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Understanding Network Meta-Analysis: A Practical Introduction for Nurses

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ABSTRACT

Aims: This paper examines network meta-analysis (NMA) as a methodological advancement in nursing research and discusses considerations for interpreting and applying NMA results in clinical practice.

Design and Methods: Methodological discussion.

Results: The NMA method simultaneously evaluates multiple interventions by combining direct and indirect evidence. The publication of NMA articles in nursing journals has been increasing. However, interpreting NMA results can be complex and challenging. In this paper, we outline the prerequisites and assumptions of NMA, provide a graphical representation, discuss effect estimation and quality of evidence and give an overview of applying NMA results in clinical practice.

Conclusion: NMA is a valuable analytical approach in nursing research that can provide high-level evidence to guide clinical decision-making. Accurate interpretation of NMA findings is necessary to inform clinical practice. This paper serves as an introduction to NMA for nurses unfamiliar with the approach.

Implications for the Profession: NMA is a powerful statistical technique for assessing the relative effectiveness of different nursing interventions and informing evidence-based nursing guidelines. When interpreting the results, nurses should consider the certainty of evidence and the practical value of the results and be cautious of misleading conclusions.

Impact: NMA is a recent analytical method in nursing research. This practical introduction seeks to enhance comprehension of NMA and the interpretation and application of NMA findings in clinical practice. NMA is a robust statistical technique to assess the relative effectiveness of various nursing interventions.

Reporting Method: In the methodological discussion guide, no new data was generated. A hypothetical dataset was used.

Patient or Public Contribution: This methodological paper contributes to understanding NMA and interpreting its results, integrating it into clinical practice, and improving patient outcomes.

1 | Introduction

Nurses must use the best evidence to support positive patient care and outcomes. Systematic reviews and meta-analyses of interventions provide robust evidence by combining data from multiple studies to generate a single effect estimate (Higgins et al. 2023). Conventional meta-analysis can estimate the efficacy of interventions at a time through head-to-head comparisons and provide the overall pooled effect (Higgins et al. 2023). A new analytical approach, network meta-analysis (NMA), has recently been reported in journal publications. These have focused on diverse nursing-related topics, including

pain (Hu et al. 2021), insomnia (Chang, Chen, and Wang 2024), wound care (Geng et al. 2023) and patient safety (Luangasanatip et al. 2015). Other examples include the effect of different home-based exercise programs on post-stroke depression (Chen et al. 2024), the comparative efficacy of non-pharmacological interventions, including psychological, behavioural and social support programs, on loneliness in community-dwelling older adults (Yu et al. 2023) and nurse-led peri-discharge interventions for reducing 30-day re-hospitalisation (Wong et al. 2021). NMA can provide reliable answers to clinical research questions and, when accurately interpreted, can be applied to clinical practice. However, interpreting results may be complex and challenging for nurses and guidance on interpreting NMA results still needs to be improved (Mbuagbaw et al. 2017). This paper outlines NMA and considerations for interpreting and applying results in clinical practice.

2 | Background

Systematic reviews incorporating meta-analysis are valuable tools for comparing the efficacy of interventions. These reviews provide direct head-to-head comparisons between two interventions, allowing for a clear assessment of their relative effectiveness (Higgins et al. 2023). However, in some cases, more evidence is needed to compare the two interventions directly. In such situations, indirect comparisons can be made by analysing two sets of trials, each comparing one of the interventions to a common comparator. This approach, known as indirect evidence, can be used to assess the two interventions' relative effects, even without direct comparisons. By synthesising all available evidence, both direct and indirect, systematic reviews and meta-analyses provide a comprehensive and rigorous assessment of the comparative effectiveness of different interventions (Chaimani et al. 2019).

Network meta-analysis is a method that concurrently evaluates several interventions by combining direct and indirect evidence (Chaimani et al. 2019). It requires a systematic search of databases, assessment of study quality, data abstraction and head-to-head pairwise outcomes analysis like conventional meta-analysis. This approach provides more accurate effect estimates and can guide nurses in making informed decisions in their research and practice. Direct evidence comes from studies comparing different pairs of interventions, while indirect evidence comes from common comparators. NMA is particularly useful when three or more interventions are available for a given condition.

