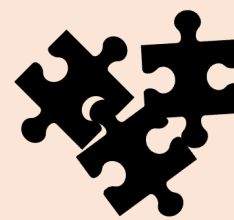


Figure Q&A on Meta-Analysis with ChatGPT

- Q1: Why is it important to create a protocol for conducting a systematic review?
- Q2: Please provide a list of five commonly used review management software for meta-analysis.
- Q3: Please list the five most common types of outcome data in systematic reviews.
- Q4: What are the elements included in the second version of the risk of bias tool for randomized controlled trials?
- Q5: How to choose between random effects model and fixed effects model in meta-analysis?
- Q6: Please list the common methods for effect estimation in meta-analysis.
- Q7: What are the methods commonly used for addressing heterogeneity in meta-analysis?
- Q8: How to handle missing data in meta-analysis?
- Q9: What factors should be considered when conducting a GRADE assessment in meta-analyses of cohort studies?
- Q10: What are the conditions for using a funnel plot to assess publication bias in meta-analysis?



A1: It is important to create a protocol for conducting a systematic review for several reasons:

- 1) Transparency: A protocol outlines the methods and procedures for conducting a systematic review in a transparent and systematic manner. This allows readers to understand how the review was conducted and assess its reliability and validity.
- 2) Reproducibility: A protocol ensures that the systematic review can be reproduced by other researchers. This is important for ensuring the accuracy and reliability of the review and allowing other researchers to build upon it.
- 3) Consistency: A protocol ensures that the review is conducted consistently and systematically, reducing the risk of bias and ensuring that all relevant studies are included.
- 4) Efficiency: A protocol helps to streamline the review process by providing a clear plan of action and identifying potential issues or challenges in advance. This can help to save time and resources and ensure that the review is completed in a timely manner.
- 5) Peer review: A protocol allows for peer review of the review methods and procedures, which can help to improve the quality of the review and increase its impact.

Overall, creating a protocol for conducting a systematic review is essential for ensuring transparency, reproducibility, consistency, efficiency, and peer review of the review methods and procedures.

- A2:**
- 1) Covidence: Covidence is a web-based software designed to facilitate systematic reviews and meta-analyses. It offers features such as importing references from various databases, screening and selection tools, data extraction, and risk of bias assessment.
 - 2) RevMan: RevMan is a software developed by the Cochrane Collaboration specifically for systematic reviews and meta-analyses. It allows reviewers to import references, assess risk of bias, extract data, and perform statistical analysis.
 - 3) DistillerSR: DistillerSR is a web-based software that offers tools for systematic review and meta-analysis. It includes features such as reference screening, data extraction, risk of bias assessment, and statistical analysis.
 - 4) EPPI-Reviewer: EPPI-Reviewer is a web-based software that facilitates the management of systematic reviews and meta-analyses. It includes features such as reference screening, data extraction, and risk of bias assessment.
 - 5) Stata: Stata is a statistical software that is commonly used for meta-analysis. It offers a range of features for data management, statistical analysis, and graphics. Stata allows reviewers to perform meta-analyses using various models, including fixed-effects and random-effects models.

- A3:**
- 1) Dichotomous data: This type of data has two possible outcomes, either "yes" or "no," or "present" or "absent." Examples of dichotomous data include mortality (death or no death), presence or absence of a disease or condition, and adverse events (occurrence or absence of a side effect).
 - 2) Continuous data: This type of data has a range of possible values that can be measured on a continuous scale, such as blood pressure, cholesterol levels, or body mass index (BMI).
 - 3) Time-to-event data: This type of data measures the time it takes for an event to occur, such as time to disease recurrence, time to death, or time to recovery.
 - 4) Ordinal data: This type of data represents an ordered set of categories, such as pain severity (mild, moderate, severe), level of functional impairment (mild, moderate, severe), or quality of life (excellent, good, fair, poor).
 - 5) Binary data: This type of data represents outcomes that can be measured as either a success or a failure, such as successful completion of a treatment program or attainment of a particular health goal.

A4: The second version of the Risk of Bias (RoB 2) tool for randomized controlled trials (RCTs) includes five domains for assessing the risk of bias in RCTs. These domains are:

- 1) Bias arising from the randomization process: This domain assesses the risk of bias in the randomization process, including sequence generation, allocation concealment, and implementation of the randomization.
- 2) Bias due to deviations from intended interventions: This domain assesses the risk of bias due to deviations from the intended interventions, including differences in the care provided to the intervention and control groups, co-interventions, and adherence to the intervention.
- 3) Bias due to missing outcome data: This domain assesses the risk of bias due to missing outcome data, including the reasons for missing data and the methods used to handle missing data.
- 4) Bias in the measurement of the outcome: This domain assesses the risk of bias in the measurement of the outcome, including blinding of outcome assessors, the validity and reliability of outcome measures, and the timing of outcome assessments.
- 5) Bias in the selection of the reported result: This domain assesses the risk of bias in the selection of the reported results, including selective outcome reporting, selective analysis reporting, and other biases in the reporting of results.

