We reply to the Ioannidis's paper "Effectiveness of antidepressants; an evidence based myth constructed from a thousand controlled trials." We disagree that antidepressants have no greater efficacy than placebo. We present the efficacy from hundreds of trials in terms of the percentage of patients with a substantial clinical response (a 50% improvement or more symptomatic reduction). This meta-analysis finds that 42-70% of depressed patients improve with drug and 21%-39% improve with placebo. The response benefit of antidepressant treatment is 33%-11% greater than placebo. Ioannidis argues that it would be vanishingly smaller because systematic biasing in these clinical trials would reduce the drug-placebo difference to zero. Ioannidis' argument that antidepressants have no benefit is eroded by his failures of logic because he does not present any evidence that there are a large number of studies where placebo is substantially more effective than drug. (To reduce to zero, one would also have to show that some of the unpublished studies find placebo better than drug and have substantial systematic or methodological bias). We also present the empirical evidence showing that these methodological concerns generally have the opposite effect of what Ioannidis argues, supporting our contention that the measured efficacy of antidepressants likely underestimates true efficacy. Our most important criticism is Ioannidis'
basic underlying argument about antidepressants that if the existing evidence is imperfect and methods can be criticized, then this proves that antidepressant are not efficacious. He presents no credible evidence that antidepressants have zero effect size. Valid arguments can point out difficulties with the data but do not prove that a given drug had no efficacy. Indeed better evidence might prove it was more efficacious that originally found. We find no empirical or ethical reason why psychiatrists should not try to help depressed patients with drugs and/or with psychotherapeutic/behavioral treatments given evidence of efficacy even though our treatment knowledge has limitations. The immense suffering of patients with major depression leads to ethical, moral, professional and legal obligations to treat patients with the best available tools at our disposal, while diligently and actively monitoring for adverse effects and actively revising treatment components as necessary.

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