



How to assess heterogeneity for a meta-analysis? Comment évaluer l'hétérogénéité pour une méta-analyse ?

Chadli Dziri, MD, FACS

Professeur Emérite en Chirurgie Générale, Université Tunis El Manar, Faculté de Médecine de Tunis, Directeur du Centre de Simulation Honoris Medical.

TO THE EDITOR: I read the update meta-analysis from biomedical literature about MTHFR 'polymorphisms and the CML' risk, published by Turki et al. in the Apr issue of "La Tunisie Médicale" (1) with interest, and I congratulate the authors for their reported meta-analysis. However, I have some comments on the presentation of the methodology (Methods section, page 287, left column - 2nd paragraph):

1. The authors stated: «The heterogeneity was determined by calculating I^2 metric statistic. $I^2 < 50\%$ were interpreted as low, moderate, and high degrees of heterogeneity, respectively (reference 19).»

This concept is not accurate. Lopez Lopez's reference 19 does not mention the origin of this concept. Lopez Lopez should have quoted the reference of Higgins (2) who introduced this concept in 2003, which remains an opinion of expert (level 5 of evidence according to the Oxford classification). The same author Higgins with Borenstein and others published an article with the title of « I^2 is not an absolute measure of heterogeneity » (3).

In fact, heterogeneity is assessed by the variation of the true effect size which is provided by the 95% Predictive Interval (4,5) and its variance Tau squared (τ^2). The 95% predictive interval is an index of dispersion while the confidence interval is an index of precision.

2. The authors also stated: «When no heterogeneity was found with $p > 0,05$ or $I^2 < 50\%$, a fixed effect model was chosen to estimate the pooled ORs with their corresponding 95% CIs. Otherwise, a random-effects model was used (reference 20).

This concept is not accurate. When dealing with different populations, the Random Model must always be applied, whatever the I^2 , which is what the authors did in Figures 2A and 2B. Indeed, there is no place for the fixed model in this context (6).

inconsistency in Meta-Analysis. *BMJ*. 2003;327(7414):557-60. doi: 10.1136/bmj.327.7414.557. PMID: 12958120; PMCID: PMC192859.

3. Borenstein M, Higgins JP, Hedges LV, Rothstein HR. Basics of Meta-Analysis: I^2 is not an absolute measure of heterogeneity. *Res Synth Methods*. 2017;8(1):5-18. doi: 10.1002/jrsm.1230. Epub 2017 Jan 6. PMID: 28058794.
4. Borenstein M, Hedges LV, Higgins JPT, Rothstein HR. Introduction to meta-analysis, second edition, Prediction Intervals (chapter 17) - Oxford, John Wiley & Sons Ltd 2021: 119-125
5. Borenstein M, Common mistakes in meta-analysis and how to avoid them, The Prediction Interval (chapter 17) - New Jersey (USA), Biostat, Inc. 2019: 85-93
6. Borenstein M, Hedges LV, Higgins JP, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. *Res Synth Methods*. 2010;1(2):97-111. doi: 10.1002/jrsm.12. Epub 2010 Nov 21. PMID: 26061376.

REFERENCES

1. Turki F, Louati N, Kamoun H, Keskes L, Rebaii T, Frikha R. Update meta-analysis from biomedical literature about MTHFR 'polymorphisms and the CML' risk. *Tunis Med*. 2022 ; Vol 100 (04) : 285-294.
2. Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring

Correspondance

Chadli Dziri, MD, FACS

Professeur Emérite en Chirurgie Générale, Université Tunis El Manar, Faculté de Médecine de Tunis, Directeur du Centre de Simulation Honoris Medical.