Are Antidepressants Placebos?

Antidepressant drugs are now taken by around 11% of Americans over the age of 12, though that could be an underestimate. Women are more likely to take them, and almost one quarter of American women in their 40s and 50s take them. While the number of people taking them is a matter of concern, a larger question is how they work. Are antidepressants placebos? There's good evidence that they are, and that's how they work.

Evidence from clinical trials

Drug companies perform clinical trials in order to get their drugs approved by the FDA (and other agencies outside the U.S.), and may also run trials after approval. Clinical trials usually include a group of patients taking a placebo, and then any improvement in health markers of interest (depression, in the case of antidepressants) is compared to improvement, if any, in the placebo group.

Patients in clinical trials are not supposed to know whether they are receiving a placebo or the real drug, and neither are their doctors. This is known as a double-blinded trial.

When patients enter a clinical trial of antidepressants, the researchers tell them that they may receive either the active drug or a placebo, but they won't know which one. There are a couple of reasons for that.

One is that, if someone knew that he was taking, or going to take, a placebo

instead of the real drug, he'd be less likely to enter or remain in the trial.

Another is that the placebo effect may depend largely or entirely on the power of suggestion, so if a patient knows he's getting a placebo, it may not work.

In clinical trials of antidepressants, the effect of the drug over the placebo has, in most cases, been quite small. In fact, the differences between antidepressants and placebos is so small as to be clinically insignificant.

Different types of antidepressants

Now, there's something odd about clinical trials of antidepressants.

Antidepressants are of different types; that is, they allegedly affect different aspects of physiology and thus have different mechanisms.

Tricyclic antidepressants are an older type. No one is really sure how they're supposed to work.

Newer types include selective serotonin uptake inhibitors (SSRIs), selective norepinephrine uptake inhibitors (SNRIs), and even selective serotonin uptake enhancers (SSREs).

In clinical trials, the difference between placebo and drug has been remarkably similar and small, no matter what type of drug was tested. That really doesn't make much sense.

Unblinding and active placebos

As mentioned, clinical trials are supposed to be blinded, ideally double-blinded, to get objective results.

It appears that in many or most cases of clinical trials of antidepressants, a large proportion, as much as 85%, of both the subjects and their doctors become unblinded by correctly guessing whether the subjects are taking a drug or a placebo.

How does that happen? Because drugs have side effects. In the case of antidepressants, they may cause dry mouth, sexual dysfunction, insomnia, and many other things. When patients experience side effects, they know that they're taking the real drug, as do their doctors. When they experience no side effects, they assume that they're getting a placebo.

Unblinding in clinical trials is an important source of bias.

When trials have both a blinded and non-blinded observer, the non-blinded observer's estimate of the drug's effects are 36% greater than the blinded observer's.

> If we assume that the blinding is broken for all patients in the antidepressant trials, and adjust for the bias the loss of blinding causes, we will find that antidepressants have no effect (odds ratio 1.02).

One way to get around this problem is to use "active placebos", that is, placebos that have side effects. When trials have done this, they've found very little difference between antidepressants and placebos. The difference was so small as to be clinically insignificant.

The conclusion is that antidepressants are "active placebos". Patients get better because they believe that they're taking a powerful drug, which in reality is either weak or powerless, beyond its effect as a placebo.

Placebos are powerful

The fact that antidepressants have little to no efficacy over and above that of a placebo doesn't mean that they don't work, only that most or all of their efficacy is due to the placebo effect.

Placebos are powerful.

Placebos that are taken twice a day are more effective than those taken once a day.

Injectable placebos are even more effective.

A great deal, or even all, of the effectiveness of arthroscopic surgery for osteoarthritis is due to a placebo effect. In a controlled trial, placebo (sham) surgery was as effective as real surgery. Sham surgery to repair a a meniscus tear in the knee was as effective as real surgery.

Mammary ligation was a surgical procedure used for several decades to treat angina pectoris, until a trial found that it was no better than sham surgery.

These surgical procedures were believed to work, because they did. Patients reported relief, even cures, but that was all due to a placebo effect.

Patients have overdosed on placebos and required emergency treatment.

