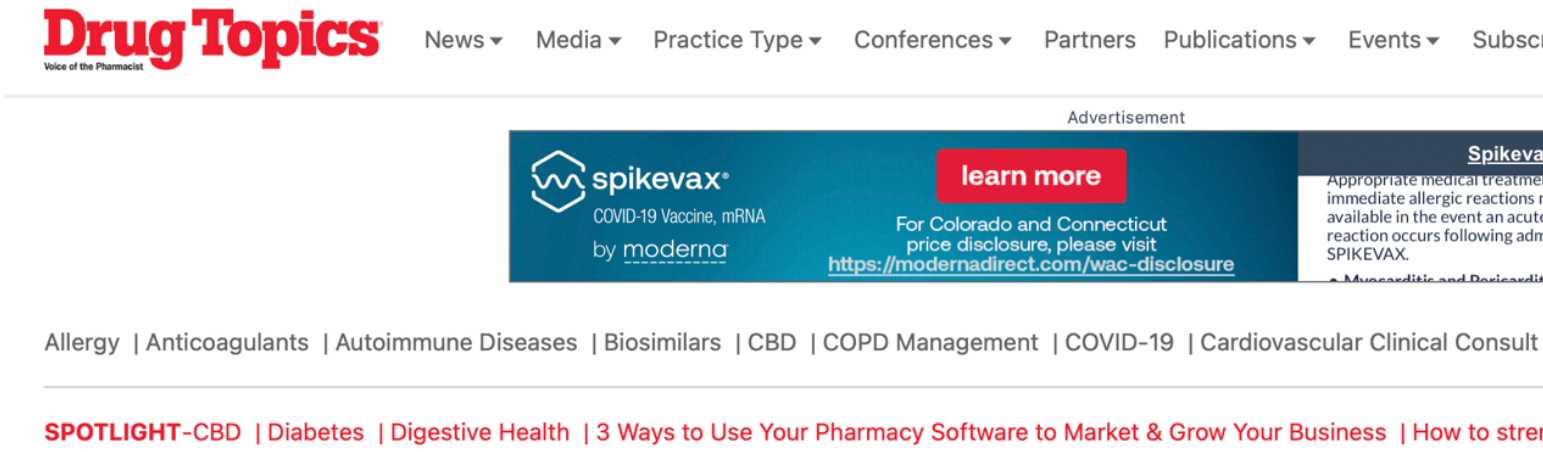
Can coffee drinking prevent COVID infection?

Coffee has undergone a dramatic rehabilitation since it was designated as a "possible" bladder carcinogen by the International Agency for Research on Cancer (IARC) in 1991.

In the past twenty years, large, prospective epidemiologic studies have pointed to an impressive but still only suggestive *reduction* in the risk of developing numerous types of cancer associated with drinking coffee. After having a brief spell as something to be shunned, coffee appears to have potential health benefits.

Now, two recent papers suggest that coffee may provide protection against COVID-19 infection. It's creating headlines across the internet. How solid is the evidence?



Coffee May Be Unexpected Protectant Against COVID-19 Infection

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Researchers in Taiwan reviewed biochemical evidence that compounds present in coffee inhibit infection with SARS-CoV-2. They also reported the results of a small study indicating that drinking 1-2 cups of coffee per day "is sufficient to inhibit infection of multiple variants of SARS-CoV-2 entry, suggesting coffee could be a dietary strategy to prevent SARS-CoV-2 infection."

The Taiwan paper published this year cites a paper by researchers at Northwestern University, which used data from the UK Biobank's prospective epidemiologic study of roughly half a million participants (aged 37 to 73) to examine the association of dietary intake with the risk of COVID infection.

The authors reasoned that factors including coffee, tea, red meat, fish, vegetables, and fruits, might influence immune function and, thereby, affect the risk of COVID infection and its sequelae.

Information on lifestyle and dietary behaviors, as well as physical measurements and blood sampling was obtained at enrollment into the study (2006-2010). Individual COVID-19 exposure was estimated using the UK's monthly positive case rate for specific geo-located populations. (It should be noted that only about 10 percent of study participants were tested for COVID-19 during the study timeframe.)

Few associations were seen with dietary factors. However, coffee intake showed a modest inverse association with COVID infection — that is, compared to people who did not drink coffee daily, those consuming 1, 2-3, or >4 cups per day had roughly a 10 percent reduction in risk of COVID infection, as shown in the table.

Table 2. Adjusted * OR (95% CI) of having a positive COVID-19 test by nutritional factors.

