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Placebo Effect

What is a placebo?

A *placebo* (pluh-SEE-bow) is a substance or other kind of treatment that looks just like a regular treatment or medicine, but is not. It's actually an inactive "look-alike" treatment or substance. This means it's not a medicine.

Typically, the person getting a placebo doesn't know for sure that the treatment isn't real. Sometimes the placebo is in the form of a "sugar pill," but a placebo can also be an injection, a liquid, or even a procedure. It's designed to seem like a real treatment, but doesn't directly affect the illness.

What is the placebo effect?

Even though they don't act on the disease, placebos affect how some people feel. This happens in up to 1 of 3 people. A change in a person's symptoms as a result of getting a placebo is called the *placebo effect*. Usually the term "placebo effect" speaks to the helpful effects a placebo has in relieving symptoms. This effect usually lasts only a short time. It's thought to have something to do with the body's natural chemical ability to briefly relieve pain and certain other symptoms.

But sometimes the effect goes the other way, and the placebo seems to cause unpleasant symptoms. These may include headaches, nervousness, nausea, or constipation, to name a few of the possible "side effects." The unpleasant effects that happen after getting a placebo are sometimes called the *nocebo effect*.

Together, these 2 types of outcomes are sometimes called *expectation effects*. This means that the person taking the placebo may experience something along the lines of what he or she expects to happen. If a person expects to feel better, that may happen. If

the person believes that he or she is getting a strong medicine, the placebo may be thought to cause the side effects. The placebo does not cause any of these effects directly. Instead, the person's belief in or experience of the placebo helps change the symptoms, or changes the way the person perceives the symptoms.

Some people can have the placebo effect without getting a pill, shot, or procedure. Some may just feel better from visiting the doctor or doing something else they believe will help. This type of placebo effect seems most related to the degree of confidence and faith the patient has in the doctor or activity.

The placebo effect can make some treatments seem like they help certain symptoms, when in fact they do nothing to directly cause a change in the disease. Other factors that are sometimes lumped in with the placebo effect can also make a treatment appear to help even when it does nothing for the illness. These are discussed in the section called "Other things that can add to or be confused with the placebo effect."

How are placebos used in research?

Placebos may be used in clinical trials. [Clinical trials](#)¹ are research studies testing new drugs or other treatments in volunteers. Before a new treatment is used on people, it's studied in the lab. If lab studies suggest the treatment will work, the next step is to test it on animals. If that also gives promising results, it may then be tested in clinical trials to see if it has value for humans. The main questions the researchers want to answer are:

- Does this treatment work?
- Does it work better than what we're now using?
- What side effects does it cause?
- Do the benefits of the treatment outweigh the risks?
- Which patients are most likely to find this treatment helpful?

If standard treatments for the disease are already available, the new treatment is usually compared to one of them. This tells researchers if the new treatment is as good as or better than the one that's currently available.

If there's no approved treatment for an illness or condition, some people in the study may be given a placebo, while others get the new treatment being tested. The main reason to have a placebo group is to be sure that any effects that happen are actually caused by the treatment and not some other factor.

The placebo looks, tastes, or feels just like the actual treatment, so that the patient and

doctor's expectations don't affect the outcomes. The placebo control makes it possible to "blind" patients and doctors to which treatment they're getting. This is called a *double-blind controlled study*, and neither the volunteers taking part in the study nor their doctors know who's getting which treatment. This study design helps avoid biases in measuring outcomes that can be caused by the researchers or the patients' expectations about the treatment. This is not as big a problem in studies of cancer treatment, where objective outcome measures are most often used. It's more likely in studies that require patient reporting for symptoms like depression, sleeplessness, or pain.

If you would like to know more about clinical trials, see [Clinical Trials: What You Need to Know²](#).

People in a study using a placebo must always be informed that there's a chance they could be getting the placebo. Please read [Informed Consent³](#) for more on this.

