News & Analysis

Medical News & Perspectives

Unpacking a Recent Study Linking Diet Soda With Stroke Risks

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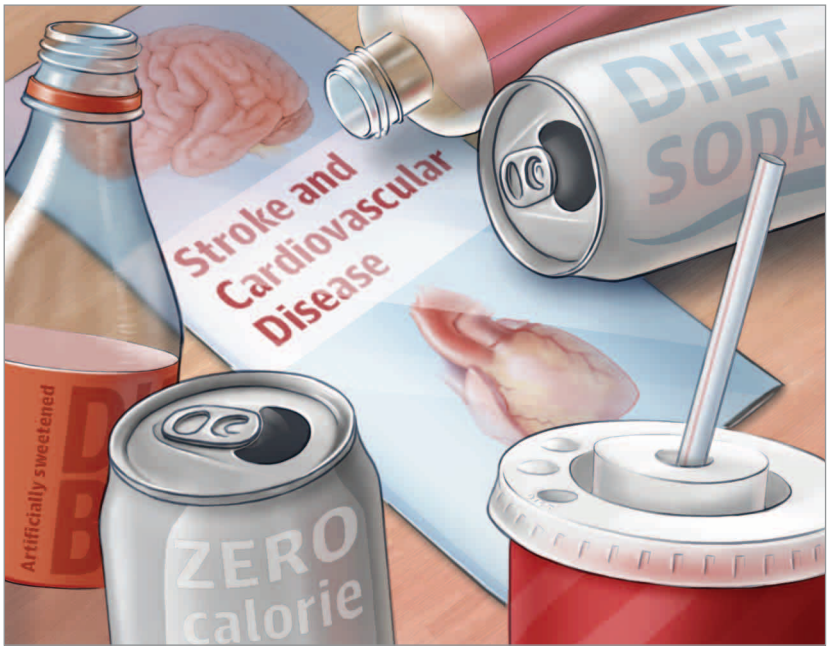

Around 2 decades ago, researchers asked tens of thousands of participants in the Women's Health Initiative study how often they consumed artificially sweetened beverages over the past 3 months. Recently, they looked at how the diet sodas and fruit drinks the women drank back then correlated with their risks of stroke, coronary heart disease, and death in the intervening years.

The results, recently published in *Stroke*, showed higher intakes of artificially sweetened beverages were associated with increased health risks. Yasmin Mossavar-Rahmani, PhD, RD, the study's lead author and an associate professor of clinical epidemiology and population health at the Albert Einstein College of Medicine in the Bronx, emphasized that the work doesn't prove cause and effect. But despite the study's limitations, "[T]his is a time to pause and look into all these associations and maybe reconsider if we're having excessive amounts of these drinks," she told *JAMA* in a recent interview.

Audio

The following is an edited version of that conversation, in which the nutrition scientist said she hopes the public doesn't walk away with the wrong message.

JAMA: Your study isn't the first to look at associations with artificially sweetened beverages and cardiovascular disease. What did the previous studies show?

DR MOSSAVAR-RAHMANI: There was another study from the Women's Health Initiative in 2014. They looked at a composite of events: [incident coronary heart disease], heart failure, myocardial infarction, coronary revascularization procedures, ischemic stroke, peripheral artery disease, and cardiovascular death. They saw [an increased] risk with high consumption of diet drinks. Then, in 2017, there was research involving the Framingham Heart Study Offspring cohort in men and women. They saw an increased risk again, specifically for stroke and Alzheimer disease. The results have been mixed in different studies. But there seems to be a certain pattern of association with cardiovascular disease.

JAMA: What's different about your study?

DR MOSSAVAR-RAHMANI: We followed 81 714 women over an average of 11.9 years. The previous study in the Women's Health Initiative followed [59 614] women for about 8 years. We also looked separately at stroke and its subtypes.

JAMA: Tell us what you learned.
DR MOSSAVAR-RAHMANI: We found that 5.1% of the women drank 2 or more artificially sweetened beverages per day. But most were infrequent drinkers. About 64.1% of the women drank artificially sweetened beverages never or less than once a week.

When we looked at this group of high vs low consumers of diet drinks, we found that women who had the higher level of consumption were 23% more likely to have a fatal or nonfatal stroke; 31% more likely to have the type of stroke from a clot in the brain or ischemic stroke; 29% more likely to develop fatal or nonfatal heart disease; and 16% more likely to die from any cause.