Network meta-analysis offers many advantages, but strict assumptions and prerequisites must be met to ensure the validity of the results (Chaimani et al. 2019). The first assumption is similarity, which necessitates that the trials included in the review share methodological characteristics such as study population, interventions, comparators and outcomes. The second assumption is transitivity, which relies on effect modifiers or study characteristics that affect the intervention results being similarly distributed between direct comparisons. For instance, suppose interventions A and B have been compared to a common comparator C. If A is more effective than C, and C is more effective than B, then this implies that A is more effective than B. A should be considered more effective than B, even without a direct comparison. If this is not the case, the results may be biased and effect modifiers are not similarly distributed. The third assumption is inconsistency or coherence, which involves statistically examining transitivity based on the differences between direct and indirect comparisons (Shim et al. 2017). A recent review by Ades et al. (2024) introduced the interchangeability of treatment effects as a single assumption covering all three NMA assumptions. However, verifying this assumption and identifying deviations from it in practice takes time and effort. Therefore, the analysis is valid and supports evidence-based decision-making when all three assumptions are met.

NMA, by addressing concerns like effect modifiers, can be a powerful statistical technique to assess the relative effectiveness of different nursing interventions and inform evidence-based nursing guidelines. However, unlike other disciplines, nursing interventions can be heterogeneous in design, and a clear classification framework is important to guide the analysis; sufficient evidence on nurse-sensitive outcomes is also needed to proceed with the analysis. Guidelines, such as the Cochrane Handbook for systematic reviews of interventions (Higgins et al. 2023) and the PRISMA extension statement for reporting systematic reviews incorporating NMA (Hutton et al. 2015), provide standardised methodological guidance on performing meta-analysis.

3 | Graphical Representation—Network Geometry

NMA can be displayed in a network map plot to show how evidence forms with the included studies. The forest plot can also illustrate pooled effect estimates for pairs of interventions included in the analysis, like conventional meta-analysis (Figure 1). See the editorial by Alavi et al. (2021) on how to interpret meta-analysis forest plots. The network map plot can be created when three or more interventions are directly or indirectly related. The plot contains nodes and lines between nodes. The widths of nodes and lines are proportional to participants and the number of papers comparing each pair of interventions (Chaimani et al. 2013). Figure 2 presents a hypothetical network map plot illustrating a study evaluating the effects of six distinct nursing interventions on sleep quality in critically ill patients: Intervention A = aromatherapy; Intervention B = earplugs; Intervention C = eye mask; Intervention D = virtual reality meditation; Intervention E = music; Intervention F = relaxation. In this plot, each intervention is represented by a node, and the direct head-to-head comparisons between the interventions are defined by the edges connecting the nodes. The width of the edges corresponds to the number of trials comparing the interventions, with wider edges indicating a greater number of trials. The graph shows that interventions A and E have been compared more frequently than other interventions, as indicated by the bolder line connecting the two nodes. This network map plot visually represents the available evidence and can help identify which interventions have been studied most extensively and where further research may be needed.

Furthermore, the node proportional to intervention A shows a higher population that received this intervention. Indirect estimates can be made when evidence compares the two

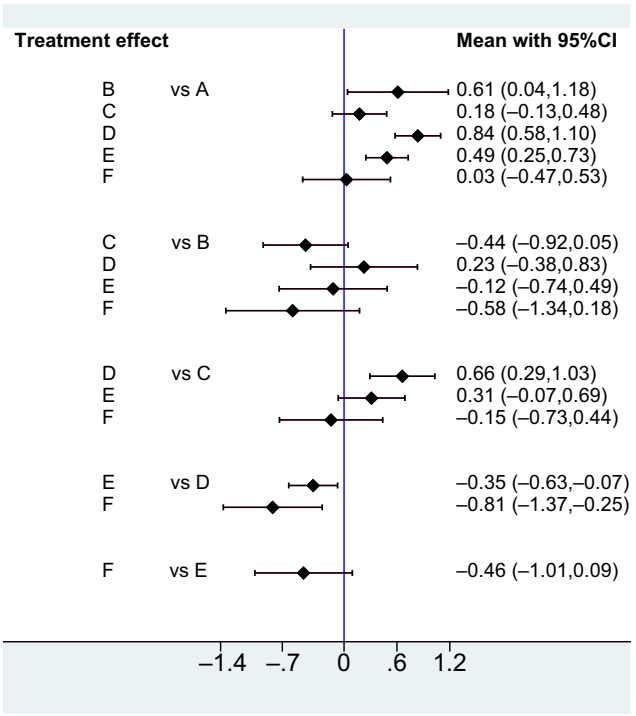

FIGURE 1 | Forest plot of pooled effect estimates for pairs of interventions included in the analysis.

