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MINIREVIEWS

Systematic reviews and meta-analyses: Why are they clinically significant?

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Abstract

This review aims to clarify the clinical significance of systematic reviews and meta-analyses by illustrating several classical examples. Firstly, systematic reviews can provide the highest level of evidence for clinical decisions. Secondly, systematic reviews can propose unresolved issues and future directions. Thirdly, systematic reviews can avoid harm to the human body. Fourthly, systematic reviews can prevent a waste of resources. Generally speaking, clinical researchers should be encouraged to perform systematic reviews and meta-analyses.

Key words: Systematic reviews; Meta-analyses; China; Publication; Science citation index

Core tip: Systematic reviews and meta-analyses are very important for clinicians and investigators because they can provide the highest level of evidence for clinical decisions, propose unresolved issues and future directions, avoid harm to the human body and prevent a waste of resources.

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INTRODUCTION

In recent years, the number of systematic reviews and meta-analyses has been steadily on the rise. By searching the PubMed database, about 500 relevant papers were published around the world in 1994 but more than 6000 relevant papers were published

in 2009[1]. Currently, systematic reviews and meta-analyses are also very hot in China. According to the statistics produced by *Ding Xiang Yuan* reporters, China contributed over 1000 meta-analysis papers in 2012[2]. There was a 40-fold increase in the annual number of meta-analyses in the genomic era for China from 2003 to 2011[3].

Investigators who perform original research need lots of time and costs for collecting clinical data and/or doing the experiments. By comparison, meta-analysis authors spend less time and fewer costs on synthesizing previously published data into a new result. It is said that a doctor wrote dozens of meta-analyses in Science Citation Index (SCI) journals with an accumulated impact factor > 200 in one year[4]. Ironically, the spectrum of his or her meta-analyses was very wide, including breast diseases, colon cancer, orthopedics, etc. As a criticism of the fact, publishing a meta-analysis in SCI journals is often regarded as opportunistic behavior. Some experts working at famous institutions strongly discourage their students from doing meta-analyses[5]. Herein, we highlight the significance of meta-analyses to correct such a distortion and encourage more investigators to perform meta-analyses.

SYSTEMATIC REVIEWS CAN PROVIDE THE HIGHEST LEVEL OF EVIDENCE FOR CLINICAL DECISIONS

According to the system produced by the Oxford Centre for Evidence-Based Medicine (March 2009), evidence for therapy/prevention and etiology/harm studies is divided into five levels[6]. They include level 1 (randomized controlled trials), level 2 (cohort studies), level 3 (case-control studies), level 4 (case series) and level 5 (expert opinion). Level 1 is further classified into level 1a (systematic review of randomized controlled trials) and 1b (individual randomized controlled trials). Similarly, systematic reviews of cohort and case-control studies are also classified as levels 2a and 3a, respectively. In the updated system produced by the Oxford Centre for Evidence-Based Medicine (2011), evidence for treatment benefit studies is also divided into five levels[7]. Systematic reviews of randomized trials provide the top level of evidence. On the other hand, the number of citations potentially reflects the hierarchy of evidence. Meta-analyses can receive the largest number of citations, followed by randomized controlled trials, cohort or case-control studies, nonsystematic review articles, decision and cost-effectiveness analyses and case reports[8].

SYSTEMATIC REVIEWS CAN PROPOSE UNRESOLVED ISSUES AND FUTURE DIRECTIONS

Systematic reviews are indispensable before initiating new clinical research[9,10]. Since August 2005, the *LANCET* editors have required authors to summarize previously published findings and explain the impact of their findings on existing knowledge[11]. In this renowned journal, the guidelines for authors obviously propose how the authors of clinical trials should do an updated systematic review if a recent systematic review is unavailable[12].

This consideration is also appropriate for every clinical researcher. In 2011, we published a meta-analysis to explore the significance of screening for JAK2 V617F mutation in patients with Budd-Chiari syndrome[13]. The prevalence of JAK2 V617F mutation was 37% and positive JAK2 V617F mutation could predict the presence and development of myeloproliferative neoplasms in such patients[13]. However, most available studies were conducted in the West and only one study was conducted in Asia (India). Given the ethnical differences between China and the West and the absence of related data from China, further evaluation of the prevalence of JAK2 V617F mutation in Chinese patients is warranted. In 2012, we reported the results of a clinical study in which the prevalence of JAK2 V617F mutation in Chinese patients with Budd-Chiari syndrome was only 4.3%[14]. This finding suggested a difference in the etiological distribution of Budd-Chiari syndrome between China and the West. Thus, we further performed a large-scale observational study to more comprehensively analyze the thrombotic risk factors for Budd-Chiari syndrome in Chinese patients[15]. Except for JAK2 V617F mutation and myeloproliferative neoplasms, paroxysmal nocturnal hemoglobinuria, factor Ⅴ Leiden mutation and prothrombin G20210A mutation were rarely found in our patients. These results were immediately confirmed by other peers[16,17].

