

Meaning, Medicine, and the “Placebo Effect”

Daniel E. Moerman

University of Michigan-Dearborn



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1 Healing and medical treatment

Ever since [ship physician] Stephen Maturin had grown rich with their first prize [about 1790] he had constantly laid in great quantities of asafetida, castoreum and other substances, to make his medicines more revolting in taste, smell and texture than any others in the fleet; and he found it answered – his hardy patients *knew* with their entire beings that they were being physicked.

Patrick O'Brian, *Master and Commander*, 1970

Even fictional doctors know that their patient's attitudes and understanding of medicine and treatment are a fundamental part of the healing process.

An ulcer trial

In the early 1990s, Dr. Frank Lanza, a gastroenterologist from Houston, Texas, led a large team of doctors in a test of a new drug for treating ulcers. Over 300 people participated in the trial which compared the effectiveness of a new drug known as lansoprazole (its trade name is "Prevacid") with another, older, drug for ulcers called ranitidine ("Zantac"). The people who entered this study were diagnosed with ulcers by having a procedure called an *endoscopy*. In this procedure, a fiber optic tube – an endoscope – is put down the patient's esophagus, and a technician examines the wall of the gut on a little television screen. In each case, only after the technician saw an ulcer in the patient's stomach was the person admitted to the study.

After this diagnosis, patients were randomly assigned to one of several groups. Some patients got Zantac (300 mg), some got Prevacid (15 mg), and no one knew who got which – neither the doctors nor the patients. After two weeks, and then another two weeks later, the patients came back to the hospital and got another endoscopy to see if the ulcers had healed. After two weeks, about 30% of patients in each group had healed ulcers. Two weeks later, things looked better. Two-thirds of the patients taking the old drug Zantac had healed ulcers, and 88% of those people taking the new drug, Prevacid, were better.

This is a classic example of the epitome of modern clinical medical research, what people routinely call the “gold standard” of medicine, the Randomized Controlled Trial (RCT); it is a way to provide highly objective and valuable information about what drugs work, and which ones work better than others.

Dr. Lanza and his colleagues wrote a (rather dense) scholarly article about their experiment and published it in one of the world’s leading journals in this field, *The American Journal of Gastroenterology* (Lanza et al. 1994). There is quite a bit of discussion in the article about how the new drug might work and why it might heal up the ulcers (it has to do with restricting the amount of acid in the stomach, which seems to help create an environment where the ulcers can heal more easily). Their explanation seems plausible, and it may even account for why Prevacid works somewhat better than Zantac does.

But this experiment had another study group. Forty-four patients in the study did not receive either Zantac or Prevacid. They received what is called a “placebo,” a pill which looked exactly like those the other patients took, but had no medicine in it at all; they took an “inert” pill. They had the same diagnosis, and were examined after two weeks, and again after two more weeks. And, like the other groups, no one knew which patients were taking the inert pills. What happened to them? After two weeks, about a third of the placebo patients were healed. After four weeks, just under half of them (nineteen of forty-four) were healed.

There’s no discussion in Dr. Lanza’s article about why *this* may have happened. What *did* happen to these people?

Whatever it was, it is very common. People have been aware for centuries that sick people, given a substance known to be inert by a doctor, frequently get better. This has, for good or ill, long been labeled the “placebo effect.”

Placebo Domino: “I shall please the Lord”

The word “placebo” has a long and colorful history. In the early years of Christianity, communities of monks organized their lives with asceticism and discipline. In many communities, they developed regimens of set times for prayer and bible reading, often from the Psalms, throughout the day and night. A supplement to Vespers (often celebrated around 4:00 pm) was read and prayed when a member of the community had died. This “Office for the Dead” began with a reading of the ninth verse of Psalm 116, which, in the Latin Vulgate, says “Placebo Domino in regione vivorum,” roughly translated as “I shall be pleasing to the Lord in the land of the living.” “Placebo” is, in this context, usually translated as “I shall please.”

Curiously, this is probably based on an inaccurate translation! The original Hebrew text has the word “eth-hal-lech” which means “I shall walk.” (Note that “I shall walk with the Lord in the land of the living” makes a lot more sense than “I shall be pleasing to Him there.”) When this was translated into Greek (probably sometime in the second century BCE), someone made a mistake and wrote “euaresaso”, which means “I shall please.” When St. Jerome translated the Bible into Latin about 500 years later, he, working from the Greek text, used the Latin word “placebo,” meaning “I shall please” (Lasagna 1986).

