With only a few approved treatments currently being available, the treatment of bipolar depression is a major challenge for frontline clinicians. The ongoing debate about the off-label use of antidepressants focuses on their efficacy and the risk of a switch into mania. Usually, empirical reports involve groups of patients; the individual patient perspective is overlooked. To fill this gap, in this paper we advocate a practical, patient-oriented approach to mania.

**GAP BETWEEN GUIDELINES AND CLINICAL PRACTICE**

Multiple studies have shown that the majority of bipolar patients are routinely treated with antidepressants for their depression. Previous authors have speculated on the considerations in the consultation rooms that encourage or warrant the use of selective serotonin reuptake inhibitors (SSRIs). The severity of bipolar depression and the estimated suicide rate of 15%-20% prompt clinicians to suggest SSRI treatment. For many patients, the side-effect profile of dopamine-serotonin receptor antagonists and the need for regular laboratory monitoring for mood stabilizers are relevant considerations. The extrapolation of antidepressant efficacy in unipolar depression may be another contributing factor.

In the past few decades, guidelines have been reluctant to endorse antidepressants as a treatment option for bipolar depression. Also, recent guidelines do not recommend tricylic antidepressants (TCA) or SSRI monotherapy but they do propose the combination of an SSRI with lithium/valproate/olanzapine as a first-line choice amongst other options such as lithium, lamotrigine, and quetiapine. Still, antidepressants have proven modestly efficacious, comparable to other treatments (number needed to treat = 5.75). A recent meta-analysis also showed that SSRI addition to lithium is superior over placebo in short-term regimes. The hesitation to award antidepressants a more prominent role in the guidelines stems from the notion that they may induce (hypo)mania, particularly TCAs and venlafaxine. The risk of SSRIs triggering (hypo)mania is considered to be much lower, however, especially when they are combined with mood stabilizers. Moreover, it is by no means certain that the mania switches are caused by the antidepressants. Previous research showed that, rather than being medication-related, the switch process in bipolar disorder may be an artefact of the depressive episodes lasting less long with resulting relapses into mania. Nevertheless, reviews and guidelines repeatedly warn against this effect, likely prompted by the ethical imperative to “first do no harm”. Experts have particularly discouraged long-term regimens because of the potentially adverse effect on disease progression, including manic switches or the induction of a rapid cycling pattern.

**NOT ALL (HYPO)MANIAS ARE HARMFUL**

We propose an alternative explanation for the widespread use of antidepressants in bipolar disorder. First, as a result of the present shared decision-making paradigm, personal considerations and subjective balancing of risks have become a focus of attention. It is possible that the clinician and/or the patient do not judge the risk of manic switches to be a relevant consideration in their specific situation. As mentioned above, for most bipolar patients the prevention of depressive episodes has high priority. Although the potential harm of mania is indisputable, it has been shown that patients judge the burden of the depression to be significantly higher than the burden of the manic episodes, while for most the depressive episodes last substantially longer. Therefore, we can assume that the severity of depression is weighted differently in relation to the risk of mania, in the final treatment decisions patients and clinicians make.
Secondly, many patients do not consider a beginning (hypo)mania to be a true burden or a serious threat of harm. They rather worry about persistent euphoria, impulsivity and disinhibition, which can lead to embarrassing situations and stigmatization. In particular, patients with a history of manias may develop considerable expertise in their “personal type of mania” and make use of a crisis plan or advance directives. This implies that these experienced patients, family members and significant others are (often, but unfortunately not always) able to identify the onset of a mania and can (help) take timely precautions, preventing harmful situations from arising.

Thirdly, some subgroups of patients even welcome (hypo)manic symptoms to a point where they are prepared to pay the price of post-manic depression. In our capacity as clinicians, we may be biased as to the harm manias can cause. We need to keep in mind that it is rare that we see outpatients with sleepless nights who are brimming with creativity and productivity waiting in our consultation rooms.

Fourthly, all patients, like all other people, have the right to make risky choices in their lives. As clinicians are trained to avoid harm, a manic conversion could easily be viewed as a “treatment failure” that should be avoided at all costs. However, referring to the concept of “dignity of risk”, patients have the right to failure as well. Still, it is imperative that the full range of consequences of mania is discussed with the patients. Subsequently, it remains the responsibility (both clinically and medico-legally) of clinicians, having broader experience in all manifestations of mania, to address all possible risks in the decision-making process.

Finally, it is important to acknowledge that patients and those close to them tend to change their treatment priorities as the disorder progresses. In the early stages, these priorities often closely follow current guidelines validating symptom control, where it is only in the later stages that the focus needs to be shifted towards the “perceptions of reality and the possibilities remaining for the patient”.

In view of the above deliberations, we posit that in many cases patients tend to value the risk of a manic switch differently than clinicians do. Given that patients have their personal perspective on the actual harm their (hypo)manias can cause, “first do no harm” to them means preventing or effectively treating their depression at all costs.

Should the practice of prescribing antidepressants to depressed bipolar patients be considered “bad medicine”, then? We say it should not. If patient-focused, the prescription of these drugs rather reflects targeted and adequate evidence-based medicine (EBM) integrating scientific evidence and clinical judgement within the context of patient values and preferences, which is fully in accordance with what SACKETT with 2 t’s and colleagues posited: “Without clinical expertise, practice risks becoming tyrannised by evidence, for even excellent external evidence may be inapplicable to or inappropriate for an individual patient.” In bipolar depression, the efficacy and tolerability of treatments differ widely at the individual level, as do the risks of undertreatment and the impact of a mania switch.

HOW HARMFUL IS MANIC EPISODE?

To determine how harmful mania is to a patient or his/her environment, we should look at its daily-life impact. Does it cause embarrassment, stigma or exclusion? What does it do to the patient’s self-esteem? Is the patient able to balance the severity of depression with the risk of mania? Is the mania insuperable? What are the psychological and psychosocial effects of mania for those close to him/her and the wider community? We call for clinician-researchers to look into these questions to ultimately provide clinicians with a practical framework for the assessment of individual patient burden and workable treatment guidelines. Although the harmfulness of mania is undoubtedly correlated with symptom severity and the absence of recovery, it is a different concept and does not necessarily foster patient-centred care. While remission may result in relevant long-term outcomes such as lasting relationships and employment, we would like to underscore that mania may not necessarily be harmful and need not always be avoided. Instead, we should consider its short-term intra-psychological and social effects and meaningfulness for the individual patient and thus rely more on his or her judgement.

As clinicians, we should not base our choice of whether and how to treat bipolar depression on scientific evidence alone. Treatment guidelines, by nature, do not apply to each and every patient. The risk of a manic switch, triggered by the use of antidepressants or not, should be determined on an individual basis. In times of shared decision making, the inevitable question should be: “How harmful is your mania to you and to others?”

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*It has not escaped our notice that this line of reasoning is also applicable to other relapsing disorders in psychiatry that also have a substantial psychosocial burden.