

Complete Process of Conducting a Meta-Analysis

A **meta-analysis** is a statistical technique that combines the results of multiple independent studies addressing the same research question to obtain an overall estimate of the effect. It is usually conducted alongside a **systematic review** and follows internationally recognized guidelines such as **PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses)**.

Recommended Study Design by Research Objective

Research Objective	Preferred Study Design
Treatment effectiveness	Randomized Controlled Trial (RCT)
Risk factor or exposure	Cohort or Case-Control
Disease prevalence	Cross-sectional
Diagnostic accuracy	Diagnostic accuracy study
Correlation between variables	Cross-sectional or Cohort
Prognosis/Survival	Cohort (often reporting Hazard Ratios)

Step 1: Define the Research Question

The first step is to formulate a clear and focused research question.

In clinical research, the **PICO framework** is commonly used:

- **P** – Population
- **I** – Intervention (or Exposure)
- **C** – Comparison
- **O** – Outcome

Examples:

- Does physical exercise reduce depression?
- Is vitamin D associated with diabetes?
- Does air pollution increase the risk of asthma?

Step 2: Develop a Research Protocol

Before starting the review, prepare a detailed protocol that describes:

- Research objectives
- Eligibility criteria
- Search strategy

- Outcomes of interest
- Data extraction methods
- Statistical analysis plan
- Risk of bias assessment

For health-related studies, protocols are often registered in **PROSPERO**.

Step 3: Conduct a Systematic Literature Search

Search multiple electronic databases to identify all relevant studies.

Common databases include:

- PubMed
- Scopus
- Web of Science
- Embase
- Cochrane Library
- Google Scholar

Example search strategy:

(diabetes OR hyperglycemia)

AND

(vitamin D)

AND

(cohort OR case-control)

Step 4: Screen and Select Studies

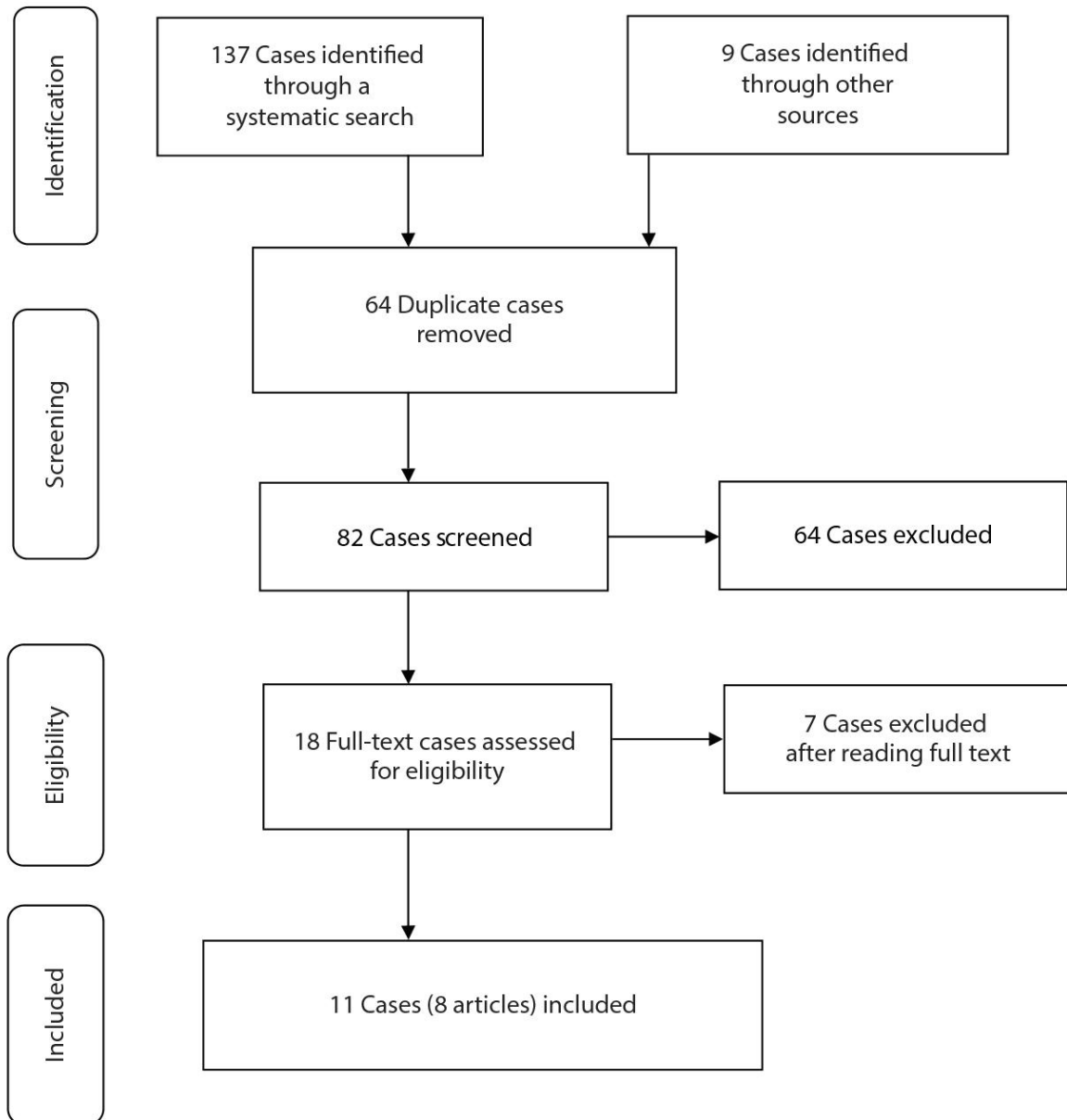
Study selection is usually performed according to the **PRISMA** guidelines.

