Trial sequential analysis for cumulative evidence: how much was believable?

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Background: Trial sequential analysis (TSA) may reduce risk of random errors due to repetitive testing of accumulating data by evaluating meta-analyses not reaching the information size.

Objective: To overview the results of TSA for evaluating the statistical reliability of data of meta-analyses.

Methods: The Cochrane library, Pubmed, Embase, ISI web of knowledge were searched at December 25 2011 without any restrictions. We included those studies, which used TSA for evaluating the statistical reliability of data or compared TSA and sequential meta-analysis (SMA) by re-analysis of a number of published meta-analyses. The outcomes were the number of meta-analyses with early spurious P <0.05, not reaching low-bias information size (LBIS), low-bias and heterogeneity-adjusted information size, $TSA_{15\%}$ (relative risk reduction [RRR]:15%), $TSA_{30\%}$ (RRR: 30%), TSA_{LBHIS} (adjusted by LBHIS).

Results: Five studies were included. Four studies investigated the statistical reliability of data using TSA, whose number of included studies ranged from one to 174. Those significant meta-analyses seemed to be with much firmer evidence using $TSA_{15\%}$ (RR 6.33, 95%CI 2.68, 14.94), $TSA_{30\%}$ (RR 3.04, 95%CI 1.96, 4.71) and TSA_{LBHIS} (RR 7.71, 95%CI 4.15, 14.29) than non-significant ones, but not in other outcomes. One study comparing TSA and SMA based on six meta-analyses showed SMA was useful to investigate the cumulative evidence.

Conclusion: Significant meta-analyses seemed to be more reliable than non-significant ones, and SMA seemed more useful than SMA in cumulative evidence. However, this was limited by few included meta-analyses, and more such studies were needed in the future.

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