The Journal of Mind and Behavior
Winter and Spring 2010, Volume 31, Numbers 1 and 2
Pages 23–36
ISSN 0271–0137

The Make-Believe World of Antidepressant Randomized Controlled Trials — An Afterword to Cohen and Jacobs (2010)

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This afterword extends and refines the arguments presented in Cohen and Jacobs (2010). The main point made by the authors is that the antidepressant randomized controlled trial world is a make-believe world in which researchers act as if a bona fide medical experiment is being conducted. From the assumed existence of the "disorder" and the assumed homogeneity of the treatment groups, through the validity of rating scales and the meaning of their scores, to the presentations of researchers' ratings as the genuine outcome of interest — all aspects of such trials are make-believe. The continued acceptance of randomized controlled trials as appropriate mechanisms to ascertain the actual effects of psychoactive drugs on human beings in distress confirms that researchers are inextricably dependent on large-scale organizational and financial interests that require the sustained production of make-believe results about psychoactive drugs.

We were invited in 2005 by the journal *Debates in Neuroscience* to take the con side in a debate on whether the safety and efficacy of antidepressant drug treatment for "Major Depressive Disorder" had been exaggerated in the professional literature. For reasons unknown to us, the pro side of the question did not materialize, and although *Debates in Neuroscience* published our article (Cohen and Jacobs, 2007) the journal discontinued publication after its second issue. Three years after the original publication, the Editor of *The Journal of Mind and Behavior* offered us the unusual opportunity to republish our article in this journal (Cohen and Jacobs, 2010) and to reflect on and refine our remarks in this Afterword.

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Our main point is this: the antidepressant randomized controlled trial world is a make-believe world in which the researchers act as if a bona fide medical experiment is being conducted. We expand on this statement below.

The "Same" Disorder Is Not "the Same"

The logic of a randomized controlled trial depends on homogeneity of the disorder, without which it makes no sense to randomly assign subjects to treatment arms and to adopt a standardized rating scale for the purpose of assessing the outcome of treatment. Although randomization provides researchers the best chance to even out unknown individual differences between treatment groups, these unknown differences pertain to everything else *but* the disorder of interest. If participants in the trial do not have the same disorder, then the results of the trial apply only to the groups at hand, and there is no rational means to apply the results of the experiment to any one else. However, in a medical experiment in which it can be physically ascertained that every participant has the same disease, the results can be applied to individuals in clinical practice because *this* individual in clinical practice can be identified as having the same disease. Without disease homogeneity, results of a randomized controlled trial of a medical treatment indicating that one group had significantly better scores than another group on some outcome give clinicians no basis to apply the results to any individual because clinicians treat individuals one at a time, not groups.

The "Limitations of the Categorical Approach" section of the *Diagnostic and Statistical Manual of Mental Disorders, fourth edition, text revision* (DSM-IV-TR, American Psychiatric Association, 2000, pp. xxxi–xxxii) candidly admits that individuals diagnosed with "the same" *DSM* disorder should not be assumed to be the same "in all important respects" (p. xxxi) — a contradiction in terms. Moreover, reading any differential diagnosis section for any primary mental disorder in the *DSM* shows that there exists no evidentiary basis for deciding in favor of one diagnosis over another (the diagnostician is simply referred back to the internal rules and criteria of the diagnoses themselves). Since diagnosis is established exclusively by interpreting what a person says and does, there can be no single "definitive" interpretation (see Jacobs, 2009).

Without disease homogeneity, a drug treatment randomized controlled trial might still hold clinical value if the scores of the drug group did not substantially overlap with those of the placebo group and if the adverse effects of drugs were insignificant — decidedly not the case for psychiatric drug treatment. For example, researchers could arrange for independent clinicians (i.e., who had *not* been administering the investigational drug throughout the course of the experiment and asking about its side effects and adjusting dosages) to evaluate

subjects blindly at the end of treatment on the basis of "Major Depressive Disorder present" or "not present." Impressive end-of-treatment results obtained with this method could suggest that the treatment drug actually has antidepressant properties. To our knowledge, however, such end-of-treatment evaluations are neither undertaken nor published. Indeed, it is precisely because the benefit of psychiatric drug treatment is so difficult to demonstrate unambiguously that researcher-scored rating scales became a critical component of psychiatric drug treatment clinical trials (Healy, 2009).

