6. Hugdahl K: The three-systems-model of fear and emotion: a critical examination. Behav Res Ther 1981; 19:75–85
7. Zinbarg RE: Concordance and synchrony in measures of anxiety and panic reconsidered: a hierarchical model of anxiety and panic. Behav Ther 1998; 29:301–323
8. Grey S, Sartory G, Rachman S: Synchronous and desynchronous changes during fear reduction. Behav Res Ther 1979; 17:137–147
9. Hodgson R, Rachman S: II. Desynchrony in measures of fear. Behav Res Ther 1974; 12:319–326
10. Koizumi A, Amano K, Cortese A, et al: Fear reduction without fear through reinforcement of neural activity that bypasses conscious exposure (letter). Nat Hum Behav 2016; 1:0006
11. Griebel G, Holmes A: 50 years of hurdles and hope in anxiolytic drug discovery. Nat Rev Drug Discov 2013; 12:667–687
12. Miller G: Is pharma running out of brainy ideas? Science 2010; 329: 502–504
13. Ericcson KA, Simon H: Protocol Analysis: Verbal Reports as Data. Cambridge, Mass, MIT Press, 1993
14. Wilson TD: The proper protocol: validity and completeness of verbal reports. Psychol Sci 1994; 5:249–252
15. Shechner T, Britton JC, Ronkin EG, et al: Fear conditioning and extinction in anxious and nonanxious youth and adults: examining a novel developmentally appropriate fear-conditioning task. Depress Anxiety 2015; 32:277–288
16. Dehaene S: Consciousness and the Brain: Deciphering How the Brain Codes Our Thoughts. New York, Penguin, 2014
17. Lau H, Rosenthal D: Empirical support for higher-order theories of conscious awareness. Trends Cogn Sci 2011; 15:365–373
18. Overgaard M, Sandberg K: Kinds of access: different methods for report reveal different kinds of metacognitive access, in The Cognitive Neuroscience of Metacognition. Edited by Fleming SM, Frith CD. Berlin; Heidelberg, Germany, Springer-Verlag, 2014, pp 67–86
19. Maniscalco B, Lau H: The signal processing architecture underlying subjective reports of sensory awareness. Neurosci Conscious 2016; 1: niw002
20. LeDoux JE, Brown R: A higher-order theory of emotional consciousness. Proc Natl Acad Sci USA 2017; 114:E2016–E2025
21. Zoellner LA, Foa EB: Applying Research Domain Criteria (RDoC) to the study of fear and anxiety: a critical comment. Psychophysiology 2016; 53:332–335

**Daniel S. Pine, M.D.**
**Joseph E. LeDoux, Ph.D.**

*From the Section on Development and Affective Neuroscience, NIMH Intramural Research Program, Bethesda, Md.; the Center for Neural Science, the Department of Psychology, the Department of Psychiatry, and the Department of Child and Adolescent Psychiatry, New York University, New York; and the Nathan Kline Institute, Orangeburg, N.Y.*

*Address correspondence to Dr. LeDoux (ledoux@cns.nyu.edu).*

*The authors' disclosures accompany the original article.*

*This reply was accepted for publication in August 2017.*

*Am J Psychiatry 2017; 174:1121–1122; doi: 10.1176/appi.ajp.2017.17070818r*

## Equivalence of Psychodynamic Therapy to Other Established Treatments: Limited Supporting Evidence and Clinical Relevance

TO THE EDITOR: Steinert and colleagues' meta-analysis (1), published in the October 2017 issue of the *Journal*, concludes that psychodynamic therapy is equivalent to established treatments. However, several shortcomings hamper the validity of this claim. The meta-analysis includes various mental conditions, and the primary efficacy outcome, "target symptoms," combines widely divergent measures of depression, social anxiety, posttraumatic stress disorder, suicidality, drug addiction, eating disorders, and even body mass index. This highly heterogeneous mix confounds the clinical relevance of the findings. Clinical significance is further stymied by lumping together diverse comparators, including medication. Even when the comparator is cognitive-behavioral therapy (CBT), its nature varies greatly among disorders.

