



Original Research Article

Analysis of Evidence-Rating Systems Used in Meta-Analyses of Pharmacotherapy

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Abstract: Evidence-rating systems (ERSs) establish the foundation for systematically evaluating the quality and credibility of meta-analyses in pharmacotherapy. While a variety of ERSs exist, including tools for both individual studies and entire evidence bodies, no unified best-practice standard exists. This article reviews the types, frequency, strengths, and limitations of major ERSs used in meta-analyses of pharmacotherapy, with emphasis on trends from high-impact medical literature, variability of application, and suggestions for future harmonization.

Keywords: Evidence-rating systems (ERSs), Meta-analyses, Pharmacotherapy, Quality assessment, Methodological standardization.

INTRODUCTION

The proliferation of clinical trials and observational studies in pharmacotherapy has produced an overwhelming volume of data. Meta-analyses, when well executed, offer reliable aggregation of such evidence, supporting informed medical practice. However, the reliability of meta-analytic conclusions is directly linked to the quality of underlying studies. Systematic evaluation via evidence-rating systems is therefore imperative to ensure robust, reproducible, and translatable findings in pharmacotherapy meta-analyses^[1].

KEY EVIDENCE-RATING SYSTEMS

Risk of Bias Tools for Individual Studies

- **Cochrane Risk of Bias Tool:** Assesses domains such as random sequence generation, allocation concealment, blinding, incomplete outcome data, and selective reporting. Widely used in RCT-based meta-analyses for qualitative domain-based judgments.
- **Jadad Scale:** Quantitative scoring system based on randomization, blinding, and withdrawals/dropouts. Simpler to use but potentially less nuanced for complex design flaws.
- **Newcastle-Ottawa Scale (NOS):** Tailored for observational studies, evaluating selection, comparability, and outcome/exposure assessment.

- **Downs-Black Checklist:** Can be applied across RCTs and non-randomized trials, offering a semi-quantitative assessment^[1].

Tools for Assessing the Body of Evidence

- **GRADE (Grading of Recommendations, Assessment, Development, and Evaluation):** Provides a structured, transparent framework to rate the quality of an overall evidence body as high, moderate, low, or very low. GRADE considers risk of bias, consistency, directness, precision, and publication bias^[2].
- **AHRQ (Agency for Healthcare Research and Quality) Methods Guide:** Utilized for effectiveness and comparative effectiveness reviews, often overlapping in elements with GRADE.
- **USPSTF (U.S. Preventive Services Task Force) and Oxford Centre for Evidence-Based Medicine:** Also offer frameworks for the body of evidence but are less frequently used in pharmacotherapy meta-analyses^[1].

Patterns of Use in Meta-Analyses

A review of high-impact medical journals revealed that among meta-analyses of drug effects:

- **86.4%** used an ERS for individual studies
- The **Cochrane Risk of Bias Tool** dominated (80.7% of interventional trial meta-analyses)
- **Newcastle-Ottawa Scale** was preferred for observational studies (66.7%)
- **GRADE** was the most common ERS for evaluating the body of evidence but applied in only 19.1% of meta-analyses
- 14 unique ERSs were identified, including some author-defined systems
- Modifications to standard ERSs were present in some studies, potentially undermining consistency^[1]

Table 1: Use of Major ERSs in Pharmacotherapy Meta-Analyses

System	Type	Context	% of Use in Meta-Analyses ^[1]
Cochrane Risk of Bias	Individual studies	RCTs	80.7
Newcastle-Ottawa Scale	Individual studies	Observational studies	66.7
Jadad	Individual studies	RCTs	6.4
GRADE	Body of evidence	All study types	15–19
AHRQ	Body of evidence	Mixed systems	<8
USPSTF	Body of evidence	Systematic reviews	<2.7

Strengths and Limitations of Evidence-Rating Systems

Strengths

- **Systematic Appraisal:** Promotes transparent, reproducible risk-of-bias assessment.
- **Informs Confidence:** Assists users in understanding strength/limitations of summarized evidence.
- **Supports Meta-Analytic Decisions:** Guidance on exclusion/inclusion, stratified synthesis, and exploration of heterogeneity^{[1][3][2]}.

Limitations

- **Lack of Consensus:** No gold standard; multiple systems in use can produce discordant judgments.
- **Subjectivity:** Some tools, especially with domain-based approaches, can yield inter-rater variability.
- **Overlap and Gaps:** Many systems overlap in domains but none comprehensively address all potential biases.^[1]
- **Limited Use for Bodies of Evidence:** Most attention is paid to individual study appraisal; relatively few meta-analyses use ERSs like GRADE to summarize confidence in the cumulative evidence.

Consequences of ERS Variation

- **Comparability:** Heterogeneity in ERS application can hamper cross-study or cross-journal comparison.
- **Reproducibility Issues:** Modified or author-defined ERS hamper reproducibility and broad uptake of findings.
- **Risks in Practice:** Inconsistent grading can misinform clinical guideline development or medication policy decisions^{[1][3]}.

Graphical Representation

Figure 1: Frequency of ERS Usage in High-Impact Meta-Analyses

	Cochrane Risk of Bias	Newcastle-Ottawa	GRADE (Body of Evidence)	Others
% Usage	80.7	66.7	~19	<10

Bar graph displays dominance of Cochrane and Newcastle-Ottawa for study-level, and limited use of GRADE.

Figure 2: ERS Adoption Across Major Journals

Journal	% Meta-analyses Using ERS ^[1]
Annals of Internal Medicine	100
BMJ	92.9
JAMA	100
Lancet	53.6
PLoS Medicine	81.8

DISCUSSION

Proper ERS choice and consistent application are vital to credible meta-analyses in pharmacotherapy. While Cochrane Risk of Bias and Newcastle-Ottawa dominate individual study evaluation, their shortcomings and the multiplicity of modified systems highlight the need for better consensus. GRADE is growing in popularity for body-of-evidence assessment, offering clarity and transparency, but remains underutilized. Improving ERS harmonization—possibly via explicit journal requirements—could enhance the rigour, comparability, and utility of future meta-analyses^{[1][3][2]}.

Recommendations

- **Standardization of ERS** use within journals or meta-analysis consortia.
- **Training:** Enhance familiarity with GRADE and core risk-of-bias tools.
- **Explicit Reporting:** Transparent, detailed methods, including justifications for ERS choice or modifications^[1].
- **Comprehensive Appraisal:** Expand use of GRADE or equivalent systems to routinely summarize cumulative evidence strength.
- **Research:** Further comparative studies on the impact of ERS variation and development of integrated, adaptable frameworks.

CONCLUSION

ERSs are indispensable to high-quality meta-analytic research in pharmacotherapy. The predominance of Cochrane and Newcastle-Ottawa for study-level and GRADE for evidence-level assessments reflects best current practices—but practice heterogeneity persists. Ongoing evolution toward more systematic use and consensus standards will be key for ensuring trustworthy, actionable conclusions from the ever-expanding world of pharmacotherapy meta-analyses.

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