The Desired Outcome Dictates Research Strategy

Let us try to follow the reasoning presented in a 1989 book chapter by Wetzler and van Praag (published by the American Psychiatric Association's [APA] own publishing company) concerning the assessment of depression as a diagnostic category and as a generic dimension of psychopathology. The authors begin by conceding that it is "a gross oversimplification to think that behavioral disorders actually exist in clearly separable categories" (p. 71). They also remind the reader that since a psychiatric diagnosis is a professional activity of clinicians, then "by definition a clinician's diagnosis is the gold standard and all other assessment methods and vantage points must be evaluated against this criterion" (p. 73). After pointing out that the Hamilton Depression Rating Scale is overly sensitive to many facets of psychopathology that are not specifically depressive, Wetzler and van Praag recommend the use of a researcher scored rating scale derived from the Hamilton Depression Rating Scale, the Montgomery–Asberg Depression Rating Scale. They specifically consider and reject self-report scales *because* these do not correlate well with researcher scored scales.

The subject's own assessment of her depression is indeed another vantage point on depression. Lasalvia, Rugerri, and Santolini (2002) confirm that researcher-scored scales of distress tend to correlate poorly with self-report scales, but these authors add that self-report scales correlate well with subjective quality of life scales. It has been variously noted that antidepressant drug treatment studies regard researcher scored scales as the primary outcome data and that studies routinely decline to use, or to report the scores of, quality of life scales (Garattini and Bertele, 2008; Hotopf, Lewis, and Normand, 1997; Ioannidis, 2008; Rief, Nestoriuc, Weiss, Welzel, Barsky, and Hoffman, 2009). As intimated above, it is unlikely that researchers in drug treatment studies who do the scoring are actually blind as to which subjects were treated with the experimental drug and which were treated with placebo. This is more than a stubborn methodological blind spot in antidepressant randomized controlled trials, since as we pointed out in our paper (Cohen and Jacobs, 2010, this issue) commercial interests now dominate the research enterprise. To further place this (bias) in perspective, negative

results are less likely to be published and can even be "spun" in published form as positive results (Jureidini, McHenry, and Mansfield, 2008; Turner, Matthews, Linardatos, Tell, and Rosenthal, 2008).

Wetzler and van Praag (1989) seem to view depression as an independent dimension of (their word) psychopathology that can be identified via psychometric methods. A valid measure of this dimension is needed if numbers are to be generated in order to show whether and to what extent a treatment drug actually has antidepressant properties. A dimensional approach avoids the issue of whether subjects in a randomized controlled trial really have the categorical disorder/specific clinical entity Major Depressive Disorder. That issue is reformulated into each subject's score on the dimension of depression. The practical question for researchers concerned with the quantitative measurement of depression is what items should appear on a rating scale of depression. Wetzler and van Praag admit that a specific, independent "dimension of depression" is a psychometric feat, not a fact of nature, because ". . . psychopathology rarely exists in these pure dimensional forms. Rather, all dimensions of psychopathology are intermingled and must therefore be disentangled by the scientist" (p. 79). A simpler way of saying this is that a person's feeling state may be so complex that describing it in words can be quite challenging. Few descriptions could be considered definitive.

Wetzler and van Praag began their chapter by admitting to the "gross oversimplification" of thinking that behavioral disorders exist in separable categories. By dint of their own reasoning and review of evidence, they asserted that all dimensions of psychopathogy are intermingled in vivo and must be disentangled psychometrically (if possible). If so, then why is it desirable to assess how subjects in a clinical trial are faring at study's end exclusively on the dimension of depression, and why should quality of life outcome measures be routinely avoided in reporting the results? If "psychopathology rarely exists . . . in pure dimensional forms," then a reason why Wetzler and van Praag reject self-report scales of depression — that they correlate highly with self report scales of anxiety, suggesting that what is actually being measured is dysphoria or generalized distress (p. 81) — seems profoundly misguided. What also seems misguided, as Wetzler and van Praag admit without seeming to realize its import, is the very idea that specific, independent dimensions of psychopathology are ontologically real and therefore can and should be measured.

Drugs are approved by the Food and Drug Administration (FDA) for the treatment of a specific medical condition, and the American Psychiatric Association identifies specific conditions in the "medical" specialty of psychiatry. Although the FDA obligingly overlooks that *DSM* primary mental disorders are identified and diagnosed with no reference whatsoever to biological findings, there must be nonetheless some kind of demonstration that a drug proposed for the treatment of such a condition is both safe and effective in order for the FDA to approve its marketing (i.e., its sale to patients through the intermediate

step of physician prescription). It would seem therefore that psychiatry has little choice but to identify discrete, autonomous disorders if it is to be regarded as a medical specialty by the FDA and if it is to be supported by the pharmaceutical industry.

