Review Article

Synthesizing Quantitative and Qualitative Studies in Systematic Reviews: The Basics of Meta-analysis and Meta-synthesis

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Introduction

It is quite challenging for researchers to stay current on all of the new and updated information being published in a research area. Summarizing the findings of a specific research topic in the form of a review can aid researchers and audiences become more informed on a research topic. Reviews provide readers the benefit of having summarized information on a research topic without reading all of the published evidence. Well-conducted reviews often provide synthesized results that are an excellent source of knowledge for evidence-based medicine and practice. Synthesized results are important, as research questions are typically studied by different researchers and findings often vary, which makes evidence-based decisions difficult. Properly synthesized results from different studies minimize bias, increase strength of evidence, and provide more reliable findings from which better conclusions and decisions can be made. In this paper, we will discuss how the results from different studies can be synthesized through two of the most common approaches: meta-analysis and meta-synthesis. Our objective is to introduce readers to these two important data synthesis processes with examples.

What is a review?

A review, commonly known as a literature review, is a process of assessing the existing literature to answer a specific research question or summarize a broad topic. Reviews involve searching the existing literature through a defined process using specific inclusion criteria and summarizing findings from the selected literature[1, 2].

Why do we need to conduct reviews?

The general objective of conducting a review is to summarize the existing knowledge on a topic and identify the gaps, if any, for further research. The literature review helps determine what is already known about a research topic, how extensively the topic has been researched in the past, and identify key questions about a topic that need further research. Other reasons for conducting a review on a specific topic include refining and generating new research ideas, assessing the current state of research in an area and creating awareness, identifying the experts and data sources in a particular research area, determining the methodologies used in past research, and demonstrating a person's understanding of a research topic. Ultimately, reviews help research move forward and provide evidence to support research findings. Reviews can be of different types and depend largely on the purpose of the review.

What are the different types of reviews?

Review articles vary based on the purpose of the review and the research question being addressed[3]. The most common types of reviews include literature reviews, critical reviews, scoping reviews, systematic reviews, qualitative systematic reviews, realist reviews, and umbrella reviews. Detailed discussions of the different types of reviews have been addressed in previous studies[2, 3].

What is the systematic way of conducting a review?

A review should be conducted through maintaining a proper process. There exist systematic methodological approaches for conducting reviews. Although there are variations in the methodological approaches of conducting reviews due to variability in the purpose and objective of the review, all reviews must follow a few common steps. These common steps include identification of a clear research question, performing a comprehensive literature search, conducting a rigorous screening, extracting data from the selected studies, and summarizing and synthesizing information from the studies [Figure 1].

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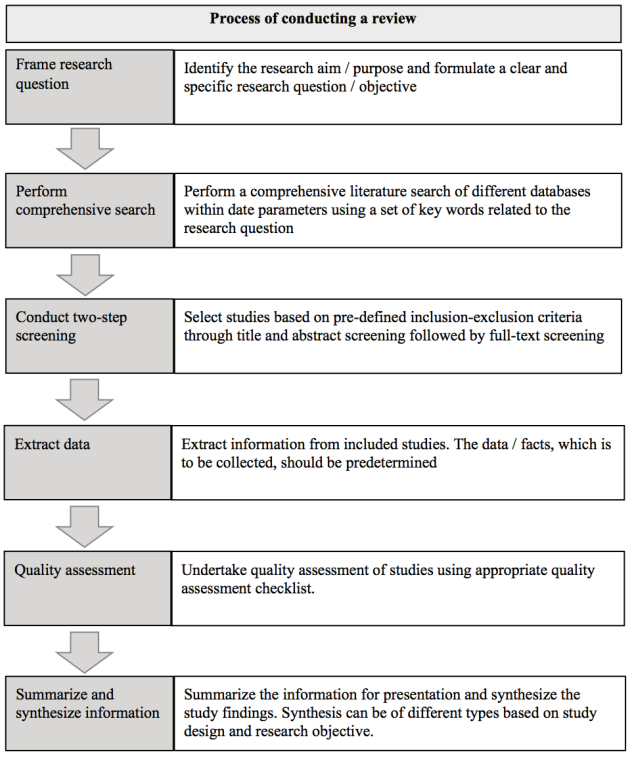

Figure 1. Process of conducting a systematic review.

