On Establishing a Standardized Chinese-Language Registration Platform for Meta-Analysis Postprints in China

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Abstract

Based on systematic reviews of extensive literature, proper Meta-analysis can yield more objective scientific evidence. Typically, foreign medical journals require authors to register their Meta-analysis and provide the registration platform and ID when submitting manuscripts. However, most domestic medical journals have no such requirements, resulting in variable quality of Chinese Meta-analyses. This article takes prognostic Meta-analyses as a sample, analyzes common errors in such literature, and recommends that China should establish a standardized Meta-analysis registration platform to improve the research quality of Chinese Meta-analyses and promote the development of evidence-based medicine.

Full Text

A Preliminary Discussion on Establishing a Standardized Chinese Registration Platform for Meta-Analysis in China

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Abstract

Based on systematic review of extensive literature, proper Meta-analysis can yield more objective scientific evidence. International medical journals typically require authors to register their Meta-analysis and provide the registration platform and ID upon submission. However, most domestic medical journals lack such requirements, resulting in inconsistent quality of Chinese Meta-analyses. This study uses prognosis-related Meta-analyses as a sample to analyze common

errors in such literature and recommends establishing a standardized Chinese registration platform for Meta-analysis to improve the quality of Chinese Meta-analysis research and promote the development of evidence-based medicine.

Keywords: Medical journals; Meta-analysis; Prognosis; Meta-analysis registration platform

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Over the 40 years since Gene Glass coined the term "Meta-analysis" in 1976, it has permeated various scientific fields and become an important tool for synthesizing research findings. Meta-analysis combines data from multiple studies to evaluate overall effects or effect sizes. It was first introduced in medicine and social sciences, particularly in clinical and epidemiological research, where humans are the subjects of study. Meta-analysis registration, similar to clinical trial registration, involves submitting a Meta-analysis research plan to a registration platform before conducting the analysis, which is then strictly followed during implementation. Currently, most international academic journals require authors to register their Meta-analysis and provide the registration platform and ID upon submission. The main registration platforms include: Cochrane Library (https://www.cochranelibrary.com), PROSPERO (https://www.crd.york.ac.uk/PROSPERO), JBI Global (https://jbi.global/), Campbell Collaboration (https://www.campbell.com/), Collaboration for Environmental Evidence (http://www.environmentalevidence.org/), and INPLASY (https://www.inplasy.com/) [1]. These platforms focus on different fields and have different emphases, with Cochrane Library, PROSPERO, and INPLASY being commonly used in the medical field.

The lack of registration requirements in the vast majority of Chinese medical journals is one reason for the inconsistent quality and even duplicate publication of Chinese Meta-analysis literature. This study uses "tumor prognosis-related Meta-analyses" published in Chinese medical academic journals as a sample to explore common errors in such literature and recommends establishing a standardized Chinese registration platform for Meta-analysis to provide an important resource platform for clinical researchers and improve the quality of Chinese Meta-analysis research.

We searched CNKI using the keywords "荟萃分析" (meta-analysis) or "Meta 分析" (Meta-analysis), limiting the document type to academic journals and the language to Chinese. We then searched the results using the keywords "肿瘤预后" (tumor prognosis) or "癌症预后" (cancer prognosis), retrieving 96 articles with data up to March 31, 2021. Since dissertations and conference papers vary in quality and do not represent the true level of Meta-analysis, this study only included literature published in academic journals. Two articles that did not provide detailed analysis data were excluded. The 94 retrieved articles were individually examined regarding literature screening criteria, statistical methods, data extraction, and description of conclusions.

1.2 Merging Single-Factor and Multi-Factor Outcome Measures

In single-factor analysis, spurious or indirect associations may occur between independent and dependent variables. For example, Gene A may have no effect on leukemia mortality risk, while Gene B is a factor influencing the outcome. However, if Gene A is simply strongly correlated with Gene B, exhibiting collinearity, single-factor analysis may show significant differences in mortality risk for leukemia patients carrying Gene A, leading to Gene A being mistakenly identified as an influencing factor and included in multi-factor analysis. In multi-factor analysis, adjusting for the effect of Gene B eliminates this "spurious association" between Gene A and leukemia mortality risk, indicating that Gene A is not actually an independent influencing factor on leukemia mortality risk. Among the 94 papers examined, 49% merged single-factor and multi-factor outcome measures, and 40% did not conduct subgroup analysis. Additionally, approximately 19% used single-factor analysis indicators even when multi-factor analysis outcome measures were available in the references. During data extraction, if the extracted data includes both single-factor and multi-factor measures, subgroup analysis should be performed to compare results between single-factor and multi-factor analyses.

