

What is a placebo effect?

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Placebo is a Latin word meaning “I shall please.” A modern definition of placebo is “A substance containing no medication and prescribed or given to reinforce a patient’s expectation to get well.” In drug clinical trials, the placebo is a pill that looks identical to the active medication being tested, but it does not contain an active ingredient. Placebos are often referred to as “sugar pills.”

Is it ethical to give placebos to patients in clinical trials?

Prior to initiation, all medication clinical trials must be reviewed and approved by an Institutional Review Board. These boards include independent scientists, ethicists, and consumer advocates. Decisions are guided by the Declaration of Helsinki, first issued in 1964. The overriding principal is that patients participating in research projects should not be exposed to unnecessary risks or have proven treatments withheld. Paragraph 29 of the Declaration says: “*The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.*”

Why are placebos used in clinical trials?

The goal of a clinical trial is to determine the true effect of a medication. The challenge for researchers is determining if the tested medication is truly responsible for the observed improvements. Other factors can and do affect a patient’s condition, including spontaneous fluctuations in the patient’s condition or improvement of the condition over time. Patients also may have hopes or expectations that can influence how they feel, including the expectation that they will get better.

Patients randomly assigned to take the placebo in a clinical trial can experience improvements due to these kinds of factors. The patients in the active-medication group will notice these effects, but they also will experience the true drug effect, which can be identified at the end of the trial by subtracting the placebo group findings from those in the actively treated group. If, for example, 52 percent of participants in the active-medication group report improvement of their condition compared to 23 percent in the placebo group, the true treatment effect is 52 minus 23, or 29 percent. It should be noted that the 23 percent improvement in the placebo group cannot be attributed to the sugar pill, since it contains only inactive ingredients. Other explanations as mentioned above are those that involve spontaneous fluctuations in the

condition or disease, improvements in the underlying condition, and high hopes of recovery (which is why it is called the “placebo effect.”)

As a potential study participant, an Informed Consent Form will indicate whether a placebo is used, and the likelihood of being assigned to the placebo treatment.

Is it ethical to treat patients in clinical practice with placebo?

Today’s patient care is based on scientific knowledge and clinical experience. Patients have the right to receive complete and truthful information from their physicians. Thus, it is not permissible to knowingly prescribe sugar pills to patients hoping for beneficial effects. However, more than half of



U.S. physicians admitted in a recent survey that they sometimes prescribed medications they considered ineffective in the hope of getting a favorable placebo effect. It is worth pointing out that a large number of Americans in 2007 spent an estimated \$4.8 billion on largely untested natural health products or dietary supplements, which may be no more effective than placebos. The important difference, though, is that we do not know whether these products have true beneficial effects. Thus, one cannot claim that they are knowingly ineffective.

How important are expectations?

Chapter 24 illustrates a clinical trial that showed how enthusiastic communication of information regarding a medication increased the benefit of penicillin for the treatment of sore throat. Other factors that tend to improve treatment response include friendly encounters, a relaxing environment, ample time for interactions, and good information about the favorable and unfavorable effects of the prescribed medication(s). Other contributing factors are the clinician's position, title, and expertise. Interestingly, for certain conditions, the color of the prescribed pill also may influence its effects. Blue and green tablets tend to reduce anxiety more than red and yellow ones. Capsules appear to be perceived as more effective for pain control than tablets. Injections are expected to be better than oral medications.

The cost of the medication is another factor, as we expect higher cost to add value. A recent clinical trial compared the effect of two placebos on pain. Patients informed that the price of their pill was \$2.50 responded much more favorably than those informed that their pill would only cost 10 cents. This may be one of the reasons patients are reluctant to accept inexpensive generic drugs.

Key messages

- ✓ A placebo is an inactive formulation used in clinical trials.
- ✓ Placebos are compared to active medications in clinical trials.
- ✓ Placebos are often reported to have beneficial effects.
- ✓ There are ethical restrictions associated with placebo use in research.