Depth of synthesis in reviews

The nature of a review also depends on the depth and amount of information to be synthesized from the selected studies [Figure 2]. Synthesizing information from different studies can be broadly classified into two categories based on the type of study being used: quantitative or qualitative. Quantitative studies are synthesized through a process called meta-analysis, while qualitative studies are synthesized through meta-synthesis. In this article, we will discuss these two very important types of synthesizing processes that represent the deepest level of data synthesis.

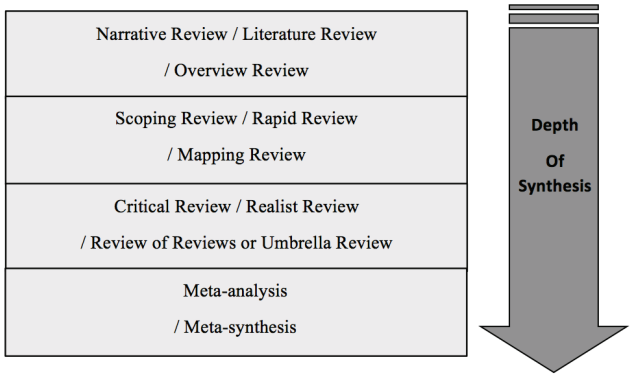

Figure 2. Reviews in relation to the depth of synthesis.

Methodological Overview - Meta-analysis of quantitative studies

Meta-analysis is a statistical procedure that helps combine/pool results from different previous quantitative studies on a specific research question and derives conclusions about that research question. Often, meta-analysis provides a more precise estimate of an outcome than an individual study alone can. Meta-analysis helps summarize findings from many quantitative studies that are often complex and conflicting in nature and plays an important role in evidence based medicine[4]. Besides pooling the results from multiple studies, meta-analysis also helps with examining the heterogeneity of study results. Meta-analysis is often considered a subset of a systematic review. It is commonly performed in conjunction with a systematic review, although a systematic review need not contain a meta-analysis[4].

Process of conducting meta-analysis with example

Meta-analyses are mostly conducted after systematic reviews. The process associated with systematic reviews is also applicable to meta-analysis. We discuss below the key steps of performing a meta-analysis on quantitative studies [Box 1].

Box 1. Meta-analysis process on quantitative studies.

Steps for Meta-analysis

- ✓ Frame an appropriate research question, purpose, or aim
- ✓ Perform a comprehensive search using carefully selected key words
- ✓ Select studies based on pre-defined, well-justified inclusion-exclusion criteria
- ✓ Extract data according to the meta-analysis objective
- ✓ Perform study quality assessment using appropriate checklist
- ✓ Summarize results from the selected studies
- ✓ Obtain pooled estimate through appropriate statistical methods
- ✓ Assess heterogeneity in the studies
- ✓ Assess publication bias in the studies
- ✓ Report and interpret findings

Step 1. Frame the research question

As with systematic reviews, a good meta-analysis is characterized by a thorough and disciplined literature search of a research question[4]. The research question should be clear, and there should be a specific purpose for conducting the meta-analysis.

Step 2. Comprehensive search to identify the relevant quantitative studies

To identify the relevant studies associated with the research question, a comprehensive search is performed on different databases within a parameter of time using a set of key words related to the research question. Typically, published papers are searched in electronic databases such as PubMed, EMBASE, MEDLINE, Web of Science, ScienceDirect, CENTRAL, Google Scholar, etc. To provide a comprehensive search, database searches are often augmented with hand searches of library resources for relevant papers, abstracts, conference proceedings, and books. In addition, undertaking a cross-reference check, following up on citations in review papers, and contacting experts working in the relevant field are also important methods of completing a comprehensive search[4].

Step 3. Screening the quantitative studies

After performing a comprehensive search, studies are included for meta-analysis based on certain pre-defined inclusion-exclusion criteria. Usually, two assessors independently decide which studies to include or exclude. If a study is excluded from meta-analysis, reasons should be given. There are no standard criteria for inclusion-exclusion of studies in meta-analysis, and it largely depends on the expertise of the researchers who are conducting the study. Screening is generally performed in two steps: title and abstract screening as a first step followed by full-text screening.