1.3 Merging HR, RR, and OR

(1) RR (Risk Ratio): Also known as relative risk (RR), it refers to the ratio of the risk of an event occurring in an exposed group to that in an unexposed group. RR is applicable to cohort studies or randomized controlled trials. **(2) OR (Odds Ratio):** OR is the ratio of the proportion of cases in the exposed group to that in the unexposed group, also known as the odds ratio. OR is typically used in case-control studies but can also be used in prospective studies (when observation times are equal). **(3) HR (Hazard Ratio):** HR = h1(t)/h2(t), where h1(t) and h2(t) are the hazard functions for exposed and unexposed groups respectively at the same time point. The hazard function refers to the hazard rate function, conditional mortality rate, and instantaneous mortality rate, generally obtained using the Cox proportional hazards model. While RR and OR only consider differences in endpoint events, HR considers not only the occurrence of endpoint events but also the time to reach the endpoint and censored data. In statistics, when incidence is rare, RR can approximate OR, and the two can be directly merged. However, HR differs by introducing a time variable and measuring instantaneous risk, which may constantly change. Therefore, HR cannot be directly merged with RR or OR. If necessary, conversion can be performed using formulas provided in research by Huang Qiao et al. [2], noting that these formulas are only applicable to prospective studies. Among the 94 papers examined, approximately 19% directly merged RR and HR without explanation. Outcome measures using different concepts in survival analysis should not be mixed.

1.4 Data Extraction Errors

During data extraction, there can be considerable variability and subjectivity in how certain data fragments are defined or expected to be defined. Some authors even privately alter numbers to make their results more statistically significant. Others use web-scraping software to directly extract data from papers, though the accuracy of such extracted data is questionable. Regardless of the extraction method, anyone who has conducted a Meta-analysis knows that slight changes to a single number can affect study heterogeneity and publication bias, and even alter the statistical significance of pooled results. Additionally, in prognosis-related Meta-analyses, using Engauge Digitizer software to extract data from Kaplan-Meier survival curves and convert them to HR is common, but this method introduces errors and heterogeneity. Therefore, data extracted using this method should be clearly labeled and subjected to subgroup analysis alongside literature with directly obtained data. Among the 94 articles examined, 36% contained data extraction errors or data that could not be verified against original sources, and 29% used software to extract and convert data to HR without conducting subgroup analysis. Furthermore, in a study by Yang Bei et al. [3], one article extracted an HR confidence interval of (-∞, +∞), which lacks statistical significance, but the authors changed the confidence interval to (0, 1000) when pooling data, a practice that significantly affects Meta-analysis heterogeneity and can even alter its statistical significance.

1.5 Description of Conclusions

Chinese Meta-analyses on gene-prognosis correlations for common diseases consistently conclude that there is significant correlation or very important significance—much larger than what is typically seen in foreign Meta-analyses. In the medical field, effect sizes of certain factors on diseases often decrease over time with new evidence. Among highly cited randomized trials conducted in the past decade, approximately one-quarter of the proposed effect sizes have been refuted or found to be exaggerated by more than double [5]. Among the 94 articles examined, 43% used descriptive terms such as "significant," "close," and "important" in their conclusions. A more appropriate description would be "there may be an association or some effect."

