



Title	The Use of Surrogate Outcomes in Model-Based, Cost-Effectiveness Analyses: A Survey of UK Health Technology Assessment Reports
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Aim

To explore the use of surrogate outcomes in health technology assessment (HTA) and provide a basis to guide their future use, validation, and reporting.

Conclusions and results

This report focuses on the role of surrogate outcomes in cost-effectiveness models (CEMs) in UK HTA reports. In our survey of UK HTA reports, about 10% of the CEMs were explicitly based on surrogate outcomes. The strength of evidence for the surrogate-final outcome relationship, transparency of quantification, and exploration of uncertainty of this relationship varied considerably. In total, 35 out of 200 UK HTA reports published in 2005 and 2006 addressed an effectiveness/efficacy question and contained a CEM. Of these, 4 (~10%) based their CEM on a surrogate outcome. All 4 reports sourced treatment-related changes in surrogate outcomes through a systematic review of the literature. However, there was variability in the consistency and transparency by which these reports provided evidence of the validation for the surrogate-final outcome relationship. One of the reports undertook a systematic review to specifically seek the evidence base for the association between surrogate and final outcomes. This was the only report to provide level-1 surrogate-final outcome validation evidence, ie, RCT data showing a strong association between the change in surrogate outcome (biopsy confirmed acute rejection) and the change in final outcome (graft survival) at an individual patient level. This report met the JAMA criteria for acceptable evidence of a surrogate. Two reports provided level-2 evidence, ie, observational study data showing the relationship between the surrogate and final outcome, and one report provided level-3 evidence, ie, a review of disease natural history. None of the 4 reports achieved a sufficient score on the Outcomes Measures in Rheumatology Clinical Trials (OMERACT) biomarker and surrogate schema to be judged to have 'acceptable' evidence of a surrogate outcome.

Recommendations

See Executive Summary link at www.hta.ac.uk/project/1674.asp.

Methods

See Executive Summary link at www.hta.ac.uk/project/1674.asp.

Further research/reviews required

1) Given both the UK focus and the relatively small number of HTA reports with a CEM explicitly based on surrogate outcomes identified, the generalizability of the findings may be limited. This supports a more extensive survey of the use of surrogate outcomes in HTA across international jurisdictions. Consideration should be given to the role of surrogate outcomes in both the clinical- and the cost-effectiveness components of these reports. Future empirical studies need to address situations in which HTA reports may combine both surrogate and final outcomes and the validity of using surrogates across technology classes. 2) The literature review in this report identified only two empirical studies designed to quantify the potential bias associated with using surrogate outcomes. Further empirical studies need to assess potential biases in using surrogate outcomes in HTA and cost-effectiveness analyses, eg, comparing the findings of cost-effectiveness analyses based on surrogate outcomes and cost-effectiveness analyses based on final outcomes. 3) Testing of the new OMERACT surrogate scoring schema and the development of similar tools. 4) Explore the transferability of the hierarchy of evidence framework for surrogate-final outcomes to the process of mapping disease-specific outcomes to health-related quality-of-life utility in CEM analyses.