Furthermore, defining equivalence margins is challenging, as presumably the clinically meaningful minimum difference varies depending on outcomes. Because equivalence testing is generally particularly prone to bias (2), this difference must be prespecified. The authors' PROSPERO registration does not describe it, and equivalence is not mentioned. Because the article was funded by a professional psychoanalysis association, with arguably vested interests, accurate outcome prespecification is especially crucial. The authors preferentially use intention-to-treat data, which are unsuitable for equivalence claims because they may artificially dilute treatment differences (2). Finally, equivalence is clinically meaningful only if the control intervention has demonstrated efficacy for the condition studied. For example, psychodynamic therapy is claimed as effective as CBT for eating disorders or addiction, but in included landmark trials on anorexia (3) or cocaine dependence (4), neither intervention proved superior to treatment as usual on the predefined primary outcomes, violating the key assumption of assay sensitivity (2) and perhaps justifying their more accurate characterization as "equally ineffective." Conversely, there is a risk of confounding of observed meaningful effects, such as in bulimia nervosa, where an equivalence verdict directly contradicts the largest trial demonstrating superiority of the comparison treatment, CBT (5). Consequently, while psychodynamic therapy may be as effective as CBT for some mental disorders, this meta-analysis offers limited supporting evidence.

### REFERENCES

1. Steinert C, Munder T, Rabung S, et al: Psychodynamic therapy: as efficacious as other empirically supported treatments? A meta-analysis testing equivalence of outcomes. Am J Psychiatry 2017; 174:943–953
2. Treadwell JR, Uhl S, Tipton K, et al: Assessing equivalence and noninferiority. J Clin Epidemiol 2012; 65:1144–1149
3. Zipfel S, Wild B, Groß G, et al: Focal psychodynamic therapy, cognitive behaviour therapy, and optimised treatment as usual in outpatients with anorexia nervosa (ANTOP study): randomised controlled trial. Lancet 2014; 383:127–137
4. Crits-Christoph P, Siqueland L, Blaine J, et al: Psychosocial treatments for cocaine dependence: National Institute on Drug Abuse Collaborative Cocaine Treatment Study. Arch Gen Psychiatry 1999; 56:493–502
5. Poulsen S, Lunn S, Daniel SI, et al: A randomized controlled trial of psychoanalytic psychotherapy or cognitive-behavioral therapy for bulimia nervosa. Am J Psychiatry 2014; 171:109–116

**Ioana A. Cristea, Ph.D.**
**Pim Cuijpers, Ph.D.**
**Florian Naudet, M.D., Ph.D.**

From the Meta-Research Innovation Center at Stanford (METRICS), Stanford University, Palo Alto, Calif.; the Department of Clinical Psychology and Psychotherapy, Babeş-Bolyai University, Cluj-Napoca, Romania; and the Department of Clinical, Neuro, and Developmental Psychology, Vrije Universiteit Amsterdam, the Netherlands.

Address correspondence to Dr. Cristea (ioana.cristea@ubbcluj.ro).

Dr. Cristea is supported by the Laura and John Arnold Foundation and the Romanian National Authority for Scientific Research and Innovation, CNCS–UEFISCDI, project number PN-II-RU-TE-2014-4-1316 (awarded to Dr. Cristea). Dr. Naudet is supported by the Laura and John Arnold Foundation, Fondation Pierre Deniker, and Rennes University Hospital (CORECT: Comité de la Recherche Clinique et Translationnelle). No funding organization had any role in the preparation of the manuscript or the decision to submit.

Dr. Naudet has received travel funding from Bristol-Myers Squibb, Janssen, Lundbeck, and Servier. Dr. Cuijpers receives expense allowances for membership on the board of directors of the Dutch Foundation for Mental Health (Fonds Psychische Gezondheid) and on a national telephone helpline (Korrelatie) and for serving as chair of the science committee of the Council for Care and Research (RZO) of the Dutch Ministry of Defense. Dr. Cristea reports no financial relationships with commercial interests.

This letter was accepted for publication in August 2017.

