Questions to ask when evaluating a new drug

The checklist below has been designed to help you assess new drugs in comparison to your current practice. You may like to use it as a basis for discussion when pharmaceutical company representatives visit you to promote new drugs.

What is new about the drug?

- Is it a member of an existing class or a new formulation, or is it a genuine innovation?

Is there good quality evidence that the new drug has an efficacy advantage over existing therapy?

- Do studies compare the new drug to the current drug of choice at effective doses?
- Is the advantage likely to be clinically significant?
- How strong is the evidence?
  - Are studies randomised and double-blind?
  - Do studies include enough patients for firm conclusions to be drawn?
  - Do studies reflect the population in which the drug will be used?
  - Do studies measure long-term effects on patient-relevant outcomes rather than relying on surrogate endpoints?

Has the new drug been shown to be safe?

- What are the incidence and severity of side-effects?
- Are long-term safety data available? Has the drug been used overseas?
- Which patients are at most risk of side-effects? Which patients should not receive the drug?
- In which patients is safety unknown (such as pregnant women or people with hepatic impairment)?

Is the new drug affordable for patients and value for money compared to existing therapy?

- If it is more expensive than existing therapy, does it have advantages that justify the extra cost?
- Is it PBS-listed? What is its PBS indication?
- Does it have a premium (such as a brand price premium or therapeutic group premium) over other drugs?
- Are there cheaper alternatives (e.g. other drugs in the same class)?

Is the drug likely to be convenient to use and acceptable to patients?

- How acceptable is the formulation, route of administration and dose frequency likely to be to patients?
- Are any special instructions needed to use it (such as drug–food interactions, or instructions for using a new device)?
- Is monitoring required?

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Glossary*

Below are definitions for some commonly used evidence-based medicine terms, which you may like to refer to when reading clinical papers. Definitions for health economics terms, which will be used in NPS Radar, are also provided.

Evidence-based medicine terms

The following scenario is provided as a basis for examples in the definitions below.

In a study of stroke prevention, 100 people take a new drug and 100 people take placebo. After 1 year of treatment, 8 people in the treatment group and 10 in the control group have had a stroke.

Absolute risk

The probability that a person will experience a specified outcome during a specified period.

Example: The absolute risk of stroke in the control group is 10/100 = 0.1, or 10%, and in the treatment group is 8/100 = 0.08, or 8%.

Absolute risk difference

The difference in absolute risk of an outcome between the control group and the treatment group, or between two treatment groups. An absolute risk difference of zero indicates no difference between the groups.

Example: The absolute risk difference between the groups is 0.1 – 0.08 = 0.02, or 2%.

Number-needed-to-treat (NNT)

The number of people that need to be treated for a given period of time with one treatment instead of another treatment for one additional person to benefit in the outcome of interest. NNT is the reciprocal of absolute risk difference.

Example: The NNT is 1/0.02 = 50. This means that to prevent one stroke you would need to treat 50 people for 1 year with the new drug, rather than control treatment.

Relative risk (or risk ratio)

The ratio of how often an event occurs in two groups receiving different treatments. A relative risk of 1.0 indicates no difference between the groups.

Example: The relative risk of stroke with treatment compared to control is 0.08/0.1 = 0.8, or 80%.

Relative risk difference

Difference between the relative risk and no effect (1 – relative risk).

Example: The relative risk difference is 1 – 0.8 = 0.2, or 20%. In other words, treatment reduced the risk of stroke by 20% compared to the control group.

Confidence interval

The range of values within which the true value for the whole population represented by the study patients is likely to lie. For example, when the confidence interval for a relative risk includes 1.0, this is interpreted as no evidence of a difference between groups.

Example: The point estimate and 95% confidence interval for the relative risk of stroke with treatment is 0.8 (0.4–1.7).

This means that the risk of stroke in the treatment group might be as low as 40% of the risk in the control group, or may be 70% more than in the control group. In this case, the results of the study do not help us to decide whether to offer the treatment to patients.

Intention-to-treat analysis

Analysis of patient outcomes based on their randomised group, regardless of whether they actually received the planned intervention. Avoids bias associated with non-random loss of participants from treatment groups.

Power

A study's ability to detect a statistically significant difference between the control and experimental groups. Factors that determine a study's power include its size, the number of outcomes that occur (e.g. strokes) and the smallest difference in outcomes between the therapy and the control groups that is considered to be clinically important.

Surrogate measure

A laboratory or physiological variable that is used as a substitute for a more clinically meaningful endpoint that defines how a patient functions or survives. For example, bone density for fracture, cholesterol for myocardial infarction, and blood pressure for stroke. Surrogates are usually measured relatively quickly and easily, so are used when observing clinical outcomes would require long follow-up.

Generalisability (or external validity)

The ability to apply the findings of a study to other circumstances.

Health economics terms

Cost-benefit analysis

Values all costs and outcomes in monetary terms.

Cost-effectiveness analysis

Describes the difference in costs and benefits of therapies with a common health outcome (e.g. blood pressure reduction). Results are presented as a ratio (e.g. cost per event prevented, cost per unit of blood pressure lowered).

Cost-minimisation analysis

An analysis conducted when two treatments are assumed to be equivalent and only costs are compared.

Cost-utility analysis

Expresses the effects of therapies as life-years adjusted by people's preferences, so includes length and quality of life. Usually expressed as cost per QALY (quality-adjusted life-year). Useful when therapies being compared have a wide range of outcomes and a common unit of measurement is needed.

Economic evaluation

Identifies and measures the costs and consequences associated with alternative health interventions. A generic term for cost-benefit, cost-effectiveness, cost-minimisation and cost-utility analyses.

Incremental cost-effectiveness ratio

The ratio generated by a cost-effectiveness analysis. Expresses the differences in costs and effects of therapies (i.e. cost A – cost B/effect A – effect B).

Modelling

Applies evidence from randomised trials to 'real-life' settings to better judge a drug's clinical and economic performance. May be used to extend surrogate outcomes (such as blood pressure reduction) to clinical endpoints (cardiovascular events prevented), to extend findings of study beyond duration to likely duration of use and to examine the impact of differences between study subjects and patients likely to receive the drug in clinical practice.

Quality-adjusted life-years (QALYs)

A measure of health status that includes both duration and quality of life.

Sensitivity analysis

Assesses how robust an analysis is to uncertainty in or assumptions about the data or methods used by testing how much the result changes when important parameters are varied.