SYSTEMATIC REVIEWS CAN AVOID HARM TO THE HUMAN BODY

Gilbert *et al*[18] performed a systematic review of observational studies and recommendations from textbooks about the association between infant sleeping position and sudden infant death syndrome. In books on infant care, the recommendation regarding whether the infants should be on a back or front sleeping position was controversial before 1989 but only a back sleeping position was recommended after that. In the meta-analysis, 25 individual studies published between 1965 and 2004 were identified. Indeed, the cumulative meta-analysis of the first two published studies (the first study was published in 1965 and the second one was published in 1970) demonstrated that the front sleeping position led to a statistically significant increase in the incidence of sudden infant death syndrome (cumulative odds ratio = 2.93, 95%CI: 1.15-7.47). In other words, if a meta-analysis was performed soon after the first two papers were published, the debate regarding the sleeping position would have disappeared, thereby

preventing more than 10000 infant deaths in the United Kingdom and more than 50000 in Europe, the United States and Australasia.

SYSTEMATIC REVIEWS CAN PREVENT A WASTE OF RESOURCES

Lau *et al*[19] performed a meta-analysis of clinical trials to compare the benefit of intravenous streptokinase *vs* placebo or no therapy for acute myocardial infarction. In the meta-analysis, 33 individual studies published between 1959 and 1988 were identified. Indeed, in the cumulative meta-analysis of the first four published studies with 962 patients, the benefit of intravenous streptokinase for acute myocardial infarction became statistically significant (P = 0.023) but the 95%CI was relatively wide. In the cumulative meta-analysis of the first 15 published studies with 4314 patients, the benefit remained significant (P < 0.001) and the odds ratio became steadier with a narrower 95%CI. Accordingly, the 18 trials published since then were unnecessary. More importantly, the additional 32660 participants should not have been enrolled because the participants assigned to the placebo/no therapy group would not have received intravenous streptokinase.

Another similar example was a meta-analysis to evaluate the risk of lung cancer in never-smoking women exposed to passive smoking by spouses[20]. Taylor *et al*[20] identified a total of 51 studies between 1981 and 2006. In the cumulative meta-analysis of the first 10 studies published before 1986, the association of passive smoking and lung cancer was significant. In the cumulative meta-analysis of the first 20 studies published before 1989, the statistical significance became steadier. Thus, the subsequent 31 studies may have been wasteful.

CONCLUSION

The importance of systematic reviews and meta-analyses in the contemporary era of evidence-based medicine needs to be clearly recognized. Clinical researchers should be accustomed to publishing their own data after the related evidence is systematically reviewed.

REFERENCES

1 **Booth A**, Clarke M, Ghersi D, Moher D, Petticrew M, Stewart L. An international registry of systematic-review protocols. *Lancet* 2011; **377**: 108-109 [PMID: 20630580 DOI: 10.1016/S0140-6736(10)60903-8]

2 Meta-analysis Lun Wen Qu Wei Tong Ji Mian Mian Guan (Article in Chinese). Available from: URL: http://paper.dxy.cn/article/26164

3 **Ioannidis JP**, Chang CQ, Lam TK, Schully SD, Khoury MJ. The geometric increase in meta-analyses from China in the genomic era. *PLoS One* 2013; **8**: e65602 [PMID: 23776510 DOI: 10.1371/journal.pone.0065602]

4 Meta-analysis- Yi Xue Ke Yan De Guai Xiang. Available from: URL: http://news.dxy.cn/bbs/topic/21336219

5 **Yang ZP**, Ye XF, Fan DM. Meta-analysis is victim to Chinese academic and educational systems. *J Formos Med Assoc* 2013; **112**: 235-236 [PMID: 23660217 DOI: 10.1016/j.jfma.2012.09.019]