Step 4. Extracting the data

Once the final papers have been selected, pre-determined data are extracted on which the meta-analysis is performed. Meta-analysis is generally performed to derive a pooled estimate of association between exposure and outcome. In this scenario, the measures of association, such as odds ratio (OR) or risk ratio (RR), are extracted from the selected studies[5]. Meta-analysis is also conducted on measures of disease burden like prevalence or proportions. In this scenario, the prevalence estimates are extracted from the selected studies[6]. In addition, meta-analysis can also be conducted for model-performance parameters. In this scenario, C-statistics or expected/observed ratio estimates are extracted from the selected studies[7].

Step 5. Study quality assessment

Quality of the studies is assessed after performing the screening based on certain criteria/checklists. Depending on the type of study and subject matter, different checklists exist from which to assess quantitative study quality, and investigators need to choose the appropriate checklist for their study. Table 1 provides name of some major study quality assessment tools/checklists to assess quality of different types of quantitative studies[8].

Table 1. Quantitative study quality assessment tools

Study Quality Assessment Tool	For Use to Assess Types of Study
The Cochrane Collaboration's Tool[9]	Randomized Controlled Trials (RCTs)
The Newcastle-Ottawa Scale[10]	Cohort and Case-control studies
The Methodological Index for Non-Randomized Studies (MINORS)[11]	Non-randomized Interventional studies
The Agency for Healthcare Research and Quality (ARHQ) Methodology Checklist[12]	Cross-sectional studies
The Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) Tool[13]	Diagnostic accuracy test studies
Assessment of Multiple Systematic Reviews (AMSTAR) Measurement Tool[14]	Systematic reviews/meta-analyses
The Appraisal of Guidelines, Research and Evaluation (AGREE)-II Instrument[15]	Clinical practice guidelines
The Systematic Review Centre for Laboratory Animal Experimentation's (SYRCLE) Risk of Bias Tool[16]	Animal studies

Step 6. Summarize information

Information from the finally selected studies is summarized for reporting. Summarized information is generally presented in tabular form for presentation.

Step 7. Obtain pooled estimate of the effect measure

Meta-analysis basically consists of pooling/combining different effect measures (e.g., odds ratio, risk ratio, prevalence) from different studies, assessing if any heterogeneity exists among the studies, and evaluating publication bias. While performing a meta-analysis, the first thing to decide is the type of model to use for the analysis. Fixed effects and random effects are the two different types of models used for the meta-analysis. These models have different underlying assumptions, and investigators need to decide which model to use in performing the meta-analysis. Different software with default commands is available to perform the meta-analysis (e.g., "metan" command in STATA software). Software provides the results of the analysis both in tabular and graphical form. A forest plot is the most popular form of graphical presentation of pooled results from meta-analysis. Figure 3 shows a forest plot of prevalence of cardiovascular disease (CVD) in the Bangladeshi population, a meta-analysis conducted by Chowdhury et al[17].

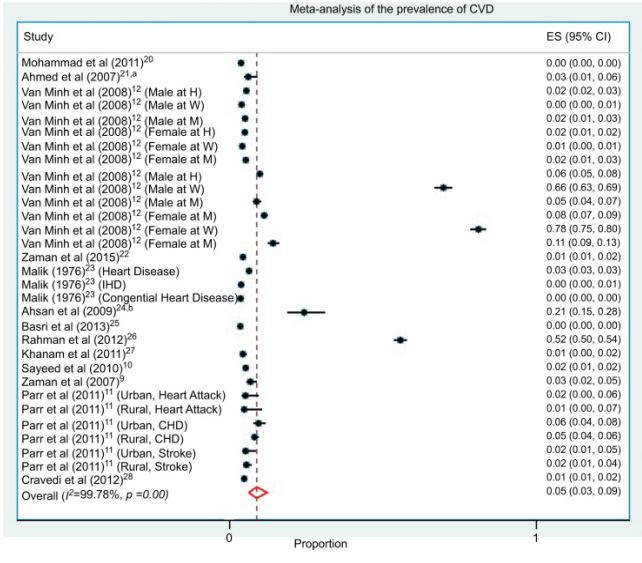

Figure 3. Forest plot of prevalence with 95% CIs of CVD in the Bangladeshi population. Reused under the Creative Commons Attribution - Non Commercial (unported, v3.0) License. From Chowdhury MZI et al. Prevalence of cardiovascular disease among Bangladeshi adult population: a systematic review and meta-analysis of the studies. Vasc Health Risk Manag. 2018; 14: 165–181.

