Is More Myth Than Science, Study Says

By GINA KOLATA

In a new report that is being met with a mixture of astonishment and sometimes disbelief, two Danish researchers say the placebo effect is a myth.

The investigators analyzed 114 published studies involving about 7,500 patients with 40 different conditions. The report found no support for the common notion that, in general, about a third of patients will improve if they are given a dummy pill and told it is real.

Instead, the researchers theorize, patients seem to improve after taking placebos because most diseases have uneven courses in which their severity waxes and wanes. In studies in which treatments are compared not just with placebos but also with no treatment at all, they said, participants given no treatment improve at about the same rate as participants given placebos.

The paper appears today in The New England Journal of Medicine. Both authors, Dr. Asbjorn Hrobjartsson and Dr. Peter C. Gotzsche, are with the University of Copenhagen and the Nordic Cochran Center, an international organization of medical researchers who review randomized clinical trials.

Dr. Hrobjartsson said he had been telling other investigators what he found and watching their responses. "People react with surprise, but also with a kind of satisfaction," he said in a telephone interview. "They start reflecting."

Experts interviewed this week had a range of responses from ready acceptance of the conclusion to great surprise to a skepticism and the desire to see the details of the analysis.

Dr. Donald Berry, for example, a statistician at the M. D. Anderson Cancer Center in Houston, said: "I believe it. In fact, I have long believed that the placebo effect is nothing more than a regression effect," referring to a well-known statistical observation that a patient who feels particularly terrible one day will almost invariably feel better the next day, no matter what is done for him.

Another physician, Dr. Jonathan Moreno, director of the Center for the Biomedical Ethics at the University of Virginia, said it rang true to him. "Maybe it is one of the urban legends of medicine," he said.
But others, like David Freedman, a statistician at the University of California, said he was not convinced. Professor Freedman said the statistical method the Danish researchers used, pooling data from many studies and using a statistical tool called metanalysis to examine them, could give misleading results.

"I just don't find this report to be incredibly persuasive," he said. "The evidence of a placebo effect is maybe a little bit less than I thought it was, but I think there's a big effect in many circumstances. This doesn't change my mind."

The researchers said they saw a slight effect of placebos on subjective outcomes reported by patients, like their descriptions of how much pain they experienced. But, Dr. Hrobjartsson said, he questions that effect.

"It could be a true effect, but it also could be a reporting bias," he said. "The patient wants to please the investigator and tells the investigator, 'I feel slightly better.'"

Placebos are still needed in clinical research, Dr. Hrobjartsson said, to prevent researchers from knowing who is getting a real treatment. Otherwise, he said, researchers can end up seeing what they want to see. For example, they may notice changes in patients who are taking an active drug while not paying as much attention to similar symptoms in patients that they know are being left untreated. Patients, he said, who are told they are not being treated may leave the study, further complicating research efforts.

Dr. Hrobjartsson and Dr. Gotzsche said they began their study out of curiosity. Over and over, medical journals and textbooks asserted that placebo effects were so powerful that, on average, 35 percent of patients would improve simply if they were told that a dummy treatment was real. The investigators began asking where this assessment came from. Every paper, Dr. Hrobjartsson said, seemed to refer to other papers. And those papers referred him to other papers. He began peeling back the onion, finally coming to the original paper. It was written by a Boston doctor, Henry Beecher, who had been chief of anesthesiology at Massachusetts General Hospital in Boston and in 1955 published a paper, "The Powerful Placebo" in The Journal of the American Medical Association.

In his paper, Dr. Beecher, who died in 1976, reviewed about a dozen studies that compared placebos with active treatments and concluded that placebos had medical effects.

"He came up with the magical 35 percent number that has entered placebo mythology," Dr. Hrobjartsson said.

But, Dr. Hrobjartsson said, diseases naturally wax and wane. And no matter how sick the person is, a truly bad spell will almost inevitably be followed by a period in which the condition seems to improve. What if the natural variation in a disease's course is behind the placebo effect, they asked?

"Of the many articles I looked through, no article distinguished between a placebo effect and the natural course of a disease," Dr. Hrobjartsson said. "This is a very banal error to make, but sometimes banal errors are made."

He and Dr. Gotzsche began looking for well-conducted studies that divided patients into three groups, giving one a real medical treatment, one a placebo and one nothing at all. That was the only way, they reasoned, to decide whether placebos had any medical effect.

But they worried that there might be so few such studies with a treated, untreated and placebo group that they would never be able to answer the question. "We thought if we could find 20, that would be a huge success," Dr. Hrobjartsson said.

To their surprise, they found 114, published between 1946 and 1998. The conditions included medical disorders,
like high blood pressure, high cholesterol levels and asthma; behavioral disorders and addictions, like alcohol abuse and smoking; neurological diseases like Alzheimer's disease, Parkinson's disease, and epilepsy, and infections, like bacterial infections and the common cold.

When they analyzed the data, they could detect no effects of placebos on objective measurements, like cholesterol levels or blood pressure.

Dr. John C. Bailar III, an emeritus professor at the University of Chicago who wrote an editorial accompanying the placebo paper, said the findings called into question some mind-body beliefs. These are arguments that use the placebo effect to conclude that the mind can so profoundly affect the course of a disease that people should be able to harness this power and think themselves well.

The findings should also give doctors pause in prescribing treatments they know are useless, like a glass of warm milk at bedtime for patients with insomnia or futile drugs for patients in the late stages of fatal diseases, Dr. Bailar said.

"I think what this ought to do is bring about a very sharp reduction in the use of placebos," he said. "My guess is that it will bring about a modest reduction and that it will take a second or third penetrating paper to bring about a real change."

But, Dr. Bailar said, he understands the reluctance many will feel to abandon their belief in placebos. He, too, is hesitant to wrench himself completely away from what he now thinks is largely a myth.

"I'm not ready to give up on placebos entirely," Dr. Bailar said. "I hope there will be a lot more research on how they work."

Or, he said, "if they work."

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