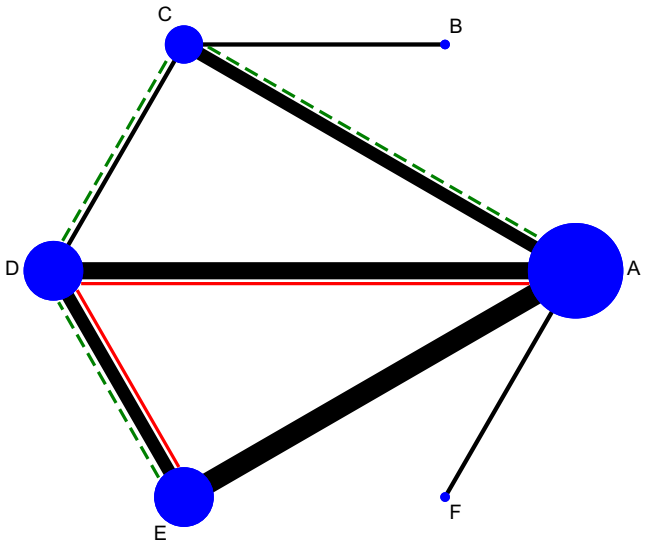

FIGURE 2 | A hypothetical network map plot of six competing interventions. *Note:* Intervention A = aromatherapy; Intervention B = earplugs; Intervention C = eye mask; Intervention D = virtual reality meditation; Intervention E = music; Intervention F = relaxation. The size of each node on the network diagram corresponds to the number of intervention participants. In contrast, the thickness of the lines linking the interventions corresponds to the number of studies included in the comparisons. Interventions A and E are compared to intervention D, resulting in a first-order loop denoted by red solid lines. Comparisons with two standard comparators (C and D) result in a second-order loop, illustrated by the green dashed lines. These loops demonstrate the presence of both direct and indirect evidence for interventions A and E.

interventions with common comparators. Otherwise, network estimates rely only on direct comparisons. The indirect head-to-head comparisons that exist between two interventions create loops. The first-order loops involve one additional intervention, while higher-order loops include more interventions. Depending on the evidence structure, one or more loops can be involved in indirect evidence between two interventions (Puhan et al. 2014). For example, in Figure 2, node F is only connected with intervention A. These interventions can only be compared directly; evidence forms on direct comparison. However, interventions A and E are compared directly and through other interventions (D and C). These created the first-order and the second-order loops. The comparisons between intervention D (common comparator) and two interventions of interest (A and E) make the first-order loop (see red solid lines in Figure 2), and comparisons with two common comparators (i.e., C and D) create a second order loop (see green dash lines in Figure 2). A close loop exists when direct and indirect evidence exists between the two interventions. No direct evidence exists between interventions A and B, so these interventions can only be compared indirectly and through common comparators (C, D and E).

4 | Effect Estimates

Network meta-analysis is a potent statistical instrument that integrates direct and indirect evidence to determine the comparative impacts of multiple treatments. The analysis results are presented in a net league table, visually representing the outcomes. The table is arranged in a triangular format that compares each intervention against all others and presents effect estimates for each combination of interventions. Nurses can refer to the table to assess the relative efficacy of interventions of interest and to identify the superiority between interventions for evidence-based decision-making by examining the size and direction of effect estimates. The effect estimates can be expressed as either risk ratio (RR) or odds ratio (OR) for dichotomous variables and as either mean difference (MD) or standardised mean difference (SMD) for continuous variables.

Along with these effect sizes, a range of possible values (confidence interval) is reported to account for an uncertainty in the true effect. The single value (point estimate) is the best estimate of the effect size based on the data. Table 1 presents the net league table for a hypothetical study. The effect estimated indicates that interventions B, D and E are significantly more effective than intervention A; intervention D is more effective than C, E and F.

5 | Treatment Ranking

Nurses may want to choose the best intervention option among those available. NMA offers options to rank interventions and identify the best one among all the interventions included compared to a reference variable. Rank probabilities, Surface Under the Cumulative Ranking (SUCRA) and p scores are used to rank treatments (Mbuagbaw et al. 2017). The network ranks interventions from 0 to 10, while SUCRA values are reported as percentages from 0 to 100. The higher the value, the more likely this intervention is to be the most

TABLE 1 | A network league table representing the relative effects of interventions from NMA.

A					
−0.61 (−1.18, −0.04)	**B**				
−0.18 (−0.48,0.13)	0.44 (−0.05,0.92)	**C**			
−0.84 (−1.10, −0.58)	−0.23 (−0.83,0.38)	**−0.66 (−1.03, −0.29)**	**D**		
−0.49 (−0.73, −0.25)	0.12 (−0.49,0.74)	−0.31 (−0.69,0.07)	**0.35 (0.07,0.63)**	**E**	
−0.03 (−0.53,0.47)	0.58 (−0.18,1.34)	0.15 (−0.44,0.73)	**0.81 (0.25,1.37)**	0.46 (−0.09,1.01)	**F**

Note: Standardised mean difference (SMD) and 95% confidence intervals (CI) are the effect estimates. SMDs higher than 0 favour the column defining the intervention, and values lower than 0 favour the row defining the intervention. Statistically significant results are bolded. Intervention A = aromatherapy; Intervention B = earplugs; Intervention C = eye mask; Intervention D = virtual reality meditation; Intervention E = music; Intervention F = relaxation. Shades of blue indicate the names of the six interventions that were included in the analysis.

