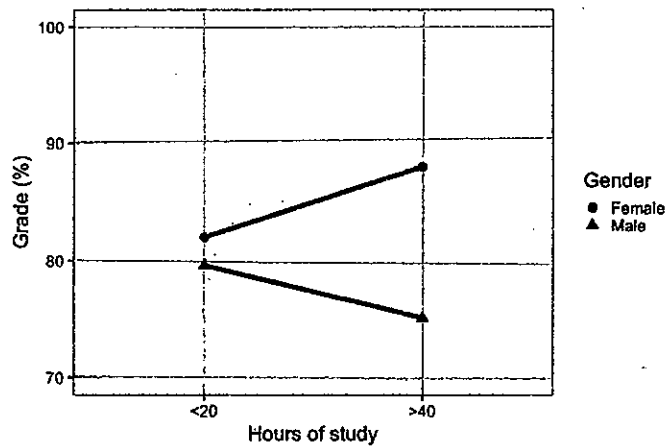
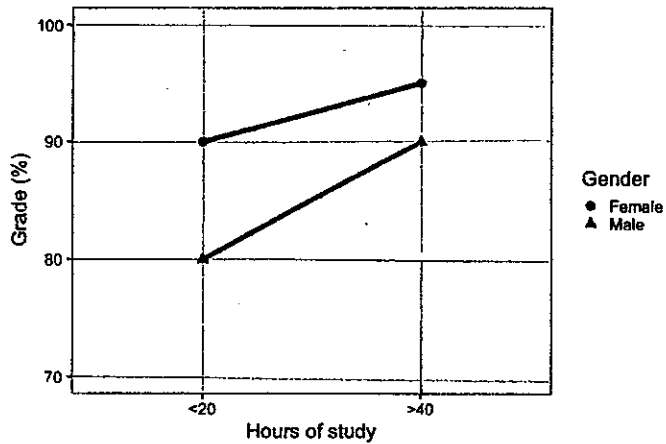


1. A group of graduate students did a quantitative study investigating the relationship between students' hours of study and their midterm grades. They analyzed data from 60 undergraduate students (30 female) and calculated the averages based on their study time. These graduate students then proposed three possible result outcomes, as illustrated below in Figure 1 (a-c).

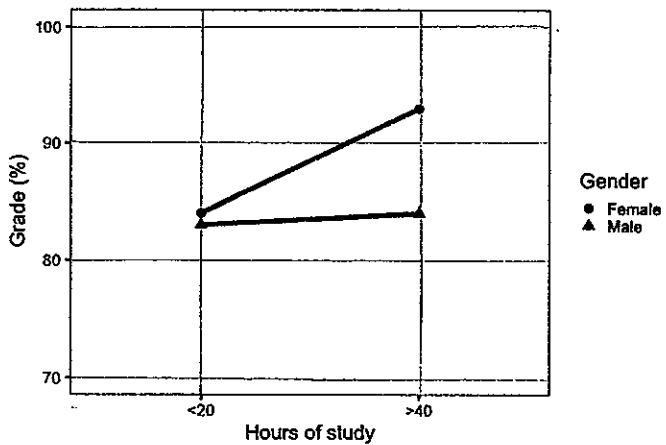
Please provide the result interpretation(s) for each sub-figure in academic English. Please be as professional and clear as possible. Limit your answer to 150 words for each sub-figure (10 points each).



