

COMMENTARY

No Magic Pill: A Prescription for Enhanced Shared Decision-Making for Depression Treatment

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For over 2 decades, there have been debates, sometimes contentious, about the efficacy and safety of antidepressants. Growing awareness of the difficulty some patients have when discontinuing these medications has intensified these debates. Recently, Cipriani and colleagues published the largest meta-analysis to date that assessed the efficacy and tolerability of antidepressants. They concluded that all were more efficacious than placebo, and they also synthesized the trial results from head-to-head studies in an effort to guide pharmacologic treatment for major depressive disorder in adults. Although the researchers acknowledged many limitations in their analysis, including the fact that effect sizes were modest at best, the media overstated the results of the study. Both the meta-analysis and the news stories reinvigorated the debates about whether or not antidepressants “work.” Unfortunately, however, the key question—how can this meta-analysis help physicians in assisting their patients with a difficult decision about depression treatment options?—was lost in the controversy. In this commentary, we identify the questions and challenges that were not addressed in the current debate and offer specific suggestions for enhancing shared decision making for physicians working in primary care settings. (J Am Board Fam Med 2019;32:6–9.)

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The publication of a recent meta-analysis on the comparative efficacy and acceptability of antidepressant medication (ADM) sparked a great deal of media attention.¹ In the largest meta-analysis to date, with over 116,000 patients and 21 antidepressants, Cipriani and colleagues¹ concluded that all the ADMs were more efficacious than placebo in adults. In an effort to inform guideline development and pharmacologic treatment decisions, they further synthesized the trial results from the head-

to-head studies and identified differences between drugs and described “the relative merits of the different antidepressants.”¹ The researchers acknowledged many limitations to their analysis, including the fact that effect sizes were modest at best, there was a novelty effect (newer medicines were more effective when older drugs were used as comparators), and that adjusting for this effect diminished differences between antidepressants. In addition, the certainty of the evidence was low or very low, with the highest rating moderate, and outcomes such as global functioning were not able to be quantified.

However, many major publications overstated the results of the study, with headlines such as “Antidepressants do work, and many more people should take them: Major international study”² and “Millions MORE of us should be taking antidepressants: Largest-ever study claims the pills DO work and GPs should be dishing them out.”³ In turn, many researchers and clinicians challenged not only the overhyped media reporting but also the research on which the meta-analysis was

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based.^{4,5} These critiques cited the short-term nature of the trials, the problematic use of nonpatient-centered outcome measures, the fact that statistical significance does not necessarily translate into clinical significance, and that the findings of efficacy were, in general, limited to people with more severe depression.

However, as is the case in political debates, the current scientific debaters seem to be ever more entrenched in their camps, talking past each other and losing sight of the most important point: how can this meta-analysis help physicians in assisting their patients with a difficult decision about depression treatment options? In this commentary, we identify what is lost in the current debate and offer a way forward for physicians working in primary care.

What Is Lost in the Current Debate?

There are Unique Challenges in the Diagnosis and Treatment of Depression

Both the diagnosis and treatment of depression are subject to ambiguity inherent in the modern understanding of the disease and in light of the available knowledge of treatments. The treatment of depression presents a unique set of challenges because there are good reasons to believe that it is unhelpful to conceptualize depression as a relatively homogeneous disorder for which a single neurobiologic etiology is responsible. When treatment with antidepressants is one's only "hammer," every patient looks like a "nail." Instead, there are several options, including lifestyle, psychotherapy, and pharmacotherapy, alone or in combination, that can be used.^{6–8} The importance of discussing uncertainty in treatment outcomes along with an explicit consideration of patients' needs and wishes, rather than considering only pharmacologic intervention, can lead to better shared understanding and decision making.⁹

The Question "Do Antidepressants work?" is an Incomplete One

Efficacy, that is, the benefit demonstrated under the ideal conditions of a clinical trial, is different from effectiveness, and often an "efficacy-effectiveness" gap exists between the results achieved in efficacy trials and those observed by usual practitioners treating real patients in common settings.¹⁰ The short duration of most studies, 12 weeks or

less, makes it difficult to determine medication effectiveness over the long-term, which is information patients struggling with depression most want to know. In addition, the question of effectiveness must also be balanced by a thorough consideration of side effects and tolerability. After all, a medication will not be remotely effective against depression if a patient stops taking it due to intolerable side effects and, worse, may bias a patient against considering further treatment choices out of fear of side effects.