JAMA: The stroke risks were higher for certain women, correct?
DR MOSSAVAR-RAHMANI: That's right. The results I just quoted were for all women. We also looked at women without previous heart disease or diabetes. In that group, [high consumers] were 2.44 times more likely to have a common type of stroke that's caused by the blockage of the very small arteries—small artery occlusion—than women with no or low levels of consumption. If you looked at all women, that risk was 1.81 times. These are small vessel strokes that, if you just have 1, it's not a big deal. But if you have many of them over time, there's an association with dementia.

Additionally, obese women without previous heart disease or diabetes were about twice as likely to have an ischemic stroke and African American women without previous history of heart disease or diabetes were about 4 times as likely.

These associations don't imply causation. And while the risk of stroke is higher in high consumers of diet drinks, the actual absolute risk is small. The incidence rate is about 2 per 1000 people per year.

JAMA: As you say, because this is an observational study, we can't know if artificial sweeteners caused the strokes and heart attacks or if they're just correlated. And, in fact, the women who drank the most artificially sweetened beverages on average were heavier, exercised less, consumed more calories, had lower-quality diets, and were more likely to smoke and have a history of diabetes, heart attack, or stroke, correct?
DR MOSSAVAR-RAHMANI: That's correct, yes.

JAMA: To what extent were you able to control for these factors?
DR MOSSAVAR-RAHMANI: We did control for all these factors. However, there could be residual confounding. The diet quality variable, for example, may not capture all the quality of the diet. The physical activity variable may not capture everything about someone's physical activity.

We're also limited by self-report. And we're limited by the fact that we asked the question in 1996 to 2001. The diet drinks at that time were limited compared to what's available now. The answer is also dependent on what the women perceived diet drinks to be. And, also, we asked the question one time. We didn't continue to ask the question [over time].

So these are the limitations. The only way we can figure out if it's the diet drink or something else that's causing [the increased risks] is to do a randomized clinical trial.

JAMA: What about reverse causality? Isn't it possible that women with obesity who already have a heightened stroke risk may be more likely to drink a lot of diet soda to try to control their weight?
DR MOSSAVAR-RAHMANI: That's one possibility. We tried to control for obesity and body mass index in the models, but there is a possibility for residual confounding. We didn't, for example, know the prediabetic status of the women. If somebody was prediabetic and was trying to have artificially sweetened beverages [for that reason], we would not have been able to capture that. That data was not available.

JAMA: The women only reported their artificially sweetened beverage intake over one 3-month period, so you don't know what they were drinking before or after. How can this limitation be addressed in the future?
DR MOSSAVAR-RAHMANI: The only way to address it is to do more studies. Follow the women over time and assess their artificial sweetened beverage consumption periodically, maybe annually.

JAMA: Are there other ways to refine the study design in an observational study? For example, using objective measures?
DR MOSSAVAR-RAHMANI: You'd need to look at biomarkers for different artificial sweeteners. Maybe with metabolomics we'll get to that level at some point. A lot of these studies have specimens that have been collected, so future researchers can take a look at that. If we have the right biomarker for these beverages, we could.

JAMA: Say the artificial sweeteners were causative. What are some of the mechanisms that could explain that?
DR MOSSAVAR-RAHMANI: There are different hypotheses. There's some evidence that they may be changing the gut microbiome. That they may affect the way glucose is used. I've also read theories about how they might affect how the brain processes or understands the taste sensation for sugar. I think we just need more evidence.

JAMA: What does your gut tell you, so to speak? Do you think it's correlation? Or causation? Or both?
DR MOSSAVAR-RAHMANI: My job is just to report what I found, which was correlation. My gut is that we just need more research. And, again, this was done at a time where there was a limited amount of artificially sweetened beverages.

Now there are drinks made with stevia, the natural sweeteners. There are synthetic sweeteners. There are nutritive sweeteners like polyols and sugar alcohols. There are new items in the market that need to be tested, both in the microbiome and other parts of our physiology.

JAMA: Are you at all concerned that, based on studies like these, people might switch from drinking artificially sweetened beverages, which the jury is still out on, to drinking sugary beverages, which we know are unhealthy?
DR MOSSAVAR-RAHMANI: I think the message is that artificially sweetened beverages should be an interim step [before switching] to water. I'm hoping that women don't go back to having sugary beverages. ■

Note: Source references are available through embedded hyperlinks in the article text online.