Each domain is evaluated based on a set of signaling questions that help assess the risk of bias. Based on the answers to these signaling questions, each domain is rated as having a low, some concerns, or high risk of bias. The overall risk of bias for a study is then determined based on the ratings of the individual domains.

A5: In meta-analysis, the choice between a random effects model and a fixed effects model depends on the nature of the heterogeneity present in the studies being combined.

Fixed effects model assumes that there is no variability in the true effect sizes beyond sampling error, and that all studies are estimating the same true effect size. Therefore, it gives more weight to larger studies with smaller standard errors, and smaller weight to smaller studies with larger standard errors. This model is appropriate when the studies are very similar in their methods, populations, and interventions.

Random effects model, on the other hand, assumes that there is variability in the true effect sizes beyond sampling error due to heterogeneity among the studies. This model gives more weight to studies with larger variability and less weight to studies with smaller variability. This model is appropriate when the studies are diverse in their methods, populations, and interventions.

To determine which model is appropriate for a particular meta-analysis, researchers often use statistical tests such as the Q-test or I-squared statistic to assess the degree of heterogeneity among the studies. If there is significant heterogeneity among the studies, then a random effects model is typically used, whereas a fixed effects model is used when there is little heterogeneity.

However, it's important to note that the choice between the two models is not always clear-cut and may depend on various factors such as the research question, the study design, and the sample size. Therefore, it's essential to consult with a statistician or meta-analysis expert to determine which model is appropriate for a particular meta-analysis.

A6: Meta-analysis is a statistical technique used to combine the results of multiple studies on the same topic to obtain a more accurate estimate of the overall effect. There are several methods for estimating the effect size in a meta-analysis, including:

- 1) Standardized Mean Difference (SMD): This method is used when studies measure the same outcome using different scales or units. It is calculated by dividing the difference in means between the treatment and control groups by the pooled standard deviation.
- 2) Odds Ratio (OR): This method is commonly used in studies that measure the association between a binary outcome and a treatment or exposure. It is calculated by dividing the odds of the outcome in the treatment group by the odds in the control group.
- 3) Risk Ratio (RR): This method is similar to OR, but it is used when the outcome is more common. It is calculated by dividing the risk of the outcome in the treatment group by the risk in the control group.
- 4) Hazard Ratio (HR): This method is used when studying time-to-event data, such as survival or recurrence. It is calculated by dividing the hazard rate in the treatment group by the hazard rate in the control group.
- 5) Mean Difference (MD): This method is used when studies measure the same outcome using the same scale or units. It is calculated by subtracting the mean in the control group from the mean in the treatment group.
- 6) Correlation Coefficient: This method is used when the studies report the correlation between two variables. It is used to estimate the strength and direction of the relationship between the variables.

It's worth noting that the choice of effect size depends on the type of data being analyzed and the research question being asked. Each method has its advantages and disadvantages, and the appropriate effect size should be selected based on the characteristics of the studies being analyzed.

A7: Heterogeneity in meta-analysis refers to the variability of effect sizes observed across studies included in the meta-analysis beyond what would be expected by chance alone. This heterogeneity can arise due to differences in study characteristics such as sample size, population characteristics, study design, interventions, and outcome measures. Heterogeneity can be assessed using statistical measures such as the I-squared statistic and Cochran's Q test.

There are several methods commonly used for addressing heterogeneity in meta-analysis, including:

- 1) Random-effects meta-analysis: This approach assumes that the true effect size varies across studies due to both random sampling error and systematic differences between studies. A random-effects model incorporates both sources of variability to estimate the overall effect size and its confidence interval.
- 2) Subgroup analysis: This approach involves dividing studies into subgroups based on relevant study characteristics and conducting separate meta-analyses for each subgroup. This allows for the examination of whether the effect size varies across subgroups and can help identify sources of heterogeneity.
- 3) Meta-regression: This approach involves modeling the relationship between the effect size and one or more study characteristics. Meta-regression can identify the study characteristics that are associated with heterogeneity and can be used to adjust for these characteristics in the meta-analysis.
- 4) Sensitivity analysis: This approach involves systematically removing one or more studies from the meta-analysis to determine their impact on the overall effect size. Sensitivity analysis can help assess the robustness of the meta-analysis results and identify influential studies that may be driving heterogeneity.