Step 8. Assess study heterogeneity

One significant feature of performing a meta-analysis is it allows investigators to examine sources of heterogeneity, if present, among studies. There could be several sources of heterogeneity, and identifying sources of heterogeneity often leads to more effective targeting of prevention and treatment strategies and helps generate new hypotheses about a research topic.

There are different statistical tools available to assess the presence of heterogeneity; Cochran's Q statistic and Inconsistency index I^2 are the two major ones. Sub-group analysis and meta-regression are the foremost ways of

examining the reasons for heterogeneity. Investigators need to be cautious when interpreting the summary results from meta-analysis when heterogeneity exists.

Step 9. Assess publication bias

Meta-analysis helps identify publication bias in studies. There is a tendency to publish large studies that contain significant positive results. Small studies with non-significant results are often ignored and are not published. Examining publication bias is important, and several methods are available to assess it. A funnel plot, a graphical way of evaluating publication bias, is perhaps the most popular method. Figure 4 provides an example of a funnel plot where the authors assessed publication bias of the studies that evaluated the prevalence of CVD in the Bangladeshi population[17].

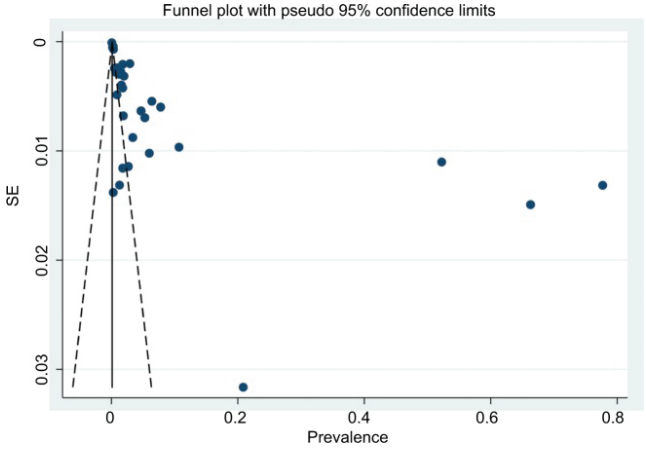

Figure 4. Funnel plot for publication bias. Reused under the Creative Commons Attribution - Non Commercial (unported, v3.0) License. From Chowdhury MZI et al. Prevalence of cardiovascular disease among Bangladeshi adult population: a systematic review and metaanalysis of the studies. Vasc Health Risk Manag. 2018;14:165–181.

Step 10. Interpreting results and reporting findings

This is the final step of meta-analysis and consists of presenting the research findings that emerged through the process of quantitative meta-analysis and interpreting the results.

Benefits of conducting meta-analysis

Meta-analyses are preformed to assess the strength of evidence that exists regarding a research question. Generally, meta-analyses are performed to produce an overall estimate of an effect and measure the precision of that estimate based on multiple studies. One key objective of meta-analysis is to obtain a single summary estimate of an effect using multiple studies that provide genuine evidence that an effect exists. Validity of a research question or hypothesis is sometimes hard to justify based on the results of a single study, as results typically vary from one study to the next. Meta-analysis provides a mechanism to synthesize data across studies by applying an objective formula and coming up with a single estimate that is often more precise and reliable. Combining individual studies allows more data to use in estimating the results more precisely and accurately along with a greater statistical power to detect an effect. Generalizing the results from a meta-analysis makes more sense than those from single studies, as the process incorporates different sets of populations into the analysis and thus accounts for variations between those groups that will most likely respond distinctively.

Case Study: synthesizing quantitative studies through meta-analysis

Chowdhury MZI et al[17]. conducted a study on the prevalence of CVD among the Bangladeshi adult population. They summarized and synthesized information on the prevalence of CVD from all published scientific literature through a systematic review and meta-analysis. It was a quantitative study (effect measure was prevalence and had numerical value) and the authors used meta-analysis to synthesize the information. The authors clearly stated their research question (to assess the prevalence of CVD); undertook a proper search strategy using a set of key words in three databases (MEDLINE, EMBASE, and PubMed) and in the grey literature; selected studies based on a set of inclusion-exclusion criteria; assessed study quality using an appropriate checklist; summarized the information; and lastly synthesized information through meta-analysis. While conducting the meta-analysis, the authors used a random effects model to pool the overall prevalence; assessed study heterogeneity using Cochran's Q statistic and I^2 statistic; assessed sources of heterogeneity through a stratified analysis and meta-regression; and assessed publication bias through a funnel plot.

