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Data: 24/12/2014 14:31  
A: andrea.messori.it@gmail.com  
CC: andrea.messori.it@gmail.com

Dear Dr Messori,

Cardiovascular safety of new oral anticoagulants: re-analysis of 27 randomized trials based on Bayesian network meta-analysis (ms no. LET-00654-14)

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Cardiovascular safety of new oral anticoagulants: re-analysis of 27 randomized trials based on Bayesian network meta-analysis

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15 December 2014

The Editor
British Journal
Of Clinical Pharmacology

Dear Editor,

We should like to submit the enclosed paper (entitled “Cardiovascular safety of new oral anticoagulants: re-analysis of 27 randomized trials based on Bayesian network meta-analysis”) for publication as a Letter.

Thank you for your kind attention.

Sincerely,

Dr. Andrea Messori
HTA Unit
Regional Health Service
50100 Firenze (Italy)
Cardiovascular safety of new oral anticoagulants: re-analysis of 27 randomized trials based on Bayesian network meta-analysis

Andrea Messori

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No. of figures: 1 (max 1)
No. of references: 12
Word count: 417 (max 800)
While the study by Loke et al. [1] has addressed an important issue concerning the safety of the new oral anticoagulants, one methodological point deserves further scrutiny. In their network meta-analysis, Loke et al. employed a frequentist statistics (the Bucher method [2]) which is recognised to have some intrinsic limitations. In fact, one drawback is that the Bucher method tends to overemphasise the statistical significance of the results; another limitation is represented by the fragmentation of its approach because as many separate analyses are needed as the number of comparisons being studied [3-6].

In recent years, the Bayesian method has increasingly been considered the new standard in the field of network meta-analysis. This approach has one main advantage in that all treatments included in the comparisons are incorporated into a single model (“all-in-one” approach). Another advantage is that the Bayesian technique enables rank ordering of the treatments concerned [7-11].

To test whether the results reported by Loke et al were influenced by the adoption of the Bucher method, we re-analysed the raw data of their analysis by applying the Bayesian method of network meta-analysis (random-effect model). The model employed in our re-analysis has been developed by the NICE Support Unit (UK) [12]. Our end-point was the occurrence of acute coronary syndrome. The data included in our re-analysis were those reported in Figures 2, 3 and 4 of Loke’s article.

Figure 1 shows the ranking histograms generated by the probabilistic analysis of our Bayesian statistics. As regards the values of odds-ratio, our results based on the Bayesian method proved to be nearly identical to those obtained by Loke et al. using the Bucher method. In fact, the odds-ratio estimated by our Bayesian statistics was 0.54 (95% credible interval: 0.38 to 0.76) for the comparison of rivaroxaban versus dabigatran and 0.60 (95% credible interval: 0.41 to 0.81) for the comparison of apixaban versus dabigatran. The corresponding estimates reported by Loke et al. were 0.54 (95% confidence interval: 0.39 to 0.76) and 0.61 (95% confidence interval: 0.44 to 0.85), respectively. Like in Loke’s analysis, the indirect comparison of rivaroxaban versus
apixaban showed, in our analysis, a result that remained far from statistical significance (odds-ratio= 0.91; 95% credible interval: 0.71 to 1.20).

In conclusion, our re-analysis indicates that, in studying this data set, the performance of the Bucher method was excellent in comparison with that of the Bayesian method. From a practical viewpoint, our re-analysis has provided a useful confirmation of the scientific robustness of the results derived from these interesting datasets.

Conflict of interests:
None

References


LEGENDS FOR FIGURES

Figure 1. Cardiovascular safety of novel oral anticoagulants: ranking histograms generated by Bayesian probabilistic analysis.

The clinical material (27 randomized trials; 4 treatments; 137,484 patients) is the same reported by Loke and co-workers [1] in their Figures 2, 3 and 4. The event is acute coronary syndrome; the treatments under comparison include apixaban, dabigatran, rivaroxaban and the treatment given to the control groups of the trials. For each of these 4 treatments, the histograms show the probability distribution of being ranked from 1 (highest safety) to 4 (lowest safety). Median ranks were the following: rivaroxaban, 1 (95% credible interval: 1 to 2); apixaban, 2 (95% credible interval: 1 to 3); control groups, 3 (95% credible interval: 2 to 3); dabigatran, 4 (95% credible interval: 4 to 4).
See text
111x236mm (72 x 72 DPI)