Author’s response to reviews

Title: Bias in a protocol for a meta-analysis of 5-HTTLPR, stress, and depression

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Version: 3 Date: 28 May 2014

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28 May 2014

Dear BMC-P Editors,

Thank you for obtaining the nice review of our letter from Dr. Matthew Keller. He notes that “the authors make cogent points and I cannot see why their views should not be published.”

Dr. Keller’s review agrees with the recommendations we make in our letter. Dr. Keller’s “…main problem with the proposed meta-analysis is that it must reply on potentially biased samples of studies.” Our letter too is about bias in the set of studies.

Like us, Dr. Keller recommends that “…the role of measurement type should be estimated alongside of sample size.” Our letter similarly says: “Culverhouse et al. include an a priori plan to test for effects of study design features on heterogeneity in findings, and include a list of five design features to be tested. We applaud this approach. However, the list of design features to be tested omits sample size.” We, like Dr. Keller, call for estimating effects of sample size.

Dr. Keller asks us to respond to one potential issue: “…downward bias in effect size introduced by lower-precision measures of stress or depression may be counterveiled by increased power afforded by larger sample size.” Thus, Dr. Keller is noting that unreliable measures might not be a problem if they are offset by large N. However, our letter’s argument is not about reliability, it is about validity. We do not argue that measures of lifetime stress and lifetime depression in the large-N studies are merely low in precision (unreliable). Instead, our letter explains how these lifetime measures are invalid, and cites empirical research that has shown they are invalid.

We realize that our letter did not contain a clear statement regarding the distinction between reliability and validity, and this might allow other readers to make the same erroneous deduction that Dr. Keller has made. To make our emphasis on validity clearer, we have added the following sentences to the middle of page 4:

“However, our concern is that lifetime measures of stress and depression in the forthcoming meta-analysis are not merely unreliable, they are also invalid, and therefore they contaminate the meta-analysis with misinformation. Increased power afforded by larger N sometimes counterveils unreliable data, but large N cannot counterveil invalid data. Unfortunately, the biasing influence of invalid data in a meta-analysis is exacerbated by large samples.”

I hope this clears up Dr. Keller’s issue.

We hope for rapid publication of our letter.

Thank you very much, Terrie Moffitt