Regardless of its origins, the term took on the somewhat different meaning in medieval English of a flatterer, sycophant, or parasite, someone out to please others with artifice rather than substance. In Chaucer’s *Canterbury Tales*, written in the late fourteenth century, Chaucer tells the story of an old (two-faced) lecher named January who wants to marry a young girl; he discusses this plan with a man named Placebo, who advises him that whatever he wants to do is fine and wise, and who is he to tell January otherwise? By the early nineteenth century, this sense of the word had been adopted by physicians – a medical dictionary published in 1811 defined placebo as “an epithet given to any medicine adapted more to please than benefit the patient.” One needn’t know too much about the violence of medicine in 1811 – with its drastic purging and bleeding of patients (it is generally agreed by historians that George Washington was bled to death by his physicians in 1799) – to see that medical benefits were, at the time, not thought to come from anything that the patient might appreciate! And by the mid-nineteenth century it was common for people to refer to such treatments not only as “placebos” but as “mere placebos” – “just a divertissement to cheer the spirits, and assist the effect of the waters.” By then, *water* was seen as a more effective medicine than a placebo.

In the twentieth century, as a result of the biological revolution which shook medicine to its roots, the term took on another meaning. Earlier, a placebo had been an inert substance given deliberately to please the patient (typically when the doctor didn’t know what else to do). By the mid-twentieth century, it had taken on another, more complex meaning as people began to consider what was called a “second sort of placebo, the type which the doctor fancies to be an effective medicament but which later investigation proves to have been all along inert” (Houston 1938:1417–8). These drugs had been (perhaps for centuries) prescribed not to please patients, but to please doctors. And, of course, even though they were equally inert, they worked just as well as (or maybe better than) those physicians prescribed knowing them to be inert.

So, for centuries in the Western world, physicians have been aware of the fact that sick people get better after taking inert drugs. And, it should

be clear that they were then (and are now) somewhat ambivalent about this. Although the reasons are complex, it must seem odd to a person who has spent twenty years learning to be a physician, studying the hundreds of medications available, to find that patients get better just because they have been in a doctor’s office for a few minutes.

Why sick people get well

There are, of course, many reasons why someone might get well after getting sick. Certainly, modern pharmaceutical drugs often help the sick get better, experience less pain, heal more quickly from a variety of conditions, and, if they don’t actually help heal diseases (like cold “remedies”), they often make such unhappy experiences more comfortable.

But other things happen as well. For ordinarily healthy people, most sicknesses are “self-limiting,” which is a fancy way of saying that they go away by themselves. Colds and headaches are the examples with which we are most familiar. Many of the upsets of babies and small children are self-limiting; this is the origin of what must be the most common “prescription” of the pediatrician – “Call me again in the morning” – by which time the problem is usually gone. And it has long been said that, left to itself, a cold will last about a week and a half, but when treated with all the armamentarium of modern medicine will last only about ten days.

A more complicated version of this goes by the unpleasant name “regression to the mean.” The idea here is that chronic diseases (ones that don’t ordinarily go away “by themselves”) regularly wax and wane. Such conditions get worse for a while, then get better for a while, and then worse again. And, the argument goes (although I don’t think I have ever seen anyone really prove it), people tend to seek medical care when their conditions are severe. The disease is likely to start getting better by itself (at least for a while) just as the patient shows up in the doctor’s office.¹ While I don’t think this happens often, there clearly are situations where regression is a real factor. If people are selected for a study based on their displaying an extreme condition – like very high blood pressure, or very high levels of cholesterol – there is good reason to believe that, after some period of time, their extreme measurement will be less extreme simply because the body seeks homeostasis.

Can these factors – the self-limiting character of many illnesses and “regression to the mean” – account for the placebo effect? Certainly not.

¹ Consider an alternate hypothesis for which there is probably just about as much data (that is, none). The patient tends to call his doctor for an appointment at the time when his condition is worst; under managed care, he will get an appointment in about six weeks, by which time he will probably be much better.

They do account for some portion of *any* set of healing rates, although we will see that there is a good deal more to it than this.