Those who get placebos in medical studies serve an important role. Their responses help provide a good way to measure the actual effect of the treatment being tested. The placebo group provides an important baseline with which to compare the treatment group. It helps researchers see what would have happened without the treatment, though both groups may still have some short-term effects based on what the patient expects. For instance, illnesses that sometimes go away on their own might be thought to get better because of the medicine, unless there's a placebo group and those people get better too. On the other side, bad effects that were going to happen anyway, or that occur from some unrelated cause, may be blamed on the treatment unless they also happen to people in the placebo group.

How does the placebo effect work?

In the past, some researchers have questioned whether there's convincing proof that the placebo effect is a real effect. But there are studies showing that the placebo effect *is* real in some situations. For example, scientists have recorded brain activity in response to placebo. Since many scientific tests have shown that there is a placebo effect, it's one way we know for sure that the mind and body are connected.

Some scientific evidence suggests that the placebo effect on pain may be partly due to the release of *endorphins* in the brain. Endorphins are the body's natural pain killers. But it appears there's more to it than this.

The expectation effect

Many think the placebo effect occurs because the patient believes in the substance, the treatment, or the doctor. The patient's thoughts and feelings somehow cause short-term physical changes in the brain or body. The patient expects to feel better, and so he or she does feel better for some time. But even if a person feels better after taking a placebo, it doesn't mean the person's illness or symptoms were not real. For instance, the person may feel less anxious, so stress hormones drop. Taking a placebo may change their perception – for example, a person might re-interpret a sharp pain as uncomfortable tingling.

The placebo effect even plays a role in mainstream medicine. There's evidence to suggest that what a patient expects about real medicines can influence how the patient feels after the medicine is taken. Even though responses from real drugs aren't typically thought of as placebo effects, some short-term effects are affected by expectations – good ones as well as bad.

Many people feel better after they get medical treatments that they expect to work. But the opposite can also happen, and this seems to support the idea of the expectation effect even more. For example, in one study, people with Alzheimer disease got less relief from pain medicines. These patients required higher doses – possibly because they had forgotten they were getting the drugs, or they forgot that the pain medicines had worked for them before. This suggests that past experiences also play into the placebo effect.

The conditioning effect

In one study that looked at the placebo effect in pain relief, one group got a real pain medicine and the other did not. In the following days, both groups were given a placebo that looked like the real pain medicine. Those who had gotten the real pain medicine were able to tolerate more pain than those who had not gotten pain medicines before.

In the same study, people who were given a drug that raised a certain hormone level beforehand actually had a similar (but smaller) hormone response when they were given a placebo later. Those who had not gotten the real drug beforehand had no change in their hormone levels when they got the placebo, even though they were told that they would. This helped to separate the power of the researcher telling them they would have an effect from the learned experience of having the effect in the past. This type of learned response after personal experience is called the *conditioning effect*. It seems to be part of what we call the placebo effect.

The nocebo effect

The nocebo effect, in which a person has more symptoms or side effects after a placebo, is still being studied. Researchers believe it may be partly explained by a substance in the body that sends messages through the nerves. When a person is anxious, for instance, the substance is activated and the person feels more pain than a person who isn't anxious. The nocebo effect can be seen in the brain: brain-imaging studies have shown that pain is more intense when a person expects more pain than when they don't. This is linked to changes in certain brain regions on the imaging studies.

The mind-body connection

Although we may not know all the ways it might work, the idea that the mind can affect the body has been around for thousands of years and is well-proven for certain situations. Many ancient cultures depended on mind-body connections to treat illness. Shamans or medicine men would not have viewed their efforts as placebos. But their healing powers may have worked partly through the patient's strong belief that the shaman's treatments would restore health. Or it could be that a sick person was going to get better anyway, but the recovery was thought to be because of the treatment – which might have really done nothing for the illness.

Because placebos often have an effect, even if the effect doesn't last long, some people think that the placebo produced a cure. But placebos do not cure. And in studies where doctors are looking at whether a tumor shrinks, placebos have very little, if any, effect.

Still, placebos clearly can help reduce certain symptoms such as pain, anxiety, and trouble sleeping in some people. In earlier times, placebos were sometimes given by doctors out of frustration or desperation, because nothing else was available or seemed to work. A 2008 study found that nearly half of the doctors polled said that they used a placebo when they felt that it might help the patient feel better.

