Lanzhou University

Trial sequential analysis in meta-analyses: could all evidence be firm?

Lun Li[1,2], Xiangji Ying[3], Jinhui Tian[1], Kehu Yang[1,2]*, *corresponding author

1. Evidence Based Medicine Center of Lanzhou University, School of Basic Medical Science of Lanzhou University, Lanzhou 730000;
2. The first Clinical Medical College of Lanzhou University, Lanzhou 730000;
3. The second Clinical Medical College of Lanzhou University, Lanzhou 730000;

Background: Trial sequential analysis (TSA) may reduce risk of random errors, which may cause misleading evidence in meta-analyses, due to repetitive testing of accumulating data by evaluating meta-analyses not reaching the information size with monitoring boundaries.

Objective: To investigate the prevalence of using TSA in meta-analysis, and evaluate how much firm evidence is reached.

Methods: The Cochrane library, Pubmed, Embase, ISI web of knowledge were searched at December 25 2011 without any restrictions. Those meta-analyses, which used TSA for evaluating the statistical reliability of data, were included. We compared the number of conclusive outcomes before 2011 and after 2011, between different countries and diseases, between Cochrane reviews and non-Cochrane reviews using Z-test and expressing by risk ratio (RR).

Results: 33 meta-analyses were included, and most of them were published in 2011 (21, 63.6%) and in the Cochrane Collaboration (16, 48.5%), written by Danes (21, 63.6%) and about diseases of the digestive system (14, 42.4%). Out of 97 outcomes evaluated, only 21 (21.88%) outcomes reached firm evidence. There were not any statistical differences before and after 2011 (RR 0.78, 95%CI 0.33, 1.81), between Denmark and other countries (RR 0.90, 95%CI 0.42, 1.92), between digestive and other diseases (RR 0.77, 95%CI 0.28, 2.12), between Cochrane and non-Cochrane reviews (RR 1.12, 95%CI 0.52, 2.39).

Conclusion: Few meta-analyses used TSA to evaluate the statistical reliability of data, and few outcomes reached firm evidence. In the future, we recommend using TSA to evaluate the statistical reliability of data and evidence.

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