



Assessing the Strength of Scientific Evidence for Clinical Guidance: A Practical Guide for Healthcare Professionals

Purpose

Clinical guidance must be based on rigorous evaluation of scientific evidence. This document offers a concise overview to help healthcare professionals understand essential considerations for developing guidance—including for vaccines—using rigorous, systematic, evidence-based processes.

1. Core Principles of Evidence-Based Guidance

- **Systematic Review:** All relevant studies are evaluated and weighted based on quality, limitations, and bias.
- **Risk-Benefit Weighing:** Experts assess how benefits and risks apply to different patient groups.
- **Transparency:** Guidance processes must be transparent and document what data are included/excluded and why.
- **Conflict of Interest Review:** Committee members undergo strict conflict assessments.

2. The GRADE Framework

GRADE (Grading of Recommendations Assessment, Development, and Evaluation) is used by organizations like ACIP conduct rigorous review of studies to:

- Determine **level of certainty of evidence** (high to very low)
- Evaluate **clinical relevance** and **applicability**
- Rate the **strength of recommendations** (strong or conditional)

3. Study Design and Evidence Hierarchy

Healthcare providers should understand how different study types contribute to guidance:

Randomized Controlled Trials (RCTs)

- Best at limiting bias
- Volunteers randomly assigned to intervention/control
- Double-blinding adds validity
- Challenges: cost, feasibility, ethics (e.g., withholding known beneficial interventions)

Observational Studies

- Useful for large-scale or rare outcome assessment and when RCTs may not be feasible or ethical
- Require study design and data analysis strategies to reduce potential bias and [confounding](#) (e.g., ensure intervention and comparison groups are as similar as possible; conduct multivariate analyses, sensitivity analyses, etc.)

Case Reports and Anecdotes

- Rarely used in forming guidance
- May generate hypotheses or possible safety issue (e.g., J&J vaccine and clotting)

4. Key Criteria for Evaluating Study Quality

- **Design and Execution:** Was the study randomized, blinded, and appropriately controlled? For observational studies, were study design and analyses done to reduce the risk of bias and confounding?
- **Relevance:** Are populations and settings applicable to the clinical question?
- **Sample Size:** Was the study adequately powered?
- **Replication:** Do other studies show similar results? If not, why?
- **Potential Bias:** Funding sources, dropout rates, appropriate comparison group?

5. Association vs. Causation

Correlation does not imply causation. Rigorous methods are needed to confirm whether a vaccine or intervention causes an outcome—not just whether it is associated with one.

6. Cherry-Picking and Misinterpretation

- Selective use or exclusion of studies results in bias and undermines validity.
- Properly performed systematic reviews reduce bias by incorporating all relevant evidence and weighting evidence based on study quality.

7. Using Statistics Wisely

- **Confidence Intervals:** Wide or overlapping CIs suggest weaker evidence.
 - **Effect Size:** Small effects in observational data may lack clinical significance.
 - **Significance:** Statistically significant does not always mean clinically important.
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8. When RCTs Are Not Feasible or Inert Placebo Unethical

- Rare events (e.g., anaphylaxis)
- Diseases with low incidence in vaccinated populations (e.g., measles) may be best assessed via observational studies and pre/post vaccine comparisons.
- Ethical considerations (e.g., a known effective intervention exists and an inert placebo would put people at risk).

Conclusion

Trustworthy guidance is built on transparent, methodical, and expert analysis of all available data—not individual anecdotes or single studies. As a healthcare provider, understanding the basics of how evidence is evaluated supports informed decision-making and patient trust.

For detailed methods, tools, and other resources:

- GRADE Working Group: www.gradeworkinggroup.org
- ACIP Handbook: www.cdc.gov/vaccines/acip/recs/grade
- Cochrane Handbook: www.training.cochrane.org/handbook
- AHRQ Risk of Bias Tools: <https://effectivehealthcare.ahrq.gov/research-methods>.
- Institute of Medicine. <https://nap.nationalacademies.org/resource/13058/Clinical-Practice-Guidelines-2011-Report-Brief.pdf>.
- University of Oxford Centre for Evidence-based Medicine. <https://www.cebm.ox.ac.uk/resources/ebm-tools/study-designs>