COMMENTS AND RESPONSES

Response to Comment on: Pan et al. Bidirectional Association Between Depression and Metabolic Syndrome: A Systematic Review and Meta-analysis of Epidemiological Studies. Diabetes Care 2012;35: 1171-1180

e thank Dr. Kawada (1) for his interest in our article (2) and welcome the opportunity to respond. Dr. Kawada raised the issues that different definitions of metabolic syndrome (MetS) and depression have been used in different studies and that the participants' characteristics varied across studies. We acknowledge that those factors could contribute to the heterogeneity of the pooled estimates. Thus, we carefully assessed the heterogeneity using the I^2 statistics, and to be more conservative, we pooled the odds ratios using the random-effects models that allowed for between-study heterogeneity. As reported in the article (2), the I^2 was moderate (55.1%) in the meta-analysis of cross-sectional studies and moderate (56.8%) in the meta-analysis of cohort studies of MetS predicting depression risk, but it was low (0%) in the metaanalysis of cohort studies of depression predicting MetS risk. To explore the heterogeneity by various factors, we conducted the stratified analysis by study characteristics and the results have been reported in Supplementary Tables 1, 4, and 5 of our original article. The results have been generally robust and consistent across different strata of most factors that we examined.

Dr. Kawada also commented on the potential publication bias in our metaanalysis. However, we would like to emphasize that we did not conclude "no publication bias" in our article, and we only stated that "no publication bias was detected" and "[we] found no indication of publication bias in all the analyses" (2). As in any meta-analysis, we have relied on certain statistical approaches to detect the publication bias, and we cannot fully exclude the possibility of publication bias. However, we tried our best to contact the authors to clarify inquiries of their articles and provide unpublished data, if necessary, to minimize the potential publication bias.

As a statistical method, a meta-analysis has its own advantages and also limitations. The general aim of a meta-analysis is to provide a more robust estimate of the true effect size by pooling estimates from multiple studies. A meta-analysis is also useful to identify the patterns among study results and sources of disagreement across studies. However, the results from a meta-analysis should be interpreted carefully in the context of its limitations. Our meta-analysis is the first of its kind to examine the bidirectionality of the depression-MetS relationship, and the results can have significant implications for both clinical care and public health.

An Pan, phd^{1,2} Frank B. Hu, md, phd^{1,3,4}

- From the ¹Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts; the ²Saw Swee Hock School of Public Health and Yong Loo Lin School of Medicine, National University of Singapore and National University Health System, Singapore; the ³Department of Epidemiology, Harvard School of Public Health, Boston, Massachusetts; and the ⁴Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts.
- Corresponding author: Frank B. Hu, frank.hu@ channing.harvard.edu, or An Pan, ephanp@nus .edu.sg.
- DOI: 10.2337/dc12-1779
- © 2013 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered. See http:// creativecommons.org/licenses/by-nc-nd/3.0/ for details.

Acknowledgments—No potential conflicts of interest relevant to this article were reported.

- Kawada T. Comment on: Pan et al. Bidirectional association between depression and metabolic syndrome: a systematic review and meta-analysis of epidemiological studies. Diabetes Care 2012;35:1171–1180 (Letter). Diabetes Care 2013;36:e27. DOI: 10.2337/dc12-1607
- 2. Pan A, Keum N, Okereke OI, et al. Bidirectional association between depression and metabolic syndrome: a systematic review and meta-analysis of epidemiological studies. Diabetes Care 2012;35:1171–1180