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## **Evidence-based clinical practice: Overview of threats to the validity of evidence and how to minimise them**

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### **Abstract:**

Using the best quality of clinical research evidence is essential for choosing the right treatment for patients. How to identify the best research evidence is, however, difficult. In this narrative review we summarise these threats and describe how to minimise them. Pertinent literature was considered through literature searches combined with personal files. Treatments should generally not be chosen based only on evidence from observational studies or single randomised clinical trials. Systematic reviews with meta-analysis of all identifiable randomised clinical trials with Grading of Recommendations Assessment, Development and Evaluation (GRADE) assessment represent the highest level of evidence. Even though systematic reviews are trust worthier than other types of evidence, all levels of the evidence hierarchy are under threats from systematic errors (bias); design errors (abuse of surrogate outcomes, composite outcomes, etc.); and random errors (play of chance). Clinical research infrastructures may help in providing larger and better conducted trials. Trial Sequential Analysis may help in deciding when there is sufficient evidence in meta-analyses. If threats to the validity of clinical research are carefully considered and minimised, research results will be more valid and this will benefit patients and health care systems.

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