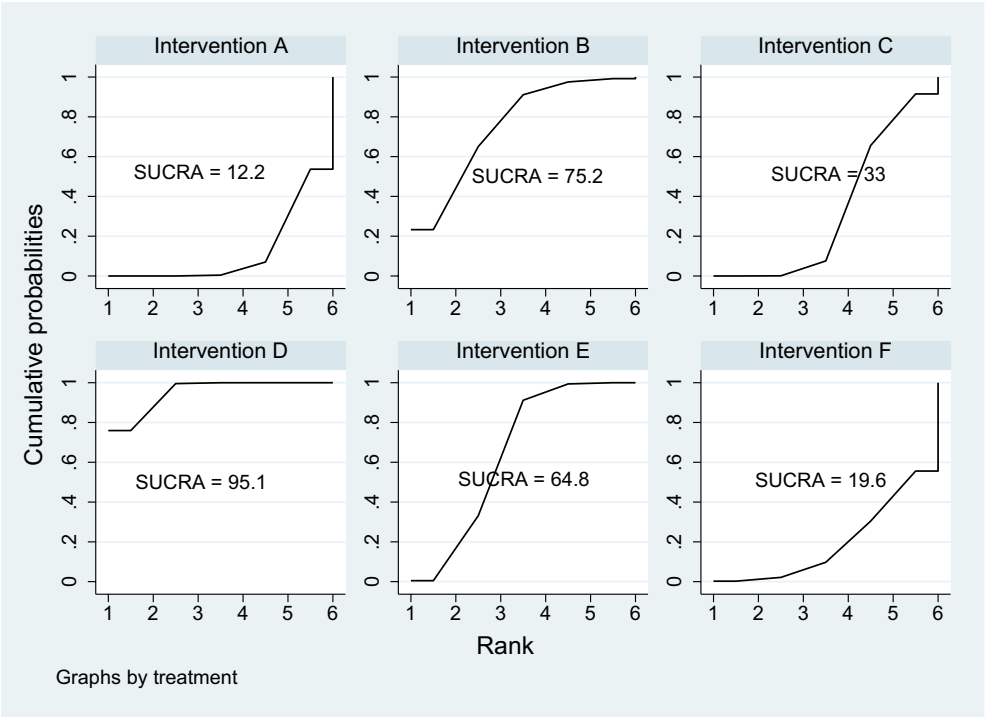

FIGURE 3 | Cumulative ranking probability plots for six interventions were included in the analysis. *Note:* The SUCRA values are reported for each plot; the higher the value, the more probable the intervention will be the best.

effective or among the most effective options. Results can also be shown graphically, with the area under each curve in SUCRA being proportional to the effect of the intervention. Figure 3 represents the cumulative rank probability plots for the hypothetical study. SUCRA values indicate that intervention D is probably the top-ranked intervention, while A has the most minor effect.

However, these rankings should be interpreted with caution. Firstly, intervention rankings may be based on low-quality and uncertain evidence, making the results unreliable. Secondly, when there are multiple related outcomes, the intervention that is best for one outcome may be the worst for another related outcome. Thirdly, the cost-benefit of interventions and their usability and acceptability by nurses and patients should also be considered. Fourthly, the analysis does not consider the magnitude of the effect difference, so the intervention that is ranked first may only be slightly better than the intervention that is ranked second. Finally, rating interventions do not consider chance probabilities (Mbuagbaw et al. 2017).

6 | Quality of Evidence

The quality of evidence should assess the trustworthiness of NMA results. Nurses must consider the quality of evidence and not rely solely on the intervention rankings. For instance, the top-ranked intervention might be estimated to have poor evidence, while the low-ranked intervention may be considered the preferred option due to its robust evidence. Hence, the quality of evidence is essential when interpreting the analysis's results.