Some scientists believe that the effects of many complementary and alternative therapies may simply be a placebo effect. If the patient believes in the treatment and wants it to work, it can seem to do so, at least for a while. If the placebo worked on an illness that usually would not get better on its own, and it lasted, it would be considered a real cure, not a placebo effect.

Remembered wellness

Some believe that placebos seem to work because many illnesses improve over time even without treatment. People may also take better care of themselves by exercising, eating healthier, or resting if they are taking a placebo. Just as natural endorphins may

relieve pain once they are released, some research shows the brain may respond to an imagined scene much as it would to something it actually sees. A placebo may help the brain remember a time before the symptoms and bring about certain chemical changes. This is a theory called *remembered wellness*.

Other things that can add to or be confused with the placebo effect

Certain other factors can affect study outcomes, and may be confused with the placebo effect. These are effects that can cause a study to report that a placebo (or even a treatment that doesn't actually work) had some effect when it really didn't.

Timing of unrelated events

Along with the placebo or nocebo effect, incidental events (unrelated effects that might have happened without the placebo) might also be linked to the placebo because of their timing. For example, a headache or rash that happens soon after taking a placebo could be caused by something else entirely, but the person might think the placebo caused it. The same can be said for good outcomes: if a person happened to start feeling better after taking a placebo, it might be thought to be due to the placebo.

Healing or changes in symptoms

A health problem that improves on its own (many do) can sometimes add to what's thought of as the placebo effect. Even in serious conditions such as cancer, some types appear to get better and worse on their own, although they continue to spread and worsen over time. This is part of the effect of timing, noted above. A person who was taking a placebo when symptoms started improving on their own is very likely to believe that the placebo had some effect. And a self-limited illness that goes away completely on its own at such a time might have the placebo-taker convinced it was a miracle drug.

Timing can have another effect when symptoms cycle through getting better and worse on their own. The patient is more likely to sign up for or be accepted into a study when their symptoms are very bad. But in cyclic illnesses, the worst symptoms are usually followed by a period when they start getting better – no matter what's done. This can make the test method seem like it works, or it can look like the placebo effect if the person ends up in the placebo group. An advantage of having a control group that's very much like the test group is that both groups should have about the same numbers of people who'll get better with or without treatment, so they balance each other out.

Patient selection and sign-up

Patients who already have some faith in a particular method are more likely to sign up for a study about that method. For example, people who have faith in their medical doctors' methods are more likely to sign up for a study on medical treatment. People who believe that acupuncture works are likely to volunteer for a study of acupuncture. Those who don't believe a method works probably won't sign up to test it. This means that the group who volunteers for the study already has some expectation effect before the study starts. Many who sign up are likely to report at least a brief improvement in symptoms with the treatment (or even with a placebo, if one is used) because they expect to be helped by the treatment. (See the section, "What is the placebo effect?")

Patient reporting

Lack of blinding can affect reporting of these kinds of coincidental timing effects and belief in what caused them. For example, people who know they're getting placebos will know that their headache is not caused by the medicine, and they probably won't report it. Those who know or believe that they are getting the real medicine are more likely to believe that the medicine is causing the headache, and are more likely to report it. Blinding and having groups that are very much alike help to balance these incidental timing effects.

Biased patient responses

Studies comparing placebo to no treatment, which would be expected to find no difference at all, instead found that patients were more likely to tell the study investigator that there was some improvement in their comfort even if they were on placebo. This was observed more often when the patient had to rank their symptoms on a scale, say, from 1 to 10. When the patients' rankings were compared with outcomes others could measure (like the amount of swelling, fever, or movement) there were often no improvements in the measurable outcomes.

Some researchers believe this is because patients want to give the investigator good news. In some studies, it may be that the patient is comparing current symptoms to what they remember, which are often the worst symptoms their problem has caused in the past. A common result is that patients report that the problem is better than it was before the study started, whether they get treatment or placebo. Again, when the study and control groups are very similar and well blinded, these effects can be recognized as unrelated to the actual treatment.