2. Significance of Establishing a Chinese Meta-Analysis Registration Platform

2.1 Providing a Resource Platform for Domestic Scholars and Reducing Meta-Analysis Bias Meta-analysis is replacing traditional (narrative) reviews as a more objective and informative way to summarize medical research. Meta-analysis registration platforms aim to improve the quality of Meta-analysis research, avoid duplication, and reduce research bias. They provide a database for uploading complete Meta-analysis protocols in advance, allowing peer experts to review and verify each step of the Meta-analysis—including literature screening criteria, statistical methods, and data extraction—to avoid the various

errors described above. Registering a complete Meta-analysis protocol in advance enables authors to anticipate potential methodological challenges, helps minimize the possibility of reporting bias, and reduces resource waste caused by duplicate Meta-analyses by different author teams. Additionally, prospective registration creates a permanent public record of key protocol elements (including inclusion criteria and expected outcomes), allowing comparison between final results and registered expectations after publication so readers can determine whether any differences may introduce bias. Using a unique registration number helps track subsequent use or citation of the analysis, encourages authors to publish their research reports, and enables clinical guideline developers to use information about upcoming reviews to assist in guideline planning and scheduling. Therefore, establishing a comprehensive Chinese Meta-analysis registration platform in China provides an important resource platform for review researchers, promotes Meta-analysis transparency, reduces Meta-analysis bias, ensures research objectivity, and contributes to the development of evidence-based medicine in China.

2.2 Helping Build Modern Journal Infrastructure and Expand Journal Influence For journal centers capable of establishing Meta-analysis registration platforms, creating systematic review platforms is significant for expanding journal influence and building modern journal infrastructure. Taking the PROSPERO platform as an example, in the ten years since its launch in February 2011, total registrations increased from 284 to over 100,000 by the end of 2020. In 2016, researchers from 210 countries and regions worldwide visited the PROSPERO website more than 30,000 times. In 2021, PROSPERO registered over 3,200 protocols related to COVID-19, helping COVID-19 researchers prioritize research plans during the pandemic. The expanding influence of the PROSPERO platform is undeniable.

3. Recommendations and Prospects

3.1 Strengthening Awareness of Meta-Analysis Registration Although Meta-analysis registration is not currently explicitly mandatory, the number of Meta-analysis articles published by Chinese researchers is increasing exponentially [6], with China' s growth rate far exceeding the global level. Many Meta-analyses contain errors or are poorly executed, and the quality varies greatly. Among the 94 articles examined in this study, 77% contained errors in various aspects. This study only searched tumor prognosis-related Meta-analyses, but the examined items are equally applicable to Meta-analyses of other disease prognoses. Therefore, medical researchers should enhance their registration awareness, medical journals should strictly implement research registration, strengthen quality review of such literature, and provide the best evidence for clinical decision-making.

3.2 Strengthening Research and Attempting to Establish a Chinese Meta-Analysis Registration Platform Standardized and transparent clin-

ical trials and Meta-analyses are both important means to serve human health. China' s primary clinical trial registration platform has already been recognized by WHO [7]. Under the policy guidance of the "Opinions on Deepening Reform and Cultivating World-Class Scientific Journals" [8] and the new requirements emphasized by General Secretary Xi Jinping to "run first-class academic journals and various academic platforms well and strengthen domestic and international academic exchanges" [9], we recommend that national administrative departments actively support organizations such as the China Association for Science and Technology, Chinese Preventive Medicine Association, Chinese Medical Association, Chinese Medical Doctor Association, or well-developed medical journal centers to lead and organize strengthened research and attempt to establish a domestic Chinese Meta-analysis registration platform. This would provide an exchange platform for resource and information sharing in medical research, better share medical research results, and provide opportunities to publish high-level clinical research papers and participate in international peer competition and cooperation. Foreign Meta-analysis registration platforms are limited by language and have slow review speeds, especially for COVID-19-related research where registration review can take half a year or even a year. While the faster INPLASY registration platform has slightly insufficient recognition in domestic and international journals. Therefore, China should attempt to establish a standardized Chinese Meta-analysis registration platform that interfaces with foreign platforms, guide authors in the proper use of statistical methods in Meta-analysis according to the Cochrane Handbook, improve the research level and paper quality of domestic review scholars, and publish Meta-analyses with practical clinical guidance significance. Domestic scholars and medical students should also actively complete Meta-analysis protocol registration in advance according to international guidelines and statements to conduct more high-quality Meta-analyses. Otherwise, Meta-analysis will become a victim of China' s academic and educational systems [10].

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Note: Figure translations are in progress. See original paper for figures.