, it’s not terribly harmful to your brain health, but it’s somewhat harmful,” Gelernter said.

## Alcohol in the brain

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Alcohol may reduce our brain reserve — the biological “hardware” — making our brain “more vulnerable to other pathologies,” Topiwala said.

Alcohol quickly permeates the cells of our body within minutes of drinking, readily crossing the blood brain barrier. In the brain, alcohol broadly amplifies neurotransmitters that inhibit neural activity, which dampens parts of the frontal cortex, and releases dopamine — which is why feeling buzzed can feel pleasant.

While alcohol’s acute effects are well studied, “the question of what it does chronically is still really unknown,” Zahrsaid.

Alcohol is a neurotoxin, and heavy drinking and alcohol use disorder — defined as a problematic pattern of alcohol use — is associated with widespread atrophy in the brain, not limited to memory centers such as the hippocampus.

Alcohol-related dementias may be distinct from other types such as Alzheimer’s since it affects other brain regions such as the thalamus and cerebellum more, Zahr said.

Another difference: Unlike Alzheimer’s, which is progressive and lacks treatment, evidencefor alcohol-related dementias suggests that “if you quit drinking, you’ll get better,” said Zahr, who wrote a recent review on alcohol’s relationship to dementia.

In studies of heavy drinkers who stop, they can recover some cognition and brain volume. “This is one of those things you don’t get with frontotemporal dementia, you don’t get with Alzheimer’s,” Zahr said

This atrophy recovery is not really understood, but to Zahr, it’s evidence that alcohol does not kill brain cells. “If it was killing brain cells, there’s no chance that you’d have as much brain recovery as you do when you quit drinking,” she said.

Previous research that carefully counted cells did not find much neuronal loss with alcohol exposure, she said.

Alcohol also disrupts our brain's white matter, the insulation that wraps around the cablelike connections that allow neurons to communicate with one another.

White matter can regenerate, but alcohol probably has "very profound effects on impairing myelin regeneration," Zahr said.

Brain imaging studies have found harmful brain outcomes even at one or two drinks a day when consumed consistently over time. Topiwala and her colleagues found that moderate alcohol intake was associated with smaller gray matter and increased iron in the brain, which has been linked to neurodegenerative diseases such as Alzheimer's and Parkinson's.

## How to manage alcohol intake

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If you want to cut back on drinking, you can try out challenges, such as Sober October or Dry January. There is also a boom in alcohol-free beverages and alcohol-free bars that can help you avoid the pressure to imbibe alcohol.

For heavier drinkers, working with a doctor is crucial to avoid the potentially dangerous effects of withdrawing too quickly.

Avoid binge drinking, which is possibly more harmful for our brains. This may be because of a "kindling effect" where repeatedly soaking your brain in alcohol and stopping leads to a "mini-withdrawal" that is thought to be more neurotoxic, Topiwala said.

Instead, "spread your intake, reduce the ethanol percentage, alternate alcohol drinks with soft drinks, reduce the volume," Topiwala said.

Gelernter compares the risk management to downhill skiing, where you're aware of the chance of broken bones.

"If you do something that might be harmful to your health, I think you should do it with an awareness of what you're doing. And you might well choose to do it anyway," he said.