

1 Levels of evidence

1.1 Management approaches

In these guidelines, the quality of scientific evidence supporting statements concerning clinical practice is indicated by the following indications of 'level of evidence':

1.1.1 Level of evidence

****	STRONG	Systematic review of multiple randomised controlled trials (RCT) OR multiple RCTs with consistent findings.
***	GOOD	At least one RCT or multiple comparative (non-randomised) studies with consistent findings.
**	MODERATE	Any form of comparative (non-randomised) study.
*	SOME	Case series (single treatment group).
NO RATING		No experimental studies – any statements are based on single case reports or clinical opinion/expertise.

This system of rating the level of evidence draws on the system used by the National Health and Medical Research Council (NH&MRC) of Australia (*A guide to the development, implementation and evaluation of clinical practice guidelines*. Canberra: NH&MRC, 1999. www.nhmrc.gov.au/publications/synopses/cp65syn.htm), and the Australian National Council on Drugs (ANCD) (Monograph 4).

1.2 Drug interactions

In these guidelines, the quality of scientific evidence supporting statements concerning drug interactions is indicated by different indications of 'level of evidence'.

As it is unethical to conduct RCTs of drug interactions in clinical populations, it is not possible to base levels of evidence on clinical RCTs. As a result, the following 'level of evidence' statements have been formulated.

1.2.1 Level of evidence

xxx	DEFINITE	<p>Multiple case reports or controlled pharmacological studies have confirmed interactions of the combination of these drugs.</p> <p>Caution: if these drugs are administered in combination with one another, interactions will occur. Alternative treatment should be sought if appropriate. Should it be necessary to combine these drugs, patients should be monitored and doses adjusted as needed to prevent adverse events.</p>
xx	LIKELY	<p>Case reports indicate that interactions have occurred in a clinical situation.</p> <p>Alternatives should be offered where appropriate. If the combination is to be administered, the individual should be monitored to confirm interactions and adjust treatment if necessary.</p>
x	THEORETICAL	<p>Based on pharmacokinetic and pharmacodynamic properties of the drugs, there is a theoretical possibility that they may interact to cause a different effect if the drugs were administered individually OR in vitro, or animal studies suggest that there may be an interaction.</p> <p>Individuals taking these combinations of drugs should be monitored.</p>