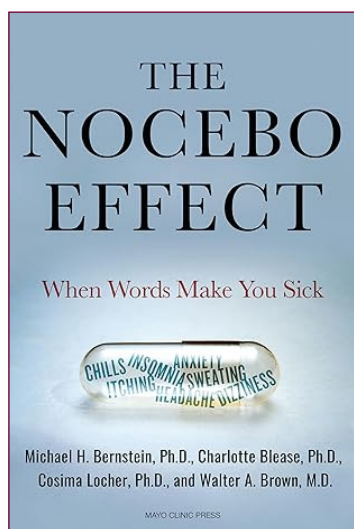


New Book Examines the Roots, Implications of the Nocebo Effect and Strategies to Address It

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From the introduction to the conclusion, the recently released book by the Mayo Clinic Press, *The Nocebo Effect: When Words Make You Sick*, is a comprehensive review of up-to-date published studies on the topic, with chapters written by multidisciplinary experts in this emerging and understudied field, with a perspective from their first-hand experiences.



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Etymology of Nocebo

The term nocebo stems from the Latin verb *nocēre*, meaning “to harm.” The noun nocebo is the first-person future indicative, meaning, “I will be harmful.” Contrast this with the noun placebo, which translates to, “I shall please,” and is derived from the Latin verb *placere*, to please.

In the mid-20th century medical literature, WP Kennedy published *The Nocebo Reaction* (*Med World*, 1961;(95):203-05) to denote this counterpart to the usage of the concept of placebo. Dr. Kennedy described it as a “quality inherent in the patient, not the remedy.”

The nocebo effect is a phenomenon that can be summarized as the occurrence of a harmful event that stems from consciously or subconsciously anticipating it. The book delves into real-world examples, such as the global administration of 12.7 billion COVID-19 vaccine doses, revealing that while vaccine hesitancy is often linked to reported side effects discussed in the media, a considerable portion of these side effects were not caused by the vaccine but by negative expectations – the nocebo effect in action.

Specific strategies are examined in several chapters in the book, directed at healthcare providers as well as patients (See **Table of Contents** for overview). Reading this book will do the reader no harm – it is sprinkled not only with strategies, examples of historical and mass “hysterical” and cultural “contagions,” (See **Book excerpts**, page 58), but humorous analogies as well.

For example, one chapter explores different psychotherapies using The Dodo Bird from *Alice is in Wonderland* as a comparative. In Part One, in the chapter, When Psychotherapy Harms, authors Cosima Locher and Helen Koechlin write: “In Lewis Carroll’s novel *Alice in Wonderland*, several characters needed to dry off after swimming around in Alice’s pool of tears. The Dodo Bird asked them to race around the lake until they were dry. Nobody cared to

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measure when a competitor started to run, or how long it took them. When the characters asked the Dodo who had won the race, he thought for a long time and then replied: “Everybody has won and all must have prizes.”

...“Despite these very different theories about how psychotherapy works, CBT, person-centered, and other approaches, all “win,” just like all the runners in *Alice in Wonderland*. Different therapies lead to a similar improvement in depression, anxiety, or whatever other symptom is being treated. In other words, it doesn’t matter much what type of therapy is used. They all work equally well.”

The chapter also delves into examples of patient scenarios and the dearth of research on the nocebo effect in psychotherapy. It is enlightening, as well as entertaining for Lewis Carroll aficionados.

Co-Editors

The four Co-editors of the book, two of whom are from Brown, include:

MICHAEL BERNSTEIN, PhD, an experimental psychologist and an Assistant Professor in The Department of Diagnostic Imaging at the Alpert Medical School. His work is focused on harnessing the placebo effect to reduce opioid use among pain patients. He is Director of the Medical Expectations Lab at Brown.

CHARLOTTE BLEASE, PhD, a philosopher and interdisciplinary health researcher at Digital Psychiatry, Beth Israel Deaconess Medical Center, Harvard Medical School, and the Department of Women’s and Children’s Health, Uppsala University, Sweden.

COSIMA LOCHER, PhD, a psychologist and researcher at the Department of Consultation-Liaison Psychiatry and Psychosomatic Medicine, University Hospital Zurich, University of Zurich, Switzerland. Dr. Locher is a co-founder of The Pain Net, an international network of researchers interested in Chronic Primary Pain, with a special focus on the placebo effect.

WALTER A. BROWN, MD, a Clinical Professor Emeritus of Psychiatry and Human Behavior at the Alpert Medical School. He has studied the placebo effect for the past 40 years, and is the author of three books, including *The Placebo Effect in Clinical Practice*.

In the conclusion they write that “...providers should be taught about the nocebo effect. We realize that medical education is already densely packed and adding more material to the curriculum is no easy feat. But even one or two seminars discussing the nocebo effect and the importance of expectation would be advisable. If doctors’ first duty is to ‘do no harm,’ then it only follows that they should be taught about the harms from the nocebo effect and ways of preventing it...Many questions remain, and we should focus our attention on answering them.”

This book is beyond a primer on the nocebo effect and side effects – it is well-researched, a fluid and focused read, illuminating as well as engaging. In the accompanying Q&A, RIMJ posed questions to Brown Co-editors, Drs. Michael Bernstein and Walter A. Brown, on the book’s genesis and focus (See Q&A). ❖

Q&A with Brown Co-Editors

Q. How did the conceptual framework for a book on this topic materialize among the four Co-editors?

A. Several years ago, Walter realized that while there were many discussions of the placebo effect in both scholarly journals and popular media, very little had been written about the nocebo effect. The time was right to assemble what we know about the topic. It has important implications for healthcare.