6 Oxford Centre for Evidence-based Medicine - Levels of Evidence (March 2009). Available from: URL: http://www.cebm.net/oxford-centre-evidence-based-medicine-levels-evidence-march-2009/

7 **Howick J**, Chalmers I, Glasziou P, Greenhalgh T, Heneghan C, Liberati A, Moschetti I, Phillips B, Thornton H. The 2011 Oxford CEBM Evidence Levels of Evidence. Available from: URL: http://www.cebm.net/ocebm-levels-of-evidence/

8 **Patsopoulos NA**, Analatos AA, Ioannidis JP. Relative citation impact of various study designs in the health sciences. *JAMA* 2005; **293**: 2362-2366 [PMID: 15900006 DOI: 10.1001/jama.293.19.2362]

9 **Clarke M**. Doing new research? Don't forget the old. *PLoS Med* 2004; **1**: e35 [PMID: 15578106 DOI: 10.1371/journal.pmed.0010035]

10 **Clarke M**, Hopewell S, Chalmers I. Clinical trials should begin and end with systematic reviews of relevant evidence: 12 years and waiting. *Lancet* 2010; **376**: 20-21 [PMID: 20609983 DOI: 10.1016/S0140-6736(10)61045-8]

11 **Young C**, Horton R. Putting clinical trials into context. *Lancet* 2005; **366**: 107-108 [PMID: 16005318 DOI: 10.1016/S0140-6736(05)66846-8]

12 The Lancet: Information for Authors. Available from: URL: http://www.thelancet.com/lancet/information-for-authors

13 **Qi X**, Yang Z, Bai M, Shi X, Han G, Fan D. Meta-analysis: the significance of screening for JAK2V617F mutation in Budd-Chiari syndrome and portal venous system thrombosis. *Aliment Pharmacol Ther* 2011; **33**: 1087-1103 [PMID: 21395632 DOI: 10.1111/j.1365-2036.2011.04627.x]

14 **Qi X**, Zhang C, Han G, Zhang W, He C, Yin Z, Liu Z, Bai W, Li R, Bai M, Yang Z, Wu K, Fan D. Prevalence of the JAK2V617F mutation in Chinese patients with Budd-Chiari syndrome and portal vein thrombosis: a prospective study. *J Gastroenterol Hepatol* 2012; **27**: 1036-1043 [PMID: 22142461 DOI: 10.1111/j.1440-1746.2011.07040.x]

15 **Qi X**, Wu F, Ren W, He C, Yin Z, Niu J, Bai M, Yang Z, Wu K, Fan D, Han G. Thrombotic risk factors in Chinese Budd-Chiari syndrome patients. An observational study with a systematic review of the literature. *Thromb Haemost* 2013; **109**: 878-884 [PMID: 23447059 DOI: 10.1160/TH12-10-0784]

16 **Wang H**, Sun G, Zhang P, Zhang J, Gui E, Zu M, Jia E, Xu H, Xu L, Zhang J, Lu Z. JAK2 V617F mutation and 46/1 haplotype in Chinese Budd-Chiari syndrome patients. *J Gastroenterol Hepatol* 2014; **29**: 208-214 [PMID: 23980667 DOI: 10.1111/jgh.12379]

17 **Cheng D**, Xu H, Lu ZJ, Hua R, Qiu H, Du H, Xu X, Zhang J. Clinical features and etiology of Budd-Chiari syndrome in Chinese patients: a single-center study. *J Gastroenterol Hepatol* 2013; **28**: 1061-1067 [PMID: 23425079 DOI: 10.1111/jgh.12140]

18 **Gilbert R**, Salanti G, Harden M, See S. Infant sleeping position and the sudden infant death syndrome: systematic review of observational studies and historical review of recommendations from 1940 to 2002. *Int J Epidemiol* 2005; **34**: 874-887 [PMID: 15843394 DOI: 10.1093/ije/dyi088]

19 **Lau J**, Antman EM, Jimenez-Silva J, Kupelnick B, Mosteller F, Chalmers TC. Cumulative meta-analysis of therapeutic trials for myocardial infarction. *N Engl J Med* 1992; **327**: 248-254 [PMID: 1614465 DOI: 10.1056/NEJM199207233270406]

20 **Taylor R**, Najafi F, Dobson A. Meta-analysis of studies of passive smoking and lung cancer: effects of study type and continent. *Int J Epidemiol* 2007; **36**: 1048-1059 [PMID: 17690135 DOI: 10.1093/ije/dym158]

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