The meta-analysis, just like the data on which it is based, provides information about group means; it does not mean that it "ends doubts" about the efficacy of antidepressants for individual patients.

Previous studies and meta-analyses assessing the efficacy of ADMs have found that, on average, antidepressants are not efficacious for people with mild depression, yet they are efficacious for people struggling with more severe depression. However, these findings mean that for some people with mild depression, antidepressants do work, and for some people with more severe depression, they do not. Although available research can give us insight into the probability that patients will benefit from treatment, it does not assure us that a patient will or will not benefit. The fact that effect sizes, as compared with placebo, are modest at best needs to be communicated to patients. Finally, complicating the efficacy question is the fact that 73% of the trials were rated at moderate risk of bias and 9% were rated at high risk. Indeed, because most bias actually escapes the standard risk of bias instruments, the results of this meta-analysis should be interpreted with caution.

Addressing What Has Been Lost in the "Yes They Do Work! No They Do Not!" Debate: A Proposed Approach To Shared Decision Making

Initiating Conversations about Medical Uncertainty

In light of the current state of the research on antidepressants, physicians bear an additional burden of initiating conversations about what is not known. Silence about uncertainty can lead to misunderstandings, which, in turn, can all too easily lead to mistrust, complaints to regulatory bodies, or even litigation.¹¹ Initiating difficult conversations is not only important from a risk management perspective, but most importantly, this type of open

and genuine discussion has the potential to enhance collaborative care and shared decision making, and potentially improve patient outcomes.^{12–15} Especially in light of the fact that effect sizes in clinical trials and in this meta-analysis were small to modest, one approach is to frame ADM as a treatment that may, in some percentage of patients, reduce but not necessarily eliminate symptoms. Establishing an expectation of partial relief is more likely to result in patients' perception of successful treatment than implying an expectation of quick, complete, and/or long-lasting cure of depressive symptoms. In addition, in light of the emerging data and literature on ADM discontinuation syndrome,^{16–18} patients should be made aware of the fact that some people experience great difficulty in stopping ADM even with tapering.

Do Not Just do Something, Stand There

As Dee Mangin, a family physician and chair in family medicine at McMaster University recently noted, "The therapeutic imperative in medicine means that we are good at rushing to do things that might 'save lives' but not good at not doing, or undoing."¹⁹ Medication treatment for depression does not, as has been implied, fit hand-in-glove like insulin for type 1 diabetes,²⁰ and it is time to rethink this model, especially for less severe forms of depression. Just as watchful waiting is recommended for acute otitis media, acute sinusitis, and early prostate cancer, perhaps a new model for psychopharmacology in general and depression treatment in particular, can be one that starts with nondrug therapy. Indeed, some treatment guidelines for depression, such as those produced by the National Institute for Health and Care Excellence, use a stepped approach for depression care.

The First Medication Choice will Likely not be The Final one, and a Multipronged Approach is Needed

There is a well-known precept and growing evidence that many depressed patients are refractory to the initial drug choice and require either a change of medication entirely or a synergy of more than one medication. At the outset of treatment, patients ought to be explicitly told that because the exact mechanism of disease and precise reasons for drug effectiveness elude current scientific knowledge, it may take several adjustments of dosage or choice of prescription before acceptable symptom control is achieved.⁸ In addition, a growing body of

research consistently demonstrates the efficacy of nonpharmacologic interventions, such as exercise, improved sleep hygiene, increased social support, and psychotherapy for the treatment of subthreshold and mild to moderate depression.^{6,7,21–28} Although a multipronged approach to the treatment of depression can be time consuming and emotionally taxing, framing drug prescription in this context may be perceived by patients as not only forthright but also reflective of a genuine interest in helping.

Conclusion

Modern American society has a taste for quick fixes, easy treatments, complete recoveries, and minimal sacrifice. In an industry-dominated climate, especially one that has heavily promoted the "chemical imbalance" theory of depression, health care providers may feel pressure to prescribe antidepressants. Certainly, it is challenging in contemporary practice to take the time to reach a level of shared understanding to make the decision about the risks, benefits, and alternatives to ADM. However, the upfront investment in later success and a reminder at each follow-up visit may very well result in better patient outcomes and satisfaction for both patients and physicians.

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To see this article online, please go to: <http://jabfm.org/content/32/1/6.full>.

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