Q. Were there any surprising revelations the Co-editors uncovered as the contributions in the book were being selected?

A. During the course of selecting chapter topics, we were surprised to see just how far-reaching the nocebo effect is. For instance, as discussed by some chapter authors, research suggests that the media can induce a nocebo effect and that nocebo is important in understanding health complaints after environmental exposure (e.g., powerlines).

Q. Given the book’s subtitle, “When Words Make You Sick,” is the target readership for the book patients or healthcare providers, or both?

A. The book is written for anyone interested in how the mind can impact your health. No special knowledge is required. We hope that both providers and the general public find it valuable.

Q. The book chapters show that the nocebo effect has been understudied and underestimated compared to the placebo effect. But would you say there is a general awareness among healthcare providers of the nocebo effect and its implications for their patients?

A. Many healthcare providers implicitly understand that expectations matter – both positive (placebo) and negative (nocebo) – from their own personal experience working with patients. However, few are probably familiar with the scientific literature on the topic. This book walks the reader through the relevant empirical evidence, and offers suggestions for how providers can minimize the impact of nocebo.

Q. What are the key takeaways in the book for clinicians/healthcare providers?

A. Be mindful of the language that you use, especially when conveying difficult information to patients. When prescribing treatments with minor side effects, consider first educating patients about the nocebo effect and then asking whether they want to learn about potential side effects. This admittedly time-consuming strategy preserves patient autonomy while likely reducing harm. ❖

[Editor's note: The following are excerpts from the book provided by its publisher, the Mayo Clinic Press, available at: <https://mcpress.mayoclinic.org/research-innovation/the-nocebo-effect-history-contemporary-applications/>]

The History of Nocebo Research: Where Did It Come From?

In the 1950s, Dr. Henry Beecher, who served as a physician in World War II, published a series of seminal papers on the placebo effect. Beecher documented instances where he gave wounded soldiers saline – that is, salt water – but told them they were receiving a powerful painkiller. Beecher did not engage in this deception out of cruelty; in fact, it was just the opposite. Dr. Beecher was an anesthesiologist and faced the difficult task of rationing an all-too-limited supply of morphine. What Beecher noticed on the battlefield has sparked seventy years of modern-day science on the placebo effect: soldiers experienced substantial pain relief from the saline.

The field started as just a few papers on the placebo effect, but it has since blossomed into a full-fledged body of theoretical and empirical work. In 2023, scholars gathered for the fourth Society of Interdisciplinary Placebo Studies conference, founded by Dr. Charlotte Blease and colleagues, and devoted to the study of placebo science. Placebo research has been published in top academic journals, but it has also captured the public imagination, with leading popular press articles in nearly all major media outlets.

The topic of nocebo has emerged largely from work on the placebo effect. And while thorough reviews of nocebo are lacking, it is still a critical factor to consider in patient care. So where did the idea of the nocebo effect originate? The answer is more confusing than you might imagine...

Psychogenic Illnesses: From the June Bug to Havana Syndrome

The mind's unfortunate ability to cause suffering is well established, and this phenomenon lies at the heart of the nocebo effect. One such example, known as "The June Bug," occurred in a textile factory in the United States in the early 1960s. Many employees began to feel dizzy and had an upset stomach. Some people vomited. Rumors of a mysterious bug that was biting employees began to circulate, and eventually sixty-two people who worked at the factory became ill. So what were these mysterious bugs? According to experts, they were nothing – literally. The CDC investigated this outbreak, but no bugs or any other cause of the illnesses could be identified. It instead appears to have been a case of what has often been labeled "mass hysteria," though it is now called *psychogenic illness*.

...But would such a mass outbreak occur today? It might be easier to imagine people from the Middle Ages, or even a half century ago, experiencing this type of bizarre illness than it would be to think of such a thing happening in the twenty-first century. During 2016 and 2017, however, twenty-one American diplomats in Cuba experienced a range of bizarre neurological symptoms such as hearing loss and nausea. News of what came to be known as "Havana Syndrome" spread, and eventually more than two hundred U.S. government personnel in diplomatic missions in several countries became ill. This case was more troubling than just a few individuals who got sick with unexplained symptoms. Speculation quickly mounted regarding nefarious acts by our foes abroad. One leading theory was that the Russian government was releasing invisible

microwaves that caused people to get sick. This might sound like a fringe conspiracy theory, but it has been discussed in leading news sources ranging from the *Washington Post* to NPR. In a 2021 meeting, the cause of Havana Syndrome was discussed among the secretary of state, the attorney general, the CIA director, and the FBI director. Would so many high-ranking U.S. officials meet if they believed that Russian interference was off the table as a potential cause?

To be clear, we do not yet know for certain the cause of these neurological conditions. It is even conceivable that the speculation about Russian interference will ultimately prove correct. However, there are plenty of similarities between what happened relatively recently in Cuba and what happened in the past in Loudun, France, and elsewhere. It should be concerning to scientists and the public alike that the *possibility* of a psychogenic reaction is not being taken seriously. As discussed by *New York Times* reporter Serge Schmemmann, the person who was hired to oversee the investigation into Havana Syndrome was pushed out of this role because she refused to take psychogenic illness off the menu of potential causes.

Germs are not the only way that illnesses can spread. Psychological outbreaks are very real, and Havana Syndrome fits the same pattern that has been observed so often before. As Mark Twain is alleged to have said, "History does not repeat itself, but it rhymes." Imagine if speculation about Russian interference gained more of a foothold. What if then-president Donald Trump had released inflammatory tweets about it? How would Vladimir Putin have responded? Could this have turned into a global incident? The nocebo effect is powerful indeed.