Am J Psychiatry 2017; 174:1122–1123; doi: 10.1176/appi.ajp.2017.17050592

## Different Standards When Assessing the Evidence for Psychodynamic Therapy? Response to Cristea et al.

TO THE EDITOR: Cristea and colleagues raise some concerns about our meta-analysis on psychodynamic therapy compared with treatments established in efficacy (1). Their concerns regard our definition of outcomes and comparators, specific methodological issues, and an alleged allegiance bias.

1. We decided to use "target symptoms" as the primary outcome because it is a disorder-specific and useful measure assessing change in the main problem area a patient presents with (e.g., depressive symptoms in major depression, weight gain in anorexia nervosa, suicidality in borderline personality disorder). This taps the symptoms most relevant to the disorder. By using "target symptoms," a strict test for psychodynamic therapy is implied because other therapies such as cognitive-behavioral therapy (CBT) focus explicitly on target symptoms. In addition, we assessed "general psychopathology" and "psychosocial functioning" as secondary outcomes, with all analyses reaching the same conclusion. In fact, combining all outcome measures assessed, as done, for example, by Wampold and colleagues (2), reaches an effect where the value of g is −0.12 and the equivalence confidence interval is −0.20 to −0.05, thus again confirming our original finding. In addition, the type of diagnosis was not found to be a significant moderator of outcome, suggesting no differences across disorders.
2. Lumping together different forms of comparison treatments is a well-established approach in meta-analysis. For example, testing against "treatment as usual" can consist of vastly different types of treatments. Cristea and colleagues themselves regularly use such an approach, for example, in their recent meta-analysis on borderline personality disorders: "Given the diversity and complexity of therapy orientations, we used an inclusive approach in delineating the psychotherapy and control conditions.… No constraints were placed on the control group, which could include (but was not restricted to) treatment as usual or other treatments not specifically developed for [borderline personality disorder]" (3, p. 320). In contrast, we included only comparison treatments with established efficacy, making this a much more homogeneous comparator despite variations in the CBT conditions. Between-study heterogeneity also was very low.
3. For their critique on equivalence testing, Cristea et al. cite an article by Treadwell and colleagues (4). However, Cristea and colleagues seem to have misunderstood what this article is about (i.e., evaluating individual trials self-identifying themselves as equivalence trials). This is a conceptual difference that cannot be directly transferred to our meta-analysis. While we agree that defining an equivalence margin is challenging, we do not see why equivalence trials or meta-analyses are particularly prone to bias. The same is true for our preference of intent-to-treat data. Both intent-to-treat and completer data are not optimal, and a researcher has to prespecify which kind of data is to be included in the analysis, which we did in our protocol. It is open to further research whether intent-to-treat analyses carry the risk of diluting treatment differences (5, 6). In our meta-analysis, only 10 (out of 23) randomized controlled trials provided intent-to-treat data, and in these cases the primary outcome was reported only for the intent-to-treat population. Thus, we used the data that were reported.

We agree that not preregistering our equivalence margin with the study protocol is a limitation. However, as reported in the article (1), we performed a thorough search on previously used equivalence margins across disorders and decided to use one of the smallest margins ever proposed (i.e., g=0.25; the smallest margin proposed was g=0.24, which specifically refers to depression [7]). Thus, preregistration would have changed neither the definition of the margin nor the outcome of our meta-analysis.

Moreover, Cristea and colleagues apply double standards as they have stated themselves, when being criticized for not preregistering one of their own meta-analyses (8), that "as meta-analyses deal with secondary observational data, the potential pernicious influence of investigator biases might be lessened."

4. It is true that our meta-analysis was funded by a professional psychoanalytic society. The sponsor was not involved in conducting this meta-analysis. In addition, we controlled for allegiance on both the level of performing this meta-analysis (by including two cognitive-behavioral colleagues, one of whom holds the chair of behavioral psychotherapy at TU Dresden) and on the study level by using the multilevel allegiance rating scale.
5. It is true that equivalence trials make sense only if control interventions proved efficacious for the condition studied. That is exactly why we ensured the efficacy of the comparator.