But not without a great deal of objection. There is much objection among physicians to the very existence of something called the placebo effect. It often seems to bother doctors enormously that the *fact* of receiving medical treatment (rather than the *content* of medical treatment) can initiate a healing process. Why? I think it is because medicine is rich in a particular kind of science. Medical education is filled with science. In the US, all students must score high on the “Medical College Admission Test” in order to be admitted to medical school. Students are allowed a total of 345 minutes to complete the exam. Eighty-five minutes are devoted to “verbal reasoning,” and 60 minutes to a “writing sample.” The remaining 200 minutes (58%) are split evenly between “physical sciences” and “biological sciences.” It is apparently important that physicians understand levers, inclined planes, the acceleration of falling bodies, the life cycle of insects, and the process of photosynthesis. The kind of science that doctors have to learn is the simpler sort of science, the mechanical kind. Physicists worked out the mechanics of simple machines (levers, planes) in the seventeenth century. In our times, they have been working on much slipperier subjects: quarks, chaos, the “weak force,” and the oddest of quantum phenomena. Cause and effect are far less easy to detect in these matters than in the study of falling bodies (although “gravity” is the most complex and least understood force in physics). But it is the latter, not the former, in which physicians are schooled. And there is very little social science in medical education where one must address the complexities and subtleties of, say, emotion, or ritual, or culture. And even in the biological sciences, while there is a good deal of biochemistry, there is very little ecology, where one must try to understand cycles of relationship between predators, prey, plants, insects, and climate (for starters).

Some definitions

An education like this is extremely helpful for understanding causal relationships, where one thing causes one other thing (or seems to) – where an antibiotic kills bacteria, or physical pressure stops bleeding. But when matters get more subtle, where a drug works twice as well in one country as it does in another; where the patient gets better even though it turns out that the drug was inert; where the drug works better when it is blue than when it is red – in these kinds of cases such an education may be as much of a hindrance as a help.

Such an education can even be seen as the source of one of the very first serious obstacles to understanding these processes. Arthur K. Shapiro, MD, spent much of his career as a psychiatrist studying the placebo effect. In 1964, he proposed a definition of the placebo and the placebo effect which I will quote at length:

A placebo is defined as any therapeutic procedure (or a component of any therapeutic procedure) which is given (1) deliberately to have an effect, or (2) unknowingly and has an effect on a symptom, syndrome, disease, or patient but which is objectively without specific activity for the condition being treated. The placebo is also used as an adequate control in research. The placebo effect is defined as the changes produced by placebos. (Shapiro 1964:136)

Thirty-three years later, in a posthumously published book, Shapiro used very nearly identical words to define these same terms (Shapiro and Shapiro 1997). But this definition, with its insistence on a simplistic sort of cause and effect, is clearly impossible. The placebo is defined as “objectively without specific activity for the condition being treated.” So if we put this definition in place of the word itself in the final sentence, here’s what we get: “The placebo effect is defined as the changes produced by things objectively without specific activity for the condition being treated.” This makes no sense whatever. Indeed, it flies clearly in the face of the obvious. The one thing that we can be absolutely sure of here is that placebos *do not* cause the placebo effect. Placebos are inert. To be inert is to not do anything. That’s what inert means. If it does something (cause changes) it isn’t inert. But placebos are inert, and changes do occur.

This definition confuses coincidence with cause. Just because two things occur at the same time doesn’t mean that one caused the other. When a gun is fired, there is a loud noise. It happens every time. But the loud noise does not cause the hole in the target.

I suggest a very different approach to this problem. I will define what I call the *meaning response*, which is “the psychological and physiological effects of *meaning* in the treatment of illness.” When such effects are “positive” (however understood), they include most of the things that have been called the placebo effect; when such effects are “negative,” they include most of what has been called the nocebo effect. Since what is positive in one situation may be negative in another, this is not a fundamental distinction.² The meaning response includes most of the

² When you take diphenhydramine (“Benadryl”) as a decongestant, if it makes you sleepy, that’s negative (it’s a negative “side effect”). If you take diphenhydramine (“Sleep-Eze”) as a sleeping pill, and it dries your mouth and nose, that’s negative (a negative “side effect”). What’s positive and negative is often a matter of context and perspective.

things that have traditionally been called the placebo effect. It also may exclude a few things (which we will consider later). More important, it includes many things that are *not* part of the placebo effect as traditionally understood; we shall see that the meaning response is attached not only to the prescription of inert medications, but to active ones as well.

To show that clearly, we must first look at the whole healing process, and see what it consists of.