Implementing NICE guidance for evidence synthesis in technology appraisals: An overview of common methodological and analytic challenges.

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Purpose and objective

• Recent guidance on appraisal methods provides a clear framework for establishing the clinical and cost-effectiveness of technologies.1 These approaches present three main challenges:
  1. All relevant/feasible interventions and comparators should be included
  2. The evidence must be complete and fit for the purpose
  3. Evidence should be synthesised in an appropriate manner.
• A recent review of the clinical and cost-effectiveness of docetaxel plus prednisone for metastatic hormone refractory prostate cancer (mHRPC) is presented as a case-study.
• Emphasis is given to overall survival for docetaxel plus prednisone 3-weekly & prednisone alone (the licensed treatments for mHRPC in the UK).

RESULTS

• The scoping search identified one study, (TAX 327) providing direct evidence on docetaxel plus prednisone versus mitoxantrone plus prednisone.
• Broader searches identified additional RCTs providing indirect evidence for docetaxel plus prednisone and other relevant comparators e.g. prednisone alone.

SYNTHESISING THE EVIDENCE

• All evidence synthesis must be appropriate and statistically robust.
• As the evidence network was incomplete, indirect comparisons were necessary.
• Using the methods proposed by Parmar, hazard ratios with 95% confidence intervals (CI) were estimated, if not directly reported using the following hierarchy of evidence:
  1. HR and number of events
  2. Number of events and p-value
  3. Survival curve with length of follow-up

Comoleting the evidence

• The most appropriate measures of treatment effect for time-to-event data in a meta-analysis are hazard ratios (HR) as these measures allow for censoring.
• Survival data were reported inconsistently between trials.
• Using the method outlined by Parmar hazard ratios with 95% confidence intervals (CI) were estimated, if not directly reported using the following hierarchy of evidence:
  1. HR and number of events
  2. Number of events and p-value
  3. Survival curve with length of follow-up

Lessons learnt

• There is a case for extending the evidence network and broadening the search strategy so that all relevant evidence is incorporated.
• Emphasis should be placed on the most clinically appropriate outcomes, e.g. overall survival. Data must be extracted to allow for appropriate synthesis methods.
• Analysis should be based on robust statistical techniques.

Conclusions

• Consideration should be given to the generalisability of results derived indirectly.

References