The screening process consists of:

1. Remove duplicate records.
2. Screen titles.
3. Screen abstracts.

4. Review full-text articles.
5. Select studies that meet the eligibility criteria.

Figure 1. PRISMA Flow Diagram Indicating the Flow of Information Through the Search and Study Selection Process



Step 5: Define Inclusion and Exclusion Criteria

Inclusion Criteria

- Original research articles
- Human studies
- English-language publications
- Studies reporting sufficient statistical information
- Appropriate study design

Exclusion Criteria

- Review articles
- Editorials
- Conference abstracts
- Animal studies
- Case reports

Step 6: Extract Data

Extract the required information from each included study using a standardized data extraction form.

Typical variables include:

- Author
- Publication year
- Country
- Study design
- Sample size
- Participant characteristics
- Intervention or exposure
- Outcome
- Effect size

- Standard error or confidence interval

Example:

Study	Year	Country	Sample Size	Effect Size	SE
Smith	2022	USA	250	0.45	0.08

Step 7: Assess Study Quality or Risk of Bias

Evaluate the methodological quality of each study.

Common assessment tools include:

- Newcastle–Ottawa Scale (NOS)
- Cochrane Risk of Bias Tool (RoB 2)
- ROBINS-I
- Joanna Briggs Institute (JBI) Checklist

Step 8: Choose an Appropriate Effect Size

The choice depends on the type of outcome.

Continuous Outcomes

- Mean Difference (MD)
- Standardized Mean Difference (SMD)
- Hedges' g

Binary Outcomes

- Odds Ratio (OR)
- Risk Ratio (RR)
- Risk Difference (RD)

Correlation Studies

- Pearson's correlation coefficient (r)
- Fisher's Z transformation

Diagnostic Accuracy Studies

- Sensitivity
- Specificity
- Diagnostic Odds Ratio (DOR)

Step 9: Calculate Effect Sizes

If the published study does not report an effect size, calculate it from the available summary statistics.

For example,

Standardized Mean Difference

$$d = \frac{\bar{X}_1 - \bar{X}_2}{S_p}$$

Odds Ratio

$$OR = \frac{ad}{bc}$$

Step 10: Compute the Variance of Each Effect Size

Each effect size must be accompanied by its sampling variance.

For Cohen's d ,

$$\text{Var}(d) = \frac{n_1 + n_2}{n_1 n_2} + \frac{d^2}{2(n_1 + n_2 - 2)}.$$

The variance is used to calculate study weights in the meta-analysis.

Step 11: Assess Heterogeneity

Evaluate the variability among study results using:

- Cochran's Q statistic
- Higgins' I^2 statistic
- Between-study variance (τ^2)

Interpretation of I^2 :

- 0–25%: Low heterogeneity
- 25–50%: Moderate heterogeneity
- 50–75%: Substantial heterogeneity
- 75%: Considerable heterogeneity

Step 12: Select the Meta-Analysis Model

Fixed-Effect Model

Appropriate when studies estimate a common true effect and heterogeneity is low.

Random-Effects Model

Appropriate when true effects are expected to differ across studies due to clinical or methodological diversity.

Step 13: Generate a Forest Plot

A forest plot summarizes:

- Individual study estimates
- Confidence intervals
- Study weights
- Overall pooled effect

Step 14: Assess Publication Bias

Publication bias can be examined using:

- Funnel plot
- Egger's regression test
- Begg's rank correlation test

Step 15: Perform Sensitivity Analysis

Evaluate the robustness of the results by:

- Removing one study at a time (leave-one-out analysis)
- Excluding low-quality studies
- Comparing alternative statistical models

Step 16: Conduct Subgroup Analysis (Optional)

Explore whether the effect differs across subgroups.

Examples include:

- Male vs. Female
- Asia vs. Europe
- Adults vs. Children
- High-income vs. Low-income countries

Step 17: Perform Meta-Regression (Optional)

Meta-regression investigates whether study-level characteristics explain heterogeneity.

Possible moderators include:

- Mean age
- Body Mass Index (BMI)
- Publication year
- Follow-up duration
- Sample size