In conditions with a large psychological component, such as depression and pain, placebo effects can be powerful. On the other hand, placebos don't lower blood sugar.

What to do about antidepressants

There are no good answers here. Depression is a serious problem that, at least in moderate to severe cases, requires treatment.

One view might be to say that if antidepressants work as placebos, then fine, just keep using them. The problem with that view is that these are drugs,

with many adverse side effects, including increased violence and suicide in some cases. It appears to be unethical to give powerful drugs that are no more effective than placebos.

On the other hand, for a doctor to tell a patient that he's giving him a placebo lowers, though it may not abolish, the effectiveness of the treatment.

And lying to a patient by giving him a placebo and telling him it's a drug also seems unethical.

My suggested alternative is to give a patient something known to have antidepressant effects, such as magnesium citrate or fish oil capsules. Feel free to poke holes in that idea.

Psychotherapy may be an alternative. It's at least as effective as second-generation antidepressants in the short term, and better in the long term, since relapse rates are lower.

Most of the information in this article comes from an excellent book, The Emperor's New Drugs: Exploding the Antidepressant Myth, by Irving Kirsch, PhD, a professor at Harvard. I couldn't put the book down, it was that good.

Relevant to what to do about antidepressants, Kirsch strongly states, "**Antidepressant medication should not be discontinued without first discussing it with your doctor**." [Emphasis in the original.]

Some quotes from the book's preface:

"When we analyzed all of the data – those that had been published and those that had been suppressed – my colleagues and I were led to the inescapable conclusion that antidepressants are little more than active placebos, drugs with very little specific therapeutic benefit, but with serious side effects."

In response to the knowledge that these drugs were approved by government regulatory agencies: "And yet I remain convinced that antidepressant drugs are not effective treatments and that the idea of depression as a chemical imbalance in the brain is a myth."

"The chemical effect of antidepressant drugs may be small or even non-existent, but these medications do produce a powerful placebo effect."

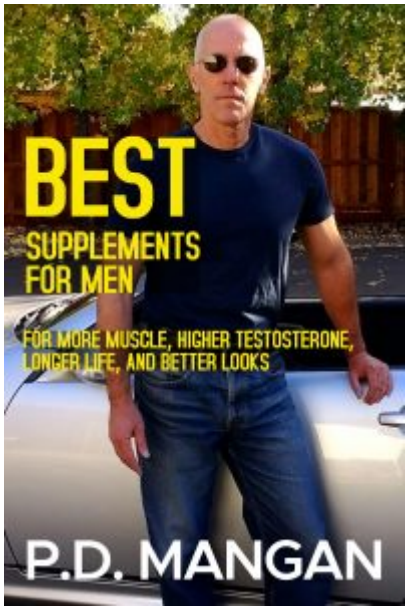
Psychiatric drugs cause harm

Psychiatric drugs, including antidepressants, may cause serious harm, especially in the elderly. Given their potential for harm, it's open to question whether many of these drugs should have been approved for human use in the first place. As Dr. Peter Gøtzsche has written, psychopharmacology is not evidence-based medicine:

> This chapter argues two evidence-based conclusions: not only are psychiatric drugs dramatically overprescribed and overvalued but the harms they unleash completely overwhelm any benefits accrued. While accepting numerous reasons for our current prescribing epidemic, this chapter focuses on the manipulation of most placebo controlled trials, the systematic underreporting of drug harms, the industry-led misrepresentation of drug safety and efficacy and the medical denial of the substantial role withdrawal and abstinence symptoms play in convincing patients to stay on drugs. This chapter concludes that a thorough and independent review of the evidence base reveals that psychiatric drugs, apart from calming some people down when taken short term, "have failed to deliver what patients want, which is to work specifically for specific mental or emotional problems." Since mental illness is rarely chronic and lifelong, it argues there is no scientific justification for the widespread lifelong use of psychiatric drugs. If we are to restore balance, and reverse these harms, a total reappraisal of what the evidence teaches must be translated into reformed prescribing guidelines.

This is yet another instance in a long series of mainstream medicine getting something very wrong.

PS: My most recent book is Best Supplements for Men.



PPS: Check out my Supplements Buying Guide for Men.