Commentary

Improving meta-analysis methodology: The necessity of prediction intervals and homogeneous data selection

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Dear Editor,

We read with interest the meta-analysis by Cho et al[1] on Obesity and mortality in patients with COVID-19: A meta-analysis of prospective studies, and congratulate the authors. However, we have a few comments concerning the methodology:

1. Pooling studies with the effect size Odds ratio (OR) and others with Hazard Ratio (HR) in the same meta-analysis may affect the validity of the results because these two measures reflect different statistical concepts: ORs evaluate static probabilities, but HRs consider a temporal dimension.[2] Combining OR and HR may introduce significant bias in the analysis, resulting in total estimates that are clinically meaning-less. The authors should transform all OR and HR to RR:

• When the prevalence in the reference group (r) is known to be low enough (<10%), relative risk (RR) and hazard ratio are quite close. In fact, the smaller the r, the closer RR and HR are. In these cases, an approximation of RR based on HR is given by the formula (1/r)*{1-e^[HR*ln(1-r)]}.[3]

• The formula to convert odds ratios to relative risks is: Relative risk=odds ratio/[1−Po+(Po×odds ratio)] (Where Po is the baseline risk). When Po is very low OR will be close to RR.[4]

The authors did not mention the adopted methodology.

2. The authors measured inconsistency using the I^2 value to evaluate heterogeneity. In 2003, Higgins[5] recorded this approach, which is considered an opinion of experts (level 5 evidence in the Oxford classification). Higgins changed his approach concerning the assessment of heterogeneity and as a co-author with Borenstein,[6] they published an article entitled "I^2 is not an absolute measure of heterogeneity". To assess het-erogeneity, Borenstein et al.[7] and Dziri[8-10] suggested using the 95% prediction interval (PI) with its variance Tau squared (Tau^2). Cho et al.[1] did not use the PI statistic to assess how much the true effect size varies across studies.

3. We recalculated the mean effect size based on the mortality rate, using the random model (Figure 1) with the comprehensive meta-analysis software version 4. We found a mean effect size of 6.8% with a 95% confidence interval (CI) (3% to 14.4%). If we consider that the true effect size is 6.8% the 95% PI should be between 0.2% and 74.7% which testimonies a substantial heterogeneity (Figure 1). To explain this heterogeneity, we performed a meta-regression comparing the mean effect size with the moderator "percentage of obesity in each study". We did not find a link between the mortality rate and the percentage of obesity (p=0.078) (Figure 2).

According to these data, the conclusion should re-port the PI which showed a substantial heterogeneity. Obesity did not explain the mortality rate. This conclusion was different than the conclusion reported by the authors: "In the current meta-analysis of prospective studies, we found that obesity increased the risk of mortality in patients with COVID-19".

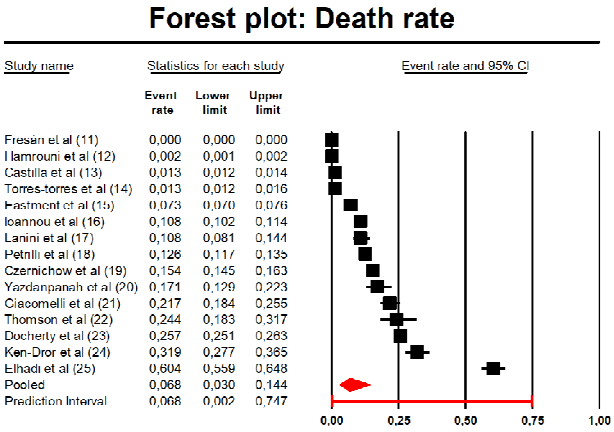

Figure 1. Forest Plot of Obesity and COVID-19 mortality prevalence

AUTHOR DISCLOSURES

The authors declare no conflict of interests.

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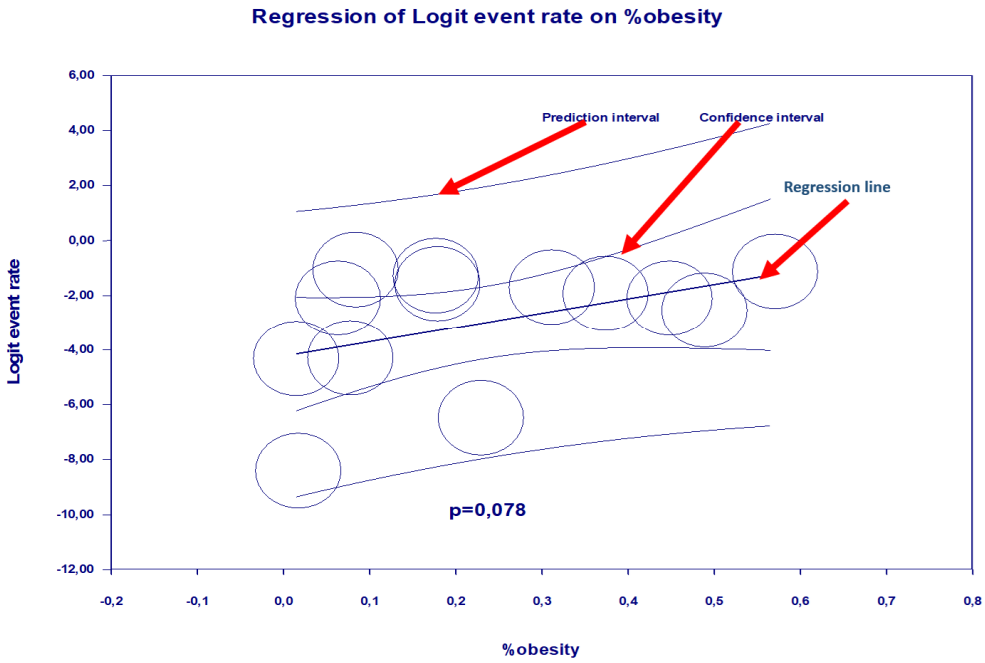

Figure 2. Meta-regression showed that obesity did not explain mortality.

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