(a) Result 1



(b) Result 2

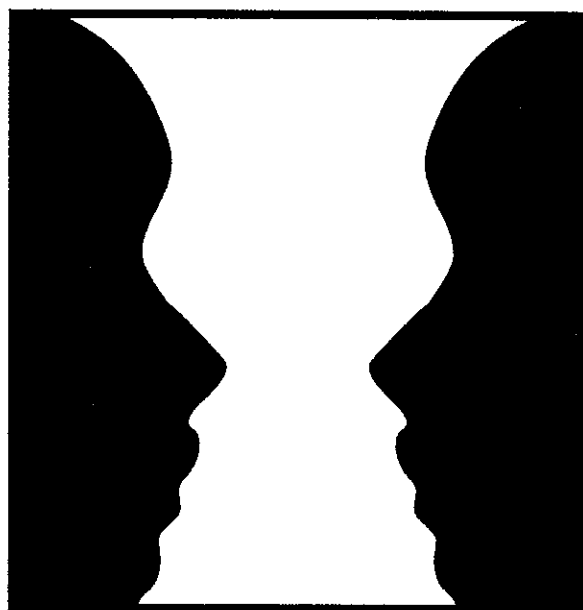
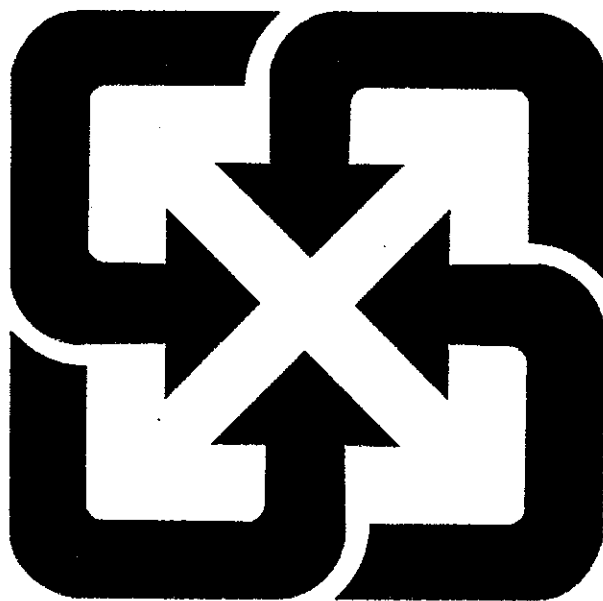


(c) Result 3

Figure 1. The relationships between hours of study and grades.

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2. Compare the following images. Please describe the phenomena that they all share. Limit your answer to 250 words. (20 points)



3. Please read the following article and answer the questions.

- (1) Why is using a placebo important in medical research? (5 pts) Why is blinding important? (5 pts) Why is it especially hard to perform blinding in cannabis research? (5 pts) The article mentioned several ways of counteracting blinding difficulties. In your opinion, what are the advantages and disadvantages of these methods? (10 pts)
- (2) Some people argue that as long as a drug works, it does not matter how it works. Other people hold the opposite view. What is the stance of the article? Please provide evidence. (5 pts) Do you agree or disagree? Please state your reasoning. (10 pts)
- (3) Please write a 200 word summary for the article. (10 pts)

Is pain relief from cannabis all in your head?

Meryl Davids Landau

For David Hao, a chronic pain physician at Massachusetts General Hospital in Boston, the conversation with a new patient experiencing severe chronic pain generally goes like this: He lays out possible treatments, including steroid injections, ablation of painful nerves, acupuncture, physical therapy, or surgery. But toward the end of the appointment, some inevitably ask, “Do you think I should try marijuana?”

Patients have heard—perhaps from family, friends, or the media—that cannabis and or compounds derived from it, called cannabinoids, may be helpful for pain like theirs. But as a scientist, Hao gives them the honest answer: “Based on the available evidence, the benefit is questionable.” Reputable studies so far have not found that cannabinoids sufficiently reduce pain, which led the International Association for the Study of Pain in 2021 to decline to endorse these drugs.

The lack of evidence was underscored late last year in a review published in *JAMA Network Open*. That study found that 67 percent of the relief from pain reported by people treated with cannabinoids was also seen among those who received a placebo. This suggests that the pain reduction was not due primarily to compounds found in cannabis but to peoples’ expectations that it would help. And that positive expectation was based in part, say the authors, on over-enthusiastic media coverage.

Medicinal cannabis includes all forms of the drug, including smokable or swallowable products containing low to elevated doses of tetrahydrocannabinol (THC)—responsible for producing the high associated with marijuana—or cannabidiol (CBD), a compound that doesn’t generate a high. Articles in the popular press, including large mainstream newspapers, regularly tout the plant as a treatment for pain, the *JAMA* study found.

The *JAMA Network Open* analysis found that positive articles appeared in the media even when the research conclusions being reported were neutral or negative, says Karin Jensen, who spearheaded the study and is a researcher in the pain neuroimaging lab at Sweden’s Karolinska Institute. *National Geographic* could not independently verify this finding due to a confidentiality agreement between the researchers and the London-based data collection firm Altmetric that prevents them from sharing the news articles that Jensen’s team assessed for the *JAMA* study.