Overall, it is important to use multiple methods to address heterogeneity and to report the results of all analyses conducted to ensure transparency and accuracy in meta-analysis.

A8: Missing data can be a challenge in meta-analysis, as it can affect the precision and validity of the overall estimate. Here are some steps to handle missing data in meta-analysis:

- 1) Identify the extent of missing data: Examine the data carefully to determine the percentage of missing data and the potential reasons for the missing data.
- 2) Contact study authors: If possible, contact the authors of the original studies to obtain missing data. This can include additional statistical information, such as standard errors, sample sizes, and effect sizes.
- 3) Use imputation methods: If the missing data cannot be obtained from the authors, imputation methods can be used to estimate missing data values. These methods involve replacing missing data with plausible values based on the available data and statistical assumptions.
- 4) Conduct sensitivity analysis: To evaluate the potential impact of missing data on the meta-analysis results, sensitivity analyses can be performed. These analyses involve removing studies with missing data or using different imputation methods to assess the robustness of the meta-analysis results.
- 5) Interpret the results carefully: The presence of missing data can affect the precision and validity of the meta-analysis results. Therefore, it is important to interpret the results with caution and consider the potential impact of missing data on the conclusions.

A9: GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) is a framework used to assess the quality of evidence and the strength of recommendations in systematic reviews and meta-analyses. When conducting a GRADE assessment in meta-analyses of cohort studies, the following factors should be considered:

- 1) Study limitations: The quality of the evidence should be assessed based on the limitations of the cohort studies, such as risk of bias, inconsistency, indirectness, imprecision, and publication bias.
- 2) Consistency of results: The consistency of the results across the cohort studies should be assessed. If the results are consistent, the quality of the evidence is likely to be higher.
- 3) Directness: The extent to which the cohort studies address the research question directly should be considered. If the cohort studies provide direct evidence, the quality of the evidence is likely to be higher.
- 4) Precision: The precision of the estimates should be assessed. The quality of the evidence is likely to be higher if the cohort studies provide precise estimates.
- 5) Publication bias: Publication bias should be assessed, as it can affect the quality of the evidence.
- 6) Effect size: The magnitude of the effect size should be considered. The quality of the evidence is likely to be higher if the effect size is large.
- 7) Coherence: The coherence of the results with the known biology of the disease should be considered. If the results are coherent with the known biology, the quality of the evidence is likely to be higher.
- 8) Dose-response relationship: The presence of a dose-response relationship should be assessed. If a dose-response relationship is present, the quality of the evidence is likely to be higher.
- 9) Grading the overall quality of evidence: Based on the above factors, the overall quality of evidence should be graded as high, moderate, low, or very low.

By taking into account these factors, a GRADE assessment can provide a comprehensive and transparent evaluation of the quality of evidence in meta-analyses of cohort studies.

A10: A funnel plot is a graphical method used to investigate publication bias in meta-analysis. Publication bias occurs when the publication of research results is influenced by the direction or significance of their findings, leading to a biased sample of studies included in the meta-analysis. To use a funnel plot to assess publication bias, the following conditions should be met:

- 1) The meta-analysis should include at least 10 studies. This is because the funnel plot is based on the assumption that a large number of studies will produce a symmetrical distribution of effect sizes.
- 2) The studies should have a wide range of sample sizes. Studies with larger sample sizes will generally have more precise estimates of effect size, and therefore their effect sizes will cluster closer to the true effect size. Smaller studies, on the other hand, will have wider confidence intervals around their effect sizes and will produce more scattered points on the funnel plot.
- 3) The studies should be homogeneous. Homogeneity means that the studies are similar enough in terms of their methodology, study population, and other characteristics that the effect sizes they produce are consistent. If there is significant heterogeneity among the studies, the funnel plot may not accurately reflect publication bias.
- 4) The outcome variable should be continuous. Funnel plots are not suitable for dichotomous outcomes, as the effect sizes are measured using different scales and standard errors.
- 5) The studies should be at low risk of bias. If there are significant differences in the risk of bias among the studies, the funnel plot may not accurately reflect publication bias.

If these conditions are met, a funnel plot can be a useful tool to assess publication bias in a meta-analysis. However, it should be used in conjunction with other methods, such as Egger's regression test, to provide a more comprehensive analysis of publication bias.