

Meta-analyses: learn to question their reliability

- **Studies confirm that the quality of meta-analyses depends on the quality of included data.**

Meta-analyses (quantitative systematic reviews) are often considered to be high-level evidence to support health care recommendations or decisions (1,2). However, as with clinical trials and publications in general, while some are of high quality, others contain biases, or even misleading claims (1,2).

Biased meta-analyses of apixaban. Experts from the US Food and Drug Administration (FDA) have identified falsified data in some publications of the results of the “Aristotle” clinical trial, which compared two oral anticoagulants: *apixaban*, a factor Xa inhibitor, versus *warfarin*, a vitamin K antagonist, for use in atrial fibrillation (3).

A team identified 22 meta-analyses of *apixaban* trials which included the results of the “Aristotle” trial. They then carried out the meta-analyses again without including the results of this trial. The results were found to be altered in 46% of cases, and the conclusion was different in 32% of cases, to the detriment of *apixaban* compared to *warfarin*, the reference anticoagulant (a)(3,4).

A large number of unreliable meta-analyses. This example confirms the results of other studies. A study published in 2016 dealing with 118 meta-analyses published in 2013 by the *Annals of Internal Medicine*, *BMJ*, *JAMA*, *Lancet* and the Cochrane network, showed that only half of the authors of these meta-analyses had looked in depth in the selected publications for the possibility of “research malpractice” (for example, multiple publications) which could have influenced the results (5).

A study of nearly 700 meta-analyses published in 2014 showed that the assessment of quality and risk of bias in the studies included in these meta-analyses had only been carried out in about 70% of cases (6).

The results of meta-analyses are of variable reliability, depending in large part on the methodological quality of the trials that are included. According to one medical publication specialist from Stanford University, among the burgeoning number of meta-analyses, the high proportion of “redundant, misleading and conflicted” examples makes it imperative to change the way in which they are published, so as to eliminate bias and vested interests (2).

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a- These biases alter the results for all-cause mortality in the Aristotle trial. They were taken into account in our review on the choice of oral anticoagulant in atrial fibrillation and led us to consider the difference in mortality reported in the published account of the trial to be not statistically significant. Furthermore, no meta-analyses of trials of direct-acting oral anticoagulants were included in our review. The conclusions of our review therefore remain unchanged.

Selected references from Prescrire's literature search

- 1- Prescrire Rédaction “Méta-analyse d'essais cliniques: une synthèse méthodique et quantifiée, avec des limites” *Rev Prescrire* 2014; **34** (373): 862-865.
- 2- Ioannidis JPA “The mass production of redundant, misleading, and conflicted systematic reviews and meta-analyses” *Milbank Q* 2016; **94** (3): 485-514.
- 3- Garmendia CA et al. “Evaluation of the inclusion of studies identified by the FDA as having falsified data in the results of meta-analyses: the example of the apixaban trials” *JAMA Intern Med* 2019; **179** (4): 582-584.
- 4- Prescrire Editorial Staff “Oral anticoagulants in atrial fibrillation. Warfarin or apixaban, depending on the clinical situation” *Prescrire Int* 2019; **28** (205): 159-160.
- 5- Elia N et al. “How do authors of systematic reviews deal with research malpractice and misconduct in original studies? A cross sectional analysis of systematic reviews and survey of their authors” *BMJ Open* 2016; **6**: e010442, 10 pages.
- 6- Page MJ et al. “Epidemiology and reporting characteristics of systematic reviews of biomedical research: a cross-sectional study” *PLoS Med* 2016; 10.1371: 30 pages.