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“The media seem to be fact-resistant in this case, because no matter what a trial says the media will report with a positive angle. So it’s a no-brainer why people keep asking for these medications,” Jensen says.

One-fifth of Americans currently experience chronic pain, according to the Centers for Disease Control and Prevention. That's why it is critical for patient care that future studies exploring the effect of cannabinoids on pain have results that do not skew positive because of bias, Hao says.

Blinding in research is challenging with cannabis

In any clinical study, when a participant does not receive the therapeutic compound, but an inert substitute like a sugar pill and reports positive results, the phenomenon is called the placebo effect. Gold-standard clinical trials use a protocol known as double-blind, in which neither the participants nor the scientists know who is taking the active medicine and who is taking the placebo.

Most studies testing compounds derived from cannabis used pills to deliver precise quantities of medicine (a few involved inhalation) and the researchers made sure the placebo smelled and tasted like the active drug. But participants can sometimes guess whether they have been given the active drug or the placebo depending on how they feel after taking the pill. When participants know when they received the medication versus the placebo, this can bias their perception of the drug’s effectiveness and skew the study results.

The Karolinska researchers wanted to understand how large the placebo response was in cannabis studies, so they evaluated 20 reports involving some 1,459 participants. One study they delved into, for example, compared a synthetic cannabinoid drug, nabilone, with a placebo for patients suffering from the pain condition fibromyalgia. The article’s co-authors concluded the medicine offered significant benefits. That was, in part, because of issues around blinding, which caused that study, along with many others, to overstate the drug’s value.

To counteract the ability of participants to figure out what they had been given, researchers sometimes administered the drug in low doses or gave participants formulations containing no THC so they wouldn’t get high and know they had received the medication.

But with a drug that so many people are intimately familiar with, successful blinding in cannabis studies takes tremendous effort, says Deepak D’Souza, a professor of psychiatry at Yale Medicine who has studied cannabis for more than two decades and is preparing for a large cannabinoid clinical trial at the Veterans Administration.

“There are ways of blinding well, but most studies have not done that. And even those methods are not absolutely perfect,” he says. One helpful approach is to have some people take very low doses while others take higher amounts, so at least some participants won’t have a psychoactive effect. Another way is to add a decongestant as a placebo so even these people experience some physiological symptoms. A third strategy is to give everyone placebos initially, based on the hypothesis that this will make guessing more confusing.

Measuring participants’ expectations of how much the products derived from marijuana might help is also important, D’Souza says. “Those can be done with simple questions,” then analyzed after the intervention with the foreknowledge that people who believe that cannabis will be effective will likely have more positive results, he says.

The brain’s impact on pain is a key factor

Unlike some chronic diseases, conditions that involve pain may be particularly susceptible to the placebo effect. This is the case for types of pain known as nociplastic pain. Unlike pain caused by ongoing damage to tissue or to nerves (nociceptive and neuropathic pain, respectively), this pain results from alterations in the brain's sensory pathways. Common conditions that trigger nociplastic pain include fibromyalgia, irritable bowel syndrome, and tension headaches, among others. This pain is as real and as detrimental as other types, but it may not respond to drugs and treatments commonly prescribed.

Experts don't yet understand the precise mechanisms behind nociplastic pain, but they are coming to see that thoughts play an important role. In functional MRI scans, for example, brain regions involved with pain perception and modulation light up when patients ponder especially negative thoughts about their condition.

People with this pain might be especially prone to having a placebo response, Hao believes. "I think it stands to reason that in that group of patients, the role of expectations can potentially be outsized," he says, although he emphasizes this has yet to be studied.

It may seem like it doesn't matter whether the positive results people experience in cannabis trials spring from taking the drug or thinking they did, as long as their pain is diminished. But this isn't the case, Jensen says. "It's not enough to know that something is working. We need to know *why* it is working to best help patients," she says. "If we provide treatments that are effective for other reasons than the suggested mechanism, that's not going to help people in the long run" who might be better served with other therapies.

"It may please patients in the short term for doctors to recommend cannabis," says Jensen, "but at the moment the scientific evidence does not support the treatment for pain."

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