This brings us back to the issue of demonstrating efficacy or benefit from the drug treatment in a randomized controlled trial. Independent clinical evaluation at study's end on whether the condition is present or not in the participants is useless to the sponsor because the drugs are not efficacious enough to demonstrate an advantage over placebo on the basis of such a "hard" outcome. Enter researcher-scored rating scales. But let us keep in mind that the stratagem requires the pretence that discrete, autonomous primary mental disorders actually exist, the pretence that independent dimensions of psychopathology exist and can be measured by a rating scale, and the pretence that at the end of treatment what anyone who is really interested in the clinical status of the people in the drug treatment trial want to know is confined to their scores on a rating scale of the "independent dimension of depression" filled out by the nominally blinded *researchers*.

The logic here is that if self-report scales correlate poorly with researcher scored scales there is clearly no use for them. If subjective quality of life scales fail to demonstrate any benefit of drug treatment over placebo treatment there is clearly no use for them as well. In sum, whether and to what extent the subject is depressed is considered a *professional* matter. All of this raises the question of whether the dominant, ubiquitous researcher-scored scales of the "dimension" of depression should simply be considered a misleading surrogate clinical measure (Fairclough, 2004; Fleming and DeMets, 1996; Garattini and Bertele, 2008).

Voiceless in the Medical Setting

The disparity that often exists between researcher ratings and patient ratings of patient depression at the end of an antidepressant trial might be viewed as a serious concern for researchers interested in the validity and clinical usefulness of antidepressant randomized controlled trials. This is not the case. How could researchers fail to consider this a serious matter? At the least, how could researchers justify presenting researcher scored ratings of depression as *the* findings of interest and importance when the disparity between researchers' and subjects' ratings is known to exist? It would be as if we had published something about how you felt (something that you disagreed with), without mentioning that you disagreed. You might feel you had grounds for a grievance.

The issue goes to how psychiatrists conceptualize "depression." Although depression is a common word in the vernacular, for psychiatrists Major Depressive Disorder is a professional–technical term that refers to a psychiatric illness or mental disorder that is identified by professionals, as Wetzler and van Pragg unabashedly

assert (1989, p. 73). From the psychiatric perspective, then, the victim or host of the disorder is no more in a position to authoritatively pass judgment than is the case whenever a physician examines a patient and decides on a diagnosis. Although the *only* way the psychiatrist can identify the presence of Major Depressive Disorder is through conversation–social interaction with the patient, who has what might be considered a privileged view of her own feelings, what is being identified as far as the psychiatrist is concerned is the presence of an impersonal disorder, an "it." If so, the patient's view of the matter — beyond simply recounting "symptoms" — is of little consequence and cannot compete with the researcher's view. Similar reasoning presumably applies to self-report rating scales of depression at the conclusion of an antidepressant randomized controlled trial. It is the medical framework itself that so disqualifies the participant.

The Science of Synonyms

Given Wetzler and van Praag's assertion that Major Depressive Disorder is a clinical entity to be identified by the physician (1989, p. 73), it is somewhat amusing to observe that the essential item defining depression (as entity or dimension) is the presence of depressed mood. Any attempt to clarify the definition of depressed mood resorts to the use of synonyms. For some reason neither the *DSM* nor rating scales use the most direct words to refer to what psychiatrists actually mean by depressed mood, namely *melancholy* or *depressed spirits*. The definition cannot get more exact because one is fully in the realm of metaphors and figures of speech. A mood only refers to what the speaker intends it to mean; there is no way to make "mood" more precise (look it up in the dictionary if you are in the mood). Outside of the taken-for-granted convictions of psychiatry, it does seem odd to think of depressed spirits or feeling blue or down in the dumps as something like an irregular heart beat that only a trained cardiologist can detect with a stethoscope or an exotic rash that only an experienced dermatologist can identify correctly.

Obviously the psychiatrist must ascertain something more than "this person feels depressed." The psychiatrist must also ascertain that *psychopathology* is present. This is the distinguishing professional evaluation, since no one has to study psychiatry, psychology, social work, or counseling to know that everyone feels depressed at some point. For psychopathology (mental disorder) to be present, the person must not merely be depressed, he must be suffering from a depressive disorder.

