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The American Psychiatric Association (APA) published a new guideline for Major Depressive Disorder (MDD) [1] which will undoubtedly be used by many practitioners to guide clinical decision-making. In fact, it is non-psychiatrist clinicians who prescribe the majority of antidepressants (AD) [2]. We review the APA's most recent guideline on MDD and report on our observations.

The Practice Guideline for the Treatment of Patients with Major Depressive Disorder, Third Edition is 152 typeset pages in length and the main body is 86 pages. The guideline is composed of three sections: Part A, "Treatment Recommendations"; Part B, "Background Information and Review of Available Evidence"; and Part C, "Future Research Needs." Part A is the only section that was published in print form and includes the "Executive Summary" [3]. This published summary provides recommendation statements and accompanying codes that indicate the strength of the recommendation. Part A also includes "Choice of an Initial Treatment Modality" (referred to in Table 1 as the "Clarification Section") and presents additional guidance for the implementation of recommendations. Part B, "Background Information and Review of Available Evidence," (referred to in Table 1 as the "Evidence Section") contains an extensive literature review and further explains the recommendation statements. This latter section was not published in a medical journal but is available on the publisher's web site (www.psychiatryonline.org).

This guideline does not contain a decision algorithm or tree or an explicit hierarchy of recommendations. Interventions were also not consistently rank-ordered within or between sections. In some cases, a careful reading of the complete document results in a statement that differed substantially in focus or weight from the recommendation statement in the printed summary. For example, drug therapy and psychotherapy are clearly "recommended" as

monotherapies in the printed summary. Yet later on in the guideline, it is suggested that that their combined treatment "may be used" [1, p. 18], despite the citation research showing the *superiority* of combined treatment in the evidence section. These internal inconsistencies and contradictions between sections will likely make it difficult for the clinician to discern exactly what course of action is best. Also, especially in the absence of a decision tree, when the rationale for a recommendations is vague (e.g., "If a patient with mild depression wishes to try exercise alone for several weeks as a first intervention, *there is little to argue against it* [emphasis added]" [1, p. 30], there is not enough evidence to guide clinical decision-making.

Perhaps most importantly, the guideline does not clearly link, as do many guidelines, the levels of recommendation with levels of evidence. As a result, the guideline is not transparent, and readers are left to surmise differences within a level of evidence. For example, it is unclear when and why AD medication should be the frontline treatment. Additionally, the risk/benefit issue when recommending AD medication as a first line treatment for individuals with mild depression is not adequately addressed. Although recent meta-analyses questioning the efficacy of ADs are cited in the guideline [4, 5], the context in which they are referenced does not convey the primary conclusions drawn by both meta-analyses: AD medication should not be the default recommendation for mild to moderate depression. Instead, the following statement is made in the guideline's executive summary: "Response rates in clinical trials typically range from 50-75% of patients, with some evidence suggesting greater efficacy relative to placebo in individuals with severe depressive symptoms as compared to those with mild to moderate symptoms" [1, p. 31]. Thus, the reader is left with the erroneous impression [6, 7] that there is a clear evidence base for generally recommending the use of ADs as the initial treatment for mild to moderate depression, and ADs work even more effectively for severe depression. This lack of clarity and the

recommendation of antidepressants as a first-line choice for mild depression stand in contrast to guidelines produced by non-specialty organizations such as the National Institute for Clinical Excellence (NICE), which addresses the risk/benefit issue and explicitly states that antidepressant medication should not be a first line choice for individuals with mild depression [8].

Given the length of this CPG it is likely that a typical reader—a busy clinician—will focus reading on the Executive Summary, which by itself does not provide sufficient guidance or acknowledge existing uncertainty and controversy in the field. On the other hand, a clinician seeking to understand the Executive Summary by reference to the text will find differing recommendations in the various sections. Indeed, like the parable of the blind men and the elephant, readers of this guideline will receive different guidance based on what part they read.

It is also noteworthy that in the case of this CPG, every APA work group member reported commercial ties to the companies that manufacture the medications recommended in the guideline, and the majority (4/6), including the chair, serve on speakers bureaus or advisory boards [1, pp. 2-3]. Financial conflicts of interest have been a problem for many CPGs, and the APA attempted to mitigate any biasing effect by adding a review panel that would evaluate the guidelines for possible industry influence (they concluded there was none). Given the primacy of pharmacotherapy, specifically newer, branded medications, these financial associations raise questions about the objectivity and integrity of the guideline because they give the appearance of undue industry influence. In fact, the IOM's most recent report states clearly that individuals with financial relationships with industry should be prohibited from participating on guideline development committees [9].

The APA leadership noted that the goal of these guidelines was to provide a "full range of treatment options" [10]. This is a laudable and important goal and certainly many patients benefit from pharmacotherapy. However, we believe that the usefulness of this practice guideline could be enhanced by linking levels of recommendations with levels of evidence; by including a decision tree or algorithm; and by addressing more fully the controversies that exist regarding the risk, benefits, and alternatives to psychotropic medications. Additionally, and in keeping with recent guideline development standards such as those identified in the IOM report, future guidelines produced by the APA should be authored by a multidisciplinary team of experts who do not have industry ties [see also, 11].

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Table Heading

Table 1. Examples of Inconsistencies among Sections and Implications for Treatment.