***Osteopathic manipulative treatment does not show a reduction in length of stay and costs in preterm infants. Letter to the editor regarding* „Osteopathic manipulative treatment showed reduction of length of stay and costs in preterm infants – A systematic review and meta-analysis“ by Lanaro et al.**

To the Editor,

I was greatly interested in the systematic review and meta-analysis by Lanaro et al. suggesting osteopathic manipulative treatment is clinically effective in reducing the length of stay (LOS) and costs in a large population of preterm infants.[1] Within this review my attention was drawn to Lanaro et al. use of a **fixed effect model** for calculating their primary outcome: length of hospital stay (LOS). They included five studies (n= 1306, 645 preterm were allocated in the OMT group and 661 to the control group) in their meta-analysis. The application of a fixed effect model depends on two assumptions that should be met: 1. One believes that all the studies included in the analysis are functionally equivalent and 2. that one has the goal to compute a common effect size for the identified population, and not to generalize to other populations.[2] An example for such a case would be a pharmaceutical company that uses thousand patients to compare a drug versus a placebo. The company might run a series of trials which can be considered identical in the sense that it is reasonable to assume that any variables that have an impact on the outcome should be the same across them. Further, we assume that the patients, the treatment dose, the outcomes measures and the timepoints are essentially the same. In that instance since all the studies share a common effect and the first condition is met. It also meets the second goal because the goal of the analysis which is to see if the drug works in the population from which the patients were drawn.[3]

In the case of the meta-analysis of Lanaro et al. the use of a fixed effect model is inappropriate for the meta-analysis. The study population arises form different clinics and from two different countries. The studies used different treatment techniques, different treatment durations and different frequencies of treatment. Control group conditions also differed across the trials. These reasons make it unlikely that a fixed effect model is the right choice for the analysis. A further indication of the heterogeneity between included studies is found in the relatively high I^2 value of I^2=61%[4], which can be considered moderate to high.[5]

1 Lanaro, Diego, et al. "Osteopathic manipulative treatment showed reduction of length of stay and costs in preterm infants: A systematic review and meta-analysis." *Medicine* 96.12 (2017).
2 Borenstein, Michael, et al. *Introduction to meta-analysis*. John Wiley & Sons, 2011.
3 Borenstein, Michael, et al. *Introduction to meta-analysis*. John Wiley & Sons, 2011.
4 Lanaro, Diego, et al. "Osteopathic manipulative treatment showed reduction of length of stay and costs in preterm infants: A systematic review and meta-analysis." *Medicine* 96.12 (2017).
5 Higgins, Julian PT, et al. "Measuring inconsistency in meta-analyses." *BMJ: British Medical Journal* 327.7414 (2003):

A more appropriate model for the meta-analysis of the studies is a random effects meta-analysis because it does not assume a common effect size.[6] Recreating the analysis (using RevMan Version 5.2.6) with a random effects model the overall effect is no longer statistically significant (p = 0.08) [see figure 1]. This significantly alters the conclusion that osteopathic manipulative treatment does reduce LOS and costs in preterm infants.

Authors should choose models whose assumptions best fit the research question and those assumptions should be considered in the interpretation of the data.

I would like to thank Dr Neil OConnell for his comments on this letter.

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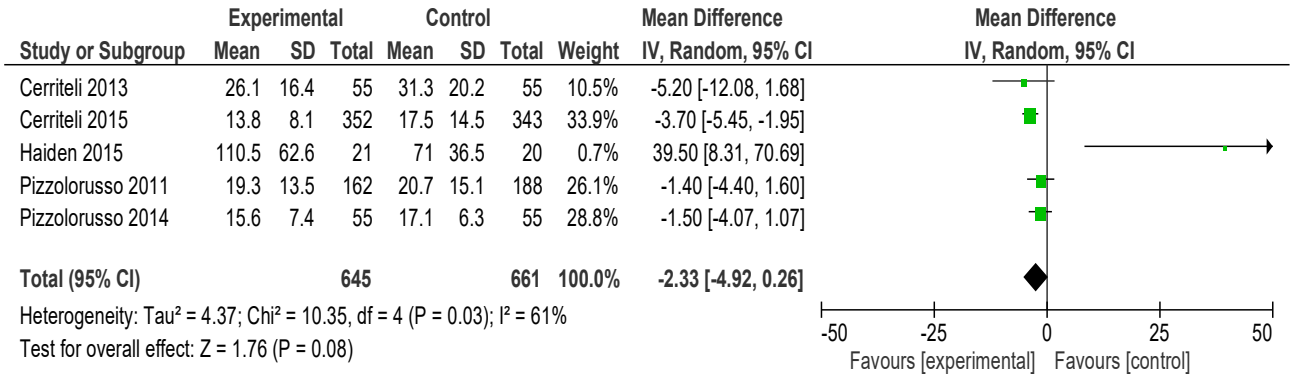

Figure 1- Reanalysis of the data with a random effects model

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6 Borenstein, Michael, et al. *Introduction to meta-analysis*. John Wiley & Sons, 2011.