The difference between feeling depressed and suffering from a depressive disorder must be a real difference if professional evaluation is to have a substantive meaning and to be considered part of science or medicine rather than something like asking the barber if you need a shave. There is by definition (of a *DSM* primary mental disorder) nothing biological to show for this purpose

(*DSM-IV-TR*, p. 181). What is required is something objective that discriminates between depression and "clinical" depression, between no mental disorder and mental disorder.

We have pondered this matter for some time (Jacobs and Cohen, 2003, in press). The *DSM* definition of mental disorder has remained basically unaltered since the publication of *DSM-III* in 1980, and the proposed new definition of mental disorder in *DSM-V*, slated for publication in 2013, is virtually identical (American Psychiatric Association, 2010). It is fair to conclude that the American Psychiatric Association considers mental disorder indefinable except in a vacuous and circular manner. The *DSM-IV-TR* admits that the distinction between no disorder and disorder is "inherently difficult" (p. 8) and leaves it at that except to advise seeking information from others about "role performance," since that may be difficult to glean in an interview. But disappointing role performance still does not indicate whether mental disorder is or is not present because there can be many reasons for disappointing role performance. The segue into what constitutes mental disorder is important for this discussion because without a real basis for the clinician to decide that mental disorder is present, it is hard to see how downplaying or ignoring the study participants' own evaluation of their depression at the conclusion of drug treatment can be justified.

The Inscrutable Meaning of Mental Disorder

After the introductory sections of the *DSM-IV-TR*, in the manual proper, the issue of how to distinguish mental disorder present from not present turns on the question of severity of distress or the presence of "clinically significant" deviation from usual and expected behavior rather than whether distress or problematic behavior can be connected to adversity. This is both a fundamental shift in meaning and at the same time allows the clinician the prerogative to make the diagnosis mental disorder present on the basis of something that is indefinable (clinical significance). The working section of the manual (under "Adjustment Disorders," p. 679) even repudiates the caveat that distress or problematic behavior should not be considered a mental disorder if intelligibly connected to adversity: ". . . a reaction to a stressor that might be considered normal and expectable can still qualify for a diagnosis of Adjustment Disorder if the reaction is sufficiently severe to cause significant impairment [in social or occupational functioning]."

In other words, if adversity of any kind or severity impairs a person's social or occupational functioning in a significant (indefinable) manner, the clinician may diagnose mental disorder (only bereavement excuses the diagnosis of Major Depressive Disorder). The clinician is at liberty to diagnose mental disorder present if a person seems clinically (indefinable) distressed or socially impaired for any reason — but the clinician need not even dismiss comprehen-

sible reasons for depression because the manual also grants the clinician liberty to ignore Axis IV (Psychosocial and Environmental Problems) if she "does not wish to" consider it (*DSM-IV-TR*, 2000, p. 37).

In sum, the meaning of mental disorder in the working part of the *DSM* reveals itself as no more than an opinion on the part of a clinician. No pretence remains that mental disorder is an objective scientific–technical term. In a paper prepared for the *Journal of the American Academy of Psychiatry and the Law*, the Chairperson of the *DSM-IV* Task Force, Allen Frances, readily admitted that the clinician's liberty to diagnose mental disorder based on personal judgment regarding clinical significance means that a clinician's "finding" of mental disorder should not be confused with a finding of fact (Frances, Sreenivasan, and Weinberger, 2008, p. 380).

The Medical Framework Is the Wrong Approach

A telling indication that the wrong approach to a problem has been adopted is the persistence over time of insoluble conceptual and methodological issues. For example, 26 years ago Prien and Levine (1984) identified three troubling issues in evaluating the therapeutic effectiveness of antidepressant drugs: 1) what rating scale should be used to measure depression, 2) how much numerical change on the rating scale from start to end of treatment should be taken to indicate clinically meaningful improvement or recovery, and 3) how to assess and report on the full range and incidence of adverse reactions and medical complications. Anyone conversant with the relevant literature knows that the identical paper could be published today. Bagby, Andrew, Schuller, and Marshall (2004) evaluated the validity of the Hamilton Depression Rating Scale and recommended its retirement on the already well-known basis that "many individual items are poorly designed and sum to generate a total score whose meaning is multidimensional and unclear" (p. 2173). They declined to discuss why use of the Hamilton scale as the outcome instrument of first choice has withstood decades of criticism.

