

COMMENTS AND RESPONSES

**Response to Comment on: Kan et al. A Systematic Review and Meta-analysis of the Association Between Depression and Insulin Resistance. Diabetes Care 2013;36:480-489**

Two key issues are raised by Dr. Kawada (1): assessment of depression and insulin resistance (IR).

The prevalence of depression varied with the method used to identify depression cases, and the author suggested the use of only one standard definition. Diagnostic interview was used in six datasets in the meta-analysis, with two datasets using the Structured Clinical Interview for Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) Disorders (SCID) and four using the Composite International Diagnostic Interview (CIDI). The latter is designed for the assessment of mental disorders according to the definitions and criteria of International Classification of Diseases, 10th Edition and DSM-IV. Moderate to good level of concordance have been demonstrated between CIDI and SCID (2), and both instruments are widely used in epidemiological studies for major depressive disorders. The aim of meta-analyses is to combine the effects of all available studies to get a precise and unbiased estimate. The Cohen *d* approach was used in this meta-analysis to calculate the standardized effect size, and the random-effect model was chosen to account for any possible heterogeneity.

Furthermore, we assessed the effect for different methods in a meta-regression. It is not realistic to expect to have only one measure or one definition of depression in any systematic review in this field, and we minimized the influence of different definitions using the above methods.

Dr. Kawada suggested that the reason for the difference in effect sizes observed between homeostasis model assessment-insulin resistance (HOMA-IR) and quantitative insulin sensitivity check index (QUICKI) was due to the lack of log transformation of HOMA-IR in the calculation of QUICKI. QUICKI was the measure used exclusively in the datasets conducted by Timonen et al. (3,4), who confirmed the appropriate calculations. It is possible that the differences in effect sizes were due to methodological or population differences of the studies reporting HOMA-IR and QUICKI methods.

The association between depression and IR remained statistically significant across the different depression and IR measures in all meta-regression analyses (effect size [95% CI]; diagnostic interviews: 0.46 [0.22–0.71]; self-report measures: 0.13 [0.05–0.21]; HOMA-IR/HOMA2-IR: 0.32 [0.12–0.53]; minimal model/QUICKI: 0.17 [0.08–0.26]) (5), suggesting that the association observed, although small, was robust. The strength of evidence for the depression-IR association was graded as low to moderate with a medium to high risk of bias, in recognition of the study designs and qualities of the datasets being included in the meta-analysis. The substantial heterogeneity in the assessment of depression and IR was discussed in the strengths and limitations section of our conclusion. The limitations raised by Dr. Kawada have already been acknowledged in our meta-analysis.

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**References**

1. Kawada T. Comment on: Kan et al. A systematic review and meta-analysis of the association between depression and insulin resistance. *Diabetes Care* 2013;36:480-489 (Letter). *Diabetes Care* 2013;36:e123. DOI: 10.2337/dc13-0403
2. Haro JM, Arbabzadeh-Bouchez S, Brugha TS, et al. Concordance of the Composite International Diagnostic Interview Version 3.0 (CIDI 3.0) with standardized clinical assessments in the WHO World Mental Health surveys. *Int J Methods Psychiatr Res* 2006;15:167-180
3. Timonen M, Laakso M, Jokelainen J, Rajala U, Meyer-Rochow VB, Keinänen-Kiukaanniemi S. Insulin resistance and depression: cross sectional study. *BMJ* 2005;330:17-18
4. Timonen M, Rajala U, Jokelainen J, Keinänen-Kiukaanniemi S, Meyer-Rochow VB, Räsänen P. Depressive symptoms and insulin resistance in young adult males: results from the Northern Finland 1966 birth cohort. *Mol Psychiatry* 2006;11:929-933
5. Kan C, Silva N, Golden SH, et al. A systematic review and meta-analysis of the association between depression and insulin resistance. *Diabetes Care* 2013;36:480-489