Nutritional Factor	Model 1		Model 2		Model 3	
	OR (95%CI)	*p* **	OR (95%CI)	*p* **	OR (95%CI)	*p* **
Coffee, Cups/Day						
None or <1 cup	Reference		Reference		Reference	
1 cup	0.90 (0.83, 0.97)	0.007	0.90 (0.83, 0.98)	0.015	0.93 (0.86, 1.01)	0.106
2–3 cups	0.89 (0.83, 0.95)	0.001	0.90 (0.83, 0.96)	0.003	0.92 (0.85, 0.99)	0.021
≥4 cups	0.92 (0.85, 0.996)	0.040	0.92 (0.84, 0.999)	0.047	0.91 (0.83, 0.99)	0.025

Summarizing their results in the conclusion section of the abstract, the authors wrote:

> In the UK Biobank, consumption of coffee, vegetables, and being breastfed as a baby were favorably associated with incident COVID-19; intake of processed meat was adversely associated.

Two things jump out immediately at any epidemiologist looking at the results for coffee. First, the reduction in risk associated with coffee drinking is small — on the order of 10 percent. As such, this result could be due to problems recalling one's diet or to confounding by some other factor. Secondly, and more striking, there is no suggestion that drinking more cups of coffee further enhances the protection against infection.

This is what is referred to as a *dose-response relationship*, and, while the absence of a dose-response relationship does not rule out the possibility of a causal association, its presence increases one's confidence in a possible causal association.

At the very least one would expect the authors to comment on these obvious features of their data. To gloss over the lack of a dose-response relationship is disingenuous.

Moreover, in the abstract and in the discussion section of the paper, where one would expect them to comment on these noteworthy aspects of the coffee data, the authors skip over these issues. They give an obligatory nod to the “limitations” of their study, but manage to avoid stating the obvious conclusion — that their data do not offer clear support for an association of coffee-drinking or other dietary factors with a risk of COVID infection.

In their discussion, they recapitulate,

> Habitual consumption of 1 or more cups of coffee per day was associated with about a 10% decrease in the risk of COVID-19 compared to less than 1 cup/day.

Rather than commenting on what this finding might mean, they launch into a discussion of the general background that suggests the possibility of an inverse (i.e., protective) association:

> Coffee is not only a source of caffeine, but contributes dozens of other constituents; including many implicated in immunity. Among many populations, coffee is the major contributor to total phenol intake, phenolic acids in particular. Coffee, caffeine, and polyphenols have antioxidant and anti-inflammatory properties.

The authors go on at length in this vein.

There is a second, surprising omission in this study. In addition to over-stating — and under-analyzing — the association of coffee with risk of COVID infection, for some reason, the authors ignore several obvious exposures/behaviors with well-studied effects on health and potential effects on immune status, namely: smoking, alcohol consumption, physical activity, and body mass index (BMI). We know that they have information on these factors since they controlled for some of them in their analyses.

These glaring issues should have been flagged in the peer review process, and the authors should have been required to address them before the paper was accepted for publication.

This paper reminds us of several realities surrounding research into lifestyle, dietary, and environmental factors that affect — or might affect — our health.

There is enormous interest in these sorts of topics among the public at large, and therefore among journalists, and even scientists themselves. These are legitimate and potentially important questions for scientists/epidemiologists to address.

First, we have to keep in mind that many reasonable and highly appealing hypotheses fail to stand up when examined with high-quality data.

It is also important to keep in mind that early studies are often “quick and dirty,” that is, crude, and are often based on small populations. Often, they were not designed to address the question under investigation. Additionally, researchers can give undue weight to a borderline result that appears to support their hypothesis.

Finally, even when the findings are extremely weak, there is often a tendency to “leave the door open” or even give the most positive/optimistic gloss on the finding, rather than coming out and saying that the data from our study do not provide particularly strong support for the notion/hypothesis — in this case, that coffee drinking reduces the risk of COVID infection.

That is what I believe happened in this study. The authors of the UK Biobank paper report their results, carefully eschewing precision, trying to have it both ways. They imply that their data on coffee convey a meaningful signal, while avoiding subjecting the data to rigorous examination. They try to paper over the yawning gap in the evidence by referring to biochemical effects of compounds present in coffee, and, at the same time, conceding that their findings “warrant independent confirmation.”

If a “medicine” as cheap and as easily available as coffee was in fact capable of reducing or eliminating the risk of infection with SARS-CoV-2, think of the enormous implications for bringing to an end, or curtailing, an evolving pandemic, which to date has caused an estimated 7 million deaths worldwide. Unfortunately, much more powerful and rigorous studies are needed before this is anything more than an appealing hypothesis.

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