

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.

Cristea and colleagues seem to assume that this needs to be the case within the trials included in the meta-analysis. However, the efficacy of the comparison condition needs to be established in principle, not necessarily in the trials being included. In both the study by Zipfel et al. on anorexia nervosa (9) and the study by Crits-Christoph et al. on cocaine dependence (10), CBT was not superior to comparison conditions, one being an enhanced version of treatment as usual (9), the other being an established treatment (i.e., individual drug counseling based on the 12-step program [10]). However, CBT is considered established (11) for these conditions, independent of the outcome of these two trials, and thus was included in the meta-analysis. Therefore, the key assumption of assay sensitivity was not violated (4).

6. It is possible that results of an individual study differ from those of a meta-analysis. However, we agree that results of psychodynamic therapy in bulimia are controversial (12–14) and that further research on bona fide psychodynamic therapy in bulimia is required.

Last, but not least, we do agree with the remark by Cristea et al. that a characterization of treatments as “equally ineffective” would have been more accurate for some of the studies. Further improvement of current mental health treatments and of the quality of the empirical studies testing them should be a shared goal. The issues raised by Cristea et al. question neither the results nor the conclusions of our meta-analysis.

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. Wampold BE, Mondin GW, Moody M, et al: A meta-analysis of outcome studies comparing bona fide psychotherapies: empirically, “all must have prizes.” *Psychol Bull* 1997; 122:203–215
3. Cristea IA, Gentili C, Cotet CD, et al: Efficacy of psychotherapies for borderline personality disorder: a systematic review and meta-analysis. *JAMA Psychiatry* 2017; 74:319–328
4. Treadwell JR, Uhl S, Tipton K, et al: Assessing equivalence and noninferiority. *J Clin Epidemiol* 2012; 65:1144–1149
5. Lesaffre E: Superiority, equivalence, and non-inferiority trials. *Bull NYU Hosp Jt Dis* 2008; 66:150–154
6. Walker E, Nowacki AS: Understanding equivalence and noninferiority testing. *J Gen Intern Med* 2011; 26:192–196
7. Cuijpers P, Turner EH, Koole SL, et al: What is the threshold for a clinically relevant effect? The case of major depressive disorders. *Depress Anxiety* 2014; 31:374–378
8. Cristea IA, Barbui C, Cuijpers P: Reviews and meta-analyses of psychotherapy efficacy for borderline personality disorder—reply (letter). *JAMA Psychiatry* 2017; 74:854–855
9. 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
10. 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
11. Nathan PE, Gorman JM: A guide to treatments that work. New York, Oxford University Press, 2015
12. Poulsen S, Lunn S: Response to Tasca et al. (letter). *Am J Psychiatry* 2014; 171:584
13. 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
14. Tasca GA, Hilsenroth M, Thompson-Brenner H: Psychoanalytic psychotherapy or cognitive-behavioral therapy for bulimia nervosa (letter). *Am J Psychiatry* 2014; 171:583–584

Christiane Steinert, Ph.D.
Thomas Munder, Ph.D.
Sven Rabung, Ph.D.
Jürgen Hoyer, Ph.D.
Falk Leichsenring, D.Sc.

From the Department of Psychosomatics and Psychotherapy, University of Giessen, Giessen, Germany; the Department of Psychology, Medical School Berlin, Berlin; Psychologische Hochschule Berlin, Berlin; the Department of Psychology, Alps-Adriatic University of Klagenfurt, Klagenfurt, Austria; and the Institute of Clinical Psychology and Psychotherapy, Technical University Dresden, Dresden, Germany.

Address correspondence to Dr. Steinert (christiane.steinert@psycho.med.uni-giessen.de).

The authors' disclosures accompany the original article.

This reply was accepted for publication in August 2017.

Am J Psychiatry 2017; 174:1123–1124; doi: 10.1176/appi.ajp.2017.17050592r