Getting treatment outside of the clinical trial

The patient who isn't getting better in a study may also seek outside medical help

without mentioning it to investigators. Or outside treatment for a related problem may help the symptom being studied in the clinical trial. This can affect outcomes for both the placebo and treatment groups. If there's no placebo group, it may make the test treatment look like it works, at least for some people.

Study dropouts

People who are not getting better in the study, including those on placebo, are more likely to leave the study before it's over. This means that people who aren't helped are less likely to be counted in the final analysis. This makes the tested treatment look like it works, or that it works better than it really does, because the people who felt better during treatment were more likely to have their results counted at the end of the study than those who didn't.

Not surprisingly, people who know that they're in the placebo group of a study (either because it isn't a blind study or because they figure it out another way) are more likely to drop out. This can shrink and otherwise change the makeup of the comparison group, which can also affect results.

Limits of the placebo effect

A 2010 review carefully analyzed more than 200 studies that included a placebo group along with a "no treatment" group. The reviewers found that placebo treatments don't have major effects on illness, but in certain settings they appear to improve patient-reported outcomes – especially pain and nausea. Placebo effects on pain varied quite widely, from almost none to significant relief. These variations in the effect of placebo were partly explained by differences in how studies were conducted and what patients were told. The reviewers noted that it's hard to tell if patient-reported effects were truly due to placebo effects or if they were just biased patient responses. Studies in which patients didn't know they were getting a placebo showed the strongest placebo effects.

The bottom line is that placebos don't cure. Sometimes they can make people feel better, but they can also make people feel worse. And placebo effects (along with other factors that can affect study outcomes) often make clinical trials that aren't carefully designed come out with falsely positive results. This is one of many reasons why good study design, like having control groups that are set up to be very similar to the test groups, are so important in human studies.

Hyperlinks

1. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials.html

2. www.cancer.org/treatment/treatments-and-side-effects/clinical-trials/what-you-need-to-know.html
3. www.cancer.org/treatment/finding-and-paying-for-treatment/understanding-financial-and-legal-matters/informed-consent.html
4. <http://www.cancer.gov/>
5. <https://nccih.nih.gov/>
6. <http://www.mskcc.org/cancer-care/integrative-medicine/about-herbs-botanicals-other-products>
7. <http://www.fda.gov/Food/DietarySupplements/default.htm>
8. <http://www.ncahf.org>

Additional resources

National Cancer Institute Website: www.cancer.gov (<http://www.cancer.gov/>)⁴ Toll-free number: 1-800-422-6237 (1-800-4-CANCER) TTY: 1-800-332-8615

- Offers information about cancer, treatment, clinical trials, and related help on many cancer topics for patients, families, and caregivers

National Center for Complementary and Integrative Health (NCCIH) Toll-free number: 1-888-644-6226 TTY: 1-866-464-3615 Website: <https://nccih.nih.gov/> (nccih.nih.gov/)⁵

- Offers details on many complementary, alternative, and other non-standard treatments for cancer-related symptoms as well as clinical trials

Memorial Sloan Kettering Cancer Center About Herbs and Botanicals Website: www.mskcc.org/cancer-care/integrative-medicine/about-herbs-botanicals-other-products (<http://www.mskcc.org/cancer-care/integrative-medicine/about-herbs-botanicals-other-products>)⁶

- Has summaries of information on a number of complementary and alternative treatments

United States Food and Drug Administration

Website: www.fda.gov/Food/DietarySupplements/default.htm

(<http://www.fda.gov/Food/DietarySupplements/default.htm>)⁷ Toll-free number: 1-888-463-6332 (1-888-INFO-FDA)

- Has information on dietary and food supplements. You can also report side effects or other adverse events from dietary supplements, drugs, or medical devices by calling Medwatch at 1-800-332-1088 (1-800-FDA-1088)

National Council Against Health Fraud Website: www.ncahf.org
(<http://www.ncahf.org>)⁸

- To help you discern scammers and fraudsters from proven cancer treatments

**Inclusion on this list does not imply endorsement by the American Cancer Society*

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Written by

The American Cancer Society medical and editorial content team
(www.cancer.org/cancer/acs-medical-content-and-news-staff.html)

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