Methodological Overview - Meta-synthesis of qualitative studies:

Meta-synthesis is a process that helps researchers synthesize qualitative studies on a specific topic and translate results into one interpretation that leads to a deeper and more complete understanding of the topic[18]. Synthesizing the findings from a group of selected qualitative studies, as well as in-depth analysis and interpretation of those findings, constitutes meta-synthesis[18]. Readers often fail to distinguish the term meta-synthesis from meta-analysis. The two terms are different and serve different purposes. The purpose of meta-analysis is to collect, aggregate, and summarize quantitative studies and express the summarized results in a common and standardized numerical value (i.e., an effect size), while the purpose of meta-synthesis is not just summarizing the findings but also interpreting the findings from the qualitative studies. Meta-analysis often helps determine cause and effect inferences, while meta-synthesis focuses on examining a deeper understanding of the meaning of a specific topic.

Process of conducting meta-synthesis with example

The meta-synthesis process consists of several steps that help researchers identify a specific research question and how to address that research question through searching, selecting, appraising, summarizing, and combining evidence from multiple studies[18]. We discuss below the key steps of conducting a meta-synthesis on qualitative studies [Box 2].

Box 2. Meta-synthesis process on qualitative studies.

Steps for Meta-Synthesis	
	✓ Frame an appropriate research question, purpose, or aim ✓ Perform a comprehensive search using carefully selected key words ✓ Select studies based on pre-defined, well-justified inclusion-exclusion criteria ✓ Perform study quality assessment using appropriate checklist ✓ Extract data according to the meta-synthesis objective ✓ Summarize results from the selected studies ✓ Perform qualitative synthesis on the selected studies through appropriate methods ✓ Report and interpret findings

Step 1. Frame the research question

Like meta-analysis, identifying the research purpose and formulating a specific research question is the first step of meta-synthesis. In meta-synthesis, research questions are often broad but can be refined and reduced in scope over the course of undertaking the synthesis.

Step 2. Comprehensive search to identify relevant qualitative studies

At this stage, a comprehensive literature search is performed. Generally, the search is performed on different databases within a parameter of dates using a set of key words related to the research question. Identifying key words related to the research question and potential databases for the search requires considerable effort. Besides the databases, studies ore often identified through a grey literature search, which includes checking reference lists, searching citations, hand searching through back issues of selected journals, searching authors, searching dissertations, theses, and research reports, etc.

Step 3. Screening the qualitative studies

Inclusion and exclusion criteria are set to screen the studies through the steps of title/abstract screening and full-text screening. Setting appropriate inclusion and exclusion criteria might be challenging. Having a more flexible criterion helps ensure inclusion of all potential studies. A set of key words, date ranges, numbers and types of databases, and inclusion-exclusion criteria all determine how many articles will be included in the meta-synthesis.

Step 4. Study quality assessment/appraisal

At this stage, a careful appraisal of selected studies is performed. This appraisal often determines whether a study should be included in the final synthesis. Studies often vary in terms of their quality, with some studies being weak. A set of criteria needs to be determined to identify a study's weakness, strength, or asses its quality. Generally, these criteria are based on comparison parameters such as a clear research question and purpose, an appropriate methodological approach and analysis for the research question, claims that are supported by sufficient evidence, etc. There are some formal checklists available that are frequently used for evaluating qualitative studies. Some of those checklists are more prescriptive and comprehensive than others, despite some overlap. Performing an appraisal of qualitative studies is not easy because the methodological approaches of these studies are quite diverse and difficult to judge. There is also debate as to whether quality criteria should be applied in qualitative research, and there is no consensus on which criteria to use and how to apply them. Table 2 provides a list of tools/checklists that can be used to assess the quality of qualitative studies.

Table 2. Qualitative study quality assessment tools

Study Quality Assessment Tool	Brief Description
The Critical Appraisal Skills Programme (CASP) Checklist[19]	A 10 questions checklist designed to deal elaborately with some of the principles or assumptions that characterize qualitative research.
The Joanna Briggs Institute Qualitative Assessment and Review Instrument (JBI-QARI)[20]	A critical appraisal tool contains 10 questions and designed to assess the methodological quality of a qualitative study and to determine the extent to which a study has addressed the possibility of bias in its design, conduct and analysis.
The Cochrane Collaboration's Qualitative Research Methods Group[21]	A supplemental handbook to guide the critical appraisal of qualitative evidence.