Two guidelines assess confidence in NMA results: the Grading of Recommendations Assessment, Development and Evaluation (GRADE) (Puhan et al. 2014) and Confidence

in Network Meta-Analysis (CINeMA) (Nikolakopoulou et al. 2020) approaches. The GRADE rates confidence for direct, indirect and NMA results with four options from very low to high. Treatment estimates that receive high quality are very confident to be close to the true effect, and estimates with deficient quality are likely to differ from the true effect estimate. The framework offers a methodical approach for evaluating the constraints of evidence by considering factors such as inconsistency, indirectness, imprecision and publication bias (Puhan et al. 2014). Inconsistency pertains to discrepancies between direct and indirect evidence, while indirectness relates to the applicability of the evidence to the research question. Imprecision denotes the presence of uncertainty in the estimates, and publication bias signifies the inclination for studies with favourable findings to be published more frequently than those with poor outcomes.

Recognising the limitations of NMA, particularly regarding transitivity and potential biases such as publication and selection bias, we propose exploring future research directions to enhance its robustness. One promising avenue lies in strategically integrating alternative quantitative methodologies alongside NMA (Lunny et al. 2024). While bias adjustment techniques can be valuable for addressing inconsistencies within the existing data used for NMA, trial sequential analysis (TSA) plays a crucial role in informing the design of future trials. It offers a complementary approach suited explicitly to strengthening the foundation of future studies feeding into the NMA. TSA can not only control for type I and type II errors, which are crucial for reliable research but also help mitigate concerns about transitivity by ensuring the design of future trials with optimal comparability across interventions.

7 | Application of Results in Clinical Practice

Accurate interpretation of NMA findings can inform clinical practice. Nurses should evaluate the requirements and assumptions for NMA and accurately depict the network architecture and interventions analysed. When making clinical decisions, it is essential to consider the size of the effect estimates and the level of certainty in the evidence (based on the GRADE or CINeMA approaches). However, considering the practical value of the results, such as their costs, benefits and potential harms, is equally important, given the available resources, cultural background and other contextual factors. Additionally, nurse–patient preferences and available resources should be considered when choosing interventions. The outcomes examined in NMA are also crucial in evidence-based conclusions. When available, consideration of both efficacy and safety outcomes is essential for understanding the clinical utility of interventions. In addition, the relevance of NMA findings to patients and nurses (nurse-sensitive and patient-important outcomes) should be considered when assessing the certainty of the evidence (Rouse, Chaimani, and Li 2017).

8 | Hands-on Guide to Data Analysis

The NMA in this paper was performed on a hypothetical dataset presented in Table 2. SMDs and their 95% confidence intervals were calculated as effect estimates, and p-values < 0.05 indicated statistical significance. A network map plot was used to display a network of comparisons. The relative effects of the interventions were presented in a network league table, and SUCRA was used to rank the treatments in order. The analysis was conducted with a frequentist framework and random effects model in STATA/MP v17 (StataCorp 2021).

TABLE 2 | Hypothetical dataset for conducting an NMA.

Study ID	Sample size	Intervention	Mean	SD
Study 1	29	A	2.32	1.54
Study 1	29	C	2.44	1.14
Study 2	26	A	3.76	1.56
Study 2	26	D	4.84	2.34
Study 2	26	E	4.32	2.08
Study 3	31	A	2.12	1.12
Study 3	31	F	2.16	1.59
Study 4	34	B	3.46	2.20
Study 4	34	C	2.66	1.32
Study 5	28	A	1.18	0.84
Study 5	28	D	1.76	1.20
Study 5	28	E	1.44	1.12
Study 6	30	A	2.84	0.89
Study 6	30	D	4.45	2.22
Study 6	29	E	3.72	1.20
Study 7	25	A	3.24	1.16
Study 7	25	E	4.36	1.35
Study 8	23	A	1.98	1.17
Study 8	24	E	2.54	1.62
Study 9	20	A	3.92	1.25
Study 9	20	C	4.28	1.84
Study 10	26	A	1.22	1.20
Study 10	26	C	1.74	1.10
Study 10	25	D	2.81	1.60

9 | Conclusion

NMA is a robust method for nurses to synthesise evidence from multiple studies, provided certain conditions are met for optimal utilisation. Nurses should be encouraged to gain knowledge about NMA through workshops or online resources and to collaborate with experts in the field. However, challenges such as insufficient high-quality data and heterogeneity in the study still need to be addressed. To enhance the effectiveness of NMA, standardised methods for reporting findings from both low- and high-quality data are necessary. This will

enable NMA to contribute to nursing research and improve patient care.

Author Contributions

Amir Masoud Sharifnia: conceptualisation, visualisation, writing – original draft; writing – review and editing. **Erik Biros:** writing – review and editing. **Michelle Cleary:** project administration, writing – review and editing.

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Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing not applicable to this article. A hypothetical dataset was used (see Table 2).

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