The basic problem is easy to see but it requires stepping outside of the disciplinary conventions and ambitions of both psychiatry and psychology. The problem could be formulated in this manner: it is one thing to think of the word depression as communication, quite another to think of depression as a substantive "it" whose meaning can be definitely pinned down and analyzed into components (the dubious contribution of psychiatry) and whose quantity can be measured (the dubious contribution of psychology).

The "need" for a rating scale cannot be divorced from the "need" to show on the basis of statistical analysis that the so-called antidepressant drug produces more positive change than placebo. If patients treated with antidepressants clearly were no longer depressed there would be no need to create a complex

rating scale that produced an uninterpretable total score for each patient that could be entered into a statistical analysis comparing the drug treated group to the placebo treated group. Again, readers should keep in mind, as we showed in our target article (Cohen and Jacobs, 2010), that *despite every advantage for the drug built into the design of antidepressant randomized controlled trials*, it still remains a challenge to generate publishable (i.e., positive) findings.

Since depression as a mood disorder or dimension to be rated on a scale is fundamentally defined as the presence of depressed mood, all additional items or considerations must be considered ancillary. Hamilton (1960) explicitly stated that a rating scale should not be used to diagnose "affective disorder of depressive type." This was because patients who were not diagnosed as suffering from this depressive disorder received high scores on the scale (including item 1, depressed mood). Hamilton did state that the rating scale was of great practical value in assessing results of treatment, but he did not elaborate.

Healy (2009) has revealed that the Hamilton Depression Rating Scale was actually created by Geigy Pharmaceuticals to use in clinical trials of imipramine. According to Healy, Hamilton's main argument for using the scale was that it facilitated the execution of clinical trials and showed that imipramine worked. Again, "worked" must be understood in a nuanced fashion since a straightforward assessment had to be avoided. Recently, much has been made of the "real world" outcomes of the state-of-the-art STAR*D depression drug treatment study sponsored by the National Institute of Mental Health, whose results began to appear late 2005. The large sequential study used the refreshing primary outcome of "remission" (whose common-sense definition is recovery from illness). Yet, remission was operationalized as a score of 5 or less on the researcher-rated Quick Inventory of Depressive Symptom rating scale. The results showed that over 90% of "remitted" patients in the study nonetheless manifested at least one "residual" symptom on the scale (median of three symptoms), usually sleep disturbance, appetite/weight disturbance, sad mood, fatigue or decreased energy, and decreased concentration (Nierenberg, Husain, Trivedi, Fava, Warden, Wisniewski, Miyahara, and Rush, 2009, pp. 3–4).

Under the heading "Factor Measurements," Hamilton (1960) briefly summarized several cases (all of hospitalized patients with serious depression, usually including suicide attempts — who are screened out of the randomized controlled trials of the newer antidepressants). Case 61 is a man described as suffering from moderate depression (severe enough to require hospitalization and electroshock, however) without feelings of guilt or suicidal ideas. Hamilton did not appear to notice the twofold problem that results from giving everyone scores on the same set of items and adding these scores to produce a total score: 1) the items on the scale are not equally relevant or even apply to everyone being rated, with the consequence that 2) people who receive the same total score numerically are not the same clinically (although the purpose of the rating

scale is clinical investigation). The deeper problem, as we have suggested, is the misguided idea that the use of the word "depression" to convey something can be decontextualized and analyzed into invariant components for a rating scale. Case 61 illustrates that it can make sense clinically to describe a person as depressed enough to need hospitalization and electroshock even though he does not feel guilty and is innocent of suicidal ideas. So much for decomposing depression into essential and invariant components. So much for deciding either in committee or through psychometric methods what depression really means.

Only the circumstances at hand and the communicative intent of the speaker make the use of a descriptive word apt. It is a basic mistake to think that a word such as depressed or guilty has an invariant meaning that can be pinned down apart from circumstances and intent. Unfortunately, looking at language as creative use in a specific situation is irrelevant to those who see psychiatry's professional task as using language to identify clinical entities that exist whether anyone uses words to identify them or not. But since depressed and similar words are context-dependent descriptive possibilities, it is futile to seek their real contextless, invariant meaning, or to suppose that their descriptive use can be validated biologically, or that some quantity exists to be measured. Psychiatry-as-medicine embraces this sort of category mistake (Ryle, 1949) as its raison d'être.