Step 5. Extract data and summarize information

Information from the finally selected papers is extracted for meta-synthesis and summarized/synthesized for the purpose of reporting, presenting, and interpreting the information. The debates among academics about the appropriateness of combining qualitative studies because of the different types of qualitative research designs, theoretical assumptions, or methods of data collections used across studies should be considered. Software like NVivo can help researchers to gain richer insights from qualitative and mixed-methods studies. NVivo offers several benefits including managing, querying and coding qualitative articles, quality assessment and help in thematic analysis of qualitative articles[22].

Step 6. Synthesize information

There are different approaches for synthesizing qualitative studies, some of which are based on methods used in primary research[18]. Table 3 presents a non-inclusive list of major approaches often used for synthesizing information from qualitative studies in greater depth. Several factors, such as the question asked, subject matter, number of studies identified, and knowledge and expertise of the study team, determine which method will be used for synthesizing the studies.

Each of these methods has its own strengths and weaknesses, but they are difficult to compare, as few guidelines exist to evaluate them[18].

Table 3. Methods for synthesizing qualitative studies

Method	Brief Description
Meta-ethnography[23]	The process involves several steps, such as the reading and re-reading of studies; determining how the studies are related by listing key concepts and comparing and contrasting them; translating the studies and synthesizing the translations to identify concepts that go beyond individual studies and can be used to produce a new interpretation or construct.
Qualitative meta-synthesis[24]	Interpretive integration of qualitative research findings across studies are conducted by examining key concepts, themes, and/or metaphors with the purpose of preserving and maintaining the integrity and context of the original manuscripts.
Qualitative meta-summary[25]	A set of techniques for the quantitative aggregation of qualitative research findings. The process includes the extraction, grouping, and formatting of findings and the calculation of frequency and intensity effect sizes, which eventually helps produce mixed research synthesis.

Step 7. Report findings

This step consists of presenting the research findings that have emerged through the process of qualitative meta-synthesis and interpreting them. Research findings are often presented through visual display (charts, figures, and tables). Some common items a report should contain include search strategy, number of studies at each stage of the search process, and a summary of the studies selected for synthesis.

Benefits of conducting meta-synthesis

There are several reasons for conducting meta-synthesis. A growing interest and increased application of qualitative research over the past decade has put more emphasis on synthesizing information from qualitative studies through meta-synthesis. Meta-synthesis can help identify common themes by synthesizing a group of qualitative studies and compare and contrast different aspects of a topic from different studies, which ultimately helps gain a deeper insight into and understanding of that topic, which a single study may fail to provide[18].

Evidence-based research, practice, and policy can be enhanced greatly through meta-synthesis as it allows us to expand our knowledge. This extended knowledge can help us understand not only why a practice or intervention is effective or not, but also when, why, or how an intervention could be more effective[18]. Meta-synthesis can also contribute where knowledge application is complicated, as different research shows different ways of managing an intervention or practice. Synthesizing those research findings can provide a solution to that problem. Finally, meta-synthesis can identify potential gaps and omissions that exist in current research, include additional dimensionality, and elaborate on the interpretation of qualitative studies.

Case study: synthesizing qualitative studies through meta-synthesis

Tong et al[26]. conducted a study where they performed a meta-synthesis of qualitative studies that explored experiences of parents whose children have chronic kidney disease. The objective of their synthesis was to inform the development, implementation, and evaluation of support strategies offered by general practitioners and multidisciplinary teams for those parents. The authors performed a search using a set of 52 words in five electronic databases. A set of inclusion-exclusion criteria was used to select the studies for the synthesis. The authors used a composite checklist to assess quality of the studies and used a constant comparison method to perform meta-synthesis.

Conclusion

Synthesizing approaches like meta-analysis and meta-synthesis are viable and necessary tools in strengthening our understanding of a research topic. Synthesizing information from multiple studies through meta-analysis and meta-synthesis can help overcome the limitations of study size, include diverse populations, provide the opportunity to evaluate new hypotheses, help researchers arrive at higher order interpretations, and generate theory from multiple studies. Having a proper understanding and knowledge of the process of synthesizing information from multiple studies is crucial for researchers. We believe this paper will provide readers with a basic understanding of this very important topic.

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