

COMMENT ON “WHICH PORTION OF PHYSIOTHERAPY TREATMENTS’ EFFECT IS NOT ATTRIBUTABLE TO THE SPECIFIC EFFECTS IN PEOPLE WITH MUSCULOSKELETAL PAIN? A META-ANALYSIS OF RANDOMIZED PLACEBO-CONTROLLED TRIALS” BY EZZATVAR ET AL

J Orthop Sports Phys Ther 2024;54(12):1-2.
doi:10.2519/jospt.2024.0201

To the editor,

We are writing to express our concerns regarding the meta-analysis that was recently published in your journal, titled “Which Portion of Physiotherapy Treatments’ Effect Is Not Attributable to the Specific Effects in People With Musculoskeletal Pain? A Meta-Analysis of Randomized Placebo-Controlled Trials.”² While we appreciate the efforts to quantify the influence of the effects that are not attributable to the specific effects of physiotherapy treatments, we believe there are fundamental flaws in the methodology and conclusions of this review.

First, one may wonder why the effect not attributable to the specific effect of an intervention might be of interest. Notably, Ezzatvar et al² concluded that “Boosting these factors consciously to enhance therapeutic outcomes represents an ethical opportunity that could benefit patients.” This is a remarkable claim since only a portion of these effects (factors) can be manipulated by the health care provider. The effects not attributable to the specific effect are also called the placebo response and depend on contextual effects, nonspecific effects, and their mutual manifestation.⁷ Contextual effects are defined as clinical outcome changes that result from exposure to factors related to the context. Nonspecific effects occur naturally over time but are not inherent to treatment.⁷ Importantly, only contextual effects can be manipulated

by the health care provider; however, the nonspecific effects (eg, natural history of the disease, regression to the mean) are not manipulable. Estimating the effects not attributable to the specific effect (ie, the placebo response) does not tell us anything about the different magnitudes of the contextual and nonspecific effects and how the manipulation of these could enhance care. That is, we wonder how Ezzatvar et al² came to this conclusion? Furthermore, it appears that manipulation of contextual effects does not offer meaningful benefit for the patient⁵ and that contextual effects are generally of a small magnitude for conservative non-pharmacological interventions.⁶

Second, we believe that the use of Proportion Attributable to Contextual Effects (PCE) as a measure in this context is inherently problematic and has led to the erroneous estimates of the placebo response (ie, the effects not attributable to the specific effect) in the systematic review by Ezzatvar et al.² More specifically, the PCE is a (misapplied) Ratio of Means,^{3,4} which is an effect measure for *treatment effects* (!) on a multiplicative scale.¹ By taking the Ratio of Means between the placebo group and the intervention group, the PCE actually calculates a treatment effect, *not* a placebo response (effects not attributable to the specific effect)⁷; furthermore, this is the same misapplied method of quantification used by the authors² in their meta-analysis. In essence, Ezzatvar et al² have calculated a specific effect for the comparison of placebo versus an intervention on a multiplicative scale and are incorrectly calling this the effect **not** attributable to the specific effect.

Third, the PCE employs change scores in its calculation that inadvertently omits studies where no change or a negative change from baseline values exists, introducing selection bias. Fourth, the method used by Ezzatvar et al² to calculate the standard error of the PCE is incorrect⁷ because it does not appropriately account for change-from-baseline measures, which

would necessitate a different formula.¹ In addition, it is also concerning that using these same methods of quantification, PCE values can exceed 1.0, leading to nonsensical assertions that the placebo response (effects not attributable to the specific effects) can explain more than 100% of the treatment effects.⁷

Given these substantial issues, we urge a critical reevaluation of the findings. Ensuring accurate and reliable interpretation in clinical research is crucial for the advancement of evidence-based practice in physical therapy.

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