Since describing a person as depressed is in effect a claim to have selected an apt description given the circumstances at hand, omitting the details that justify the proffered description leaves the recipient of the claim in the dark as to its meaning and status (something like reporting that you have seen a good movie without providing any additional information). This would resemble reading a researcher's score on the Hamilton Depression Rating Scale without an account that justifies exactly why depressed is claimed. Hamilton depicts Case 61 as moderately depressed. He does not attempt to justify/explain his description of the patient as moderately depressed in any way, but he does further say that Case 61 had difficulty falling asleep and awoke early, showed moderate loss of interest, was psychically and somatically anxious, and had poor appetite and constipation. The additional information (equivalent to various items on the Hamilton Depression Rating Scale, for example) does not justify or explain referring to Case 61 as depressed.

It should now be fairly obvious that depressed mood can be applied to an indefinite range of cases: someone who feels discouraged, someone who is feeling despair, someone who feels threatened with an important loss, and so on. In each case, it will be more informative to specify what the depressed mood is about (e.g., Tom is worried sick that his wife may be having an affair). Otherwise, the erroneous idea could be formed that each case in the series is an instance of the same condition. A person in an angry mood may be red-faced and shouting

or cold and indifferent. The search for a definitive physiognomy is quixotic, a misunderstanding of how descriptive language is creatively used *in situ* to communicate something. In each instance in which a descriptor is proffered the person proffering must be prepared to defend it as the most apt under the circumstances. This can naturally lead to much haggling, which would look bad in the medical setting. "Tom is worried sick that his wife may be having an affair" does not sound quite as medical as "Major Depressive Disorder." But as the little-noted "Limitations of the Categorical Approach" section of the *DSM-IV-TR* admits, the cost of sounding medical (by describing scores of distinct mental disorders) is that individuals diagnosed with the same disorder may not really be the same. As soon as "about" or "because" are included in a narrative description of a person whose mood is said to be depressed, the illusion that different people suffer from "the same thing" clears away.

The persistent hope in American biological psychiatry (Carpenter, 2009; First, 2008) is that descriptive language (complaints from the patient and observations from the psychiatrist) will eventually serve the same role that it does in somatic medicine: verbal clues to narrow the search for definitive biological information on what *really* ails the patient (McHugh and Slavney, 1998). Given this foundational hope and belief, it does not appear to psychiatrists that the necessity to *clarify* depressed mood as "down in the dumps" is an indication that the interpretive, metaphorical, and figurative language we use to talk to each other about the human world is not a *precursor* to anything — because there is no more fundamental reality to discover if we are talking about the human world ("Tom is worried sick that his wife may be having an affair").

Contemporary American psychiatry is committed to the proposition that the subject matter of psychiatry is not the human world, it is biology and medicine. Given the complete absence of positive evidence on this score since the great leap forward in 1980 (the *DSM-III*), it is hard to see what circumstances will lead to the abandonment of that conviction.

The Big Picture: Scientism and Vested Interests

We may now make the statement at the beginning of this Afterword more precise. The world of antidepressant randomized controlled trials is a make believe world because: (a) the diagnosis is make believe (it does not refer to a specific clinical entity), (b) the discrimination between mental disorder present and not present is make believe, (c) the identification of necessary and invariant items for a rating scale to measure depression is make believe, (d) the main item on the rating scale — "depressed mood" — refers to an endless series of cases that are only superficially the same, (e) the quantification of severity for each item on the rating scale is make believe, (f) the total scale score as a measurement of something is make believe, (g) the presentation of the researcher's ratings

as the genuine outcome of interest is make believe, (h) the substitution of statistical significance for clinical significance is make believe, (i) the minimization of the drug's psychological and medical consequences is make believe, and (j) the suppression of negative findings is make believe.

Many legitimate positions exist on the issue of whether individuals attempting to cope with the challenges of life should use psychoactive drugs. On the issue of deception, however, we believe that a single legitimate position exists: exposure and debunking. Each of the points cited in the preceding paragraph has been recognized as such, or at least as quite problematic, by one or another author in the professional literature. Yet, as far as we know, no American psychiatric journal and few psychology journals could publish the conclusion that the medical randomized controlled trial framework cannot be realistically applied to ascertain how psychiatric drugs affect troubled, distressed, or misbehaving people. If this is correct, then science and marketing in the field of psychopharmacology trials have blurred so thoroughly that many researchers in this field must be considered as de facto agents of the large-scale organizational, political, and financial interests that require the sustained production and dissemination of make-believe results about psychoactive medications.

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