Studies

The hierarchy of studies for obtaining evidence is:

- Systematic reviews of randomised controlled trials
- Randomised controlled trials
- Controlled observational studies - cohort and case control studies
- Uncontrolled observational studies - case reports

When looking at the relevance of studies or reviews, the following issues should be considered:

- Type of study or analysis: RCT, prospective vs retrospective, multi-centred, blinding
- Type of intervention.
- Size of the sample.
- Type of person included and excluded.
- Type of control group used for comparison (ideally placebo).
- How reliable is the methodology?
- Results - P value, confidence limits? What is the rate of loss of follow-up during the study? Are there possible alternative explanations for the results?
- Type of outcome; objective e.g. mortality rate or subjective – pain assessment or use of validated scales (QALY, HAD etc)
- Is there a conflict of interest?

Hierarchical systems for levels of evidence and recommendations

- A variety of grading systems for evidence and recommendations are currently in use.

Grading of evidence

- Ia: systematic review or meta-analysis of randomised controlled trials
- Ib: at least one randomised controlled trial
- IIa: at least one well-designed controlled study without randomisation
- IIb: at least one well-designed quasi-experimental study, such as a cohort study
- III: well-designed non-experimental descriptive studies, such as comparative studies, correlation studies, case–control studies and case series
- IV: expert committee reports, opinions and/or clinical experience of respected authorities

Grading of recommendations

- A: based on hierarchy I evidence
- B: based on hierarchy II evidence or extrapolated from hierarchy I evidence
- C: based on hierarchy III evidence or extrapolated from hierarchy I or II evidence
- D: directly based on hierarchy IV evidence or extrapolated from hierarchy I, II or III evidence

A simpler system of A, B or C is recommended by the US Government Agency for Health Care Policy and Research (AHCPR):

- A: requires at least one randomised controlled trial as part of the body of evidence.
- B: requires availability of well-conducted clinical studies but no randomised controlled trials in the body of evidence.
- C: requires evidence from expert committee reports or opinions and/ or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality.

Numbers Needed To Treat

The Number Needed to Treat (NNT) is the number of patients you need to treat to prevent one additional bad outcome.

Calculation

- The NNT is the inverse of the Absolute Risk Reduction (ARR).
- The ARR is the Control Event Rate (CER) minus the Experimental Event Rate (EER), or ARR = CER - EER.
- NNTs are always rounded up to the nearest whole number and accompanied by its 95% confidence interval.
- A nomogram can be used to find the NNT by using the proportion of events in the control group and the relative risk reduction.

Benefits of NNT

- NNTs used for summarising a therapeutic trial or for medical decision on an individual
- The NNT is more clinically useful for an active intervention than the use of the relative risk, the relative risk reduction or the odds ratio.

Disadvantages

- Although NNTs are easy to interpret, they cannot be used for performing a meta-analysis. Pooled numbers needed to treat derived from meta-analyses can be seriously misleading because the baseline risk often varies appreciably between the trials.
- Applying the pooled relative risk reductions calculated from meta-analyses or individual trials to the baseline risk relevant to specific patient group produces a useful number needed to treat.

Sensitivity & Specificity

SnOut – Sensitive tests rule out diagnoses

SpIn – Specific tests rule in diagnoses

	Result of gold standard test	
Result of screening test	**Disease positive** (a+c)	**Disease negative** (b+d)
Test positive (a+b)	True positive (a)	False positive (b)
Test negative (c+d)	False negative (c)	True negative (d)

Feature of the test	Alternative name	Question addressed	Formula
Sensitivity	True positive rate (positive in disease)	How good is this test at picking up people who have the condition?	a/(a + c)
Specificity	True negative rate (negative in health)	How good is this test at correctly excluding people without the condition?	d/(b + d)
Positive predictive value	Post-test probability of a positive test	If a person tests positive, what is the probability that he or she has the condition?	a/(a + b)
Negative predictive value	Post-test probability of a negative test	If a person tests negative, what is the probability that he or she does not have the condition?	d/(c + d)
Accuracy	–	What proportion of all tests have given the correct result? (true positives and true negatives as a proportion of all results)	(a + d)/(a + b + c + d)
Likelihood ratio of a positive test	–	How much more likely is a positive test to be found in a person with the condition than in a person without it?	sensitivity/(1–specificity)
Likelihood ratio of a negative test	–	How much more likely is a negative test to be found in a person without the condition than in a person with it?	(1–sensitivity)/specificity