

**Title: Characterising structural uncertainty in decision analytic models: review and application of currently available methods**

**Background**

An inappropriate model structure can potentially invalidate estimates of cost-effectiveness and estimates of the value of further research. However there are often a number of possible and credible structural assumptions which can be made. Although it is common practice to acknowledge potential limitations in model structure, there is a lack of clarity about methods to characterise structural uncertainties and their contribution to decision uncertainty.

**Methods**

This review identifies approaches to handle structural uncertainty available in health technology assessment and other disciplines. I then go on to apply these alternative methods to the assessment of structural uncertainty using a case-study model, screening for age related macular degeneration. This application provides insights into the value and practicality of the alternative methods.

**Results**

The assessment of structural uncertainty has received little attention in the health economics literature. Despite the fact that, in many circumstances, it is uncertainty over appropriate structure, which is acknowledged as most important by decision-makers. A common method to characterise structural uncertainty is to compute results for each alternative model specification, and to present alternative results as scenario analyses. It is then left to decision maker to assess the credibility of the alternative structures in interpreting the range of results. An alternative method, which has not been widely used, is 'model averaging' where alternative models, with different specifications, are built, and their results averaged, using explicit prior distributions often based on expert opinion.

In this case-study model, alternative assumptions regarding model structure have little impact on the decision regarding cost-effectiveness, but have a big impact on the value of additional research estimates.