BACKGROUND

Threshold Analysis is typically used to determine the threshold value of an input parameter at which a health care technology becomes cost-effective. Currently, threshold analysis is typically performed in a deterministic way. This approach assumes independence between input parameters and may result in biased threshold values if the relationship between input parameters and the measure of cost-effectiveness is non-linear. 2-level Monte Carlo approach is considered to be the gold standard and can provide unbiased threshold values. But it is computationally intensive and complex. However, probabilistic sensitivity analysis (PSA) might overcome the issues related to deterministic threshold analysis and 2-level Monte Carlo approach.

OBJECTIVE

Propose a probabilistic method for performing threshold analysis, namely generalized additive model, which accounts for the joint uncertainty in all input parameters, makes no assumptions about the linearity of the cost-effectiveness model, and is computationally-efficient at the same time. The estimated threshold values obtained from generalized additive models are compared with the threshold values from existing approaches.

REAL-WORLD EXAMPLE

A health economic evaluation comparing typhoid conjugate vaccination strategies in Gavi-eligible countries is chosen to compare the different approaches.

We focus on the input parameters:
• Typhoid mortality when hospitalized (Pr(DeathHOSP))
• Probability of hospitalization with typhoid (Pr(HOSP))
• Duration of illness for patients seeking medical care (DOICare)

METHODS & RESULTS

Deterministic threshold analysis

1. Define the uncertain parameter of interest, \( \theta_i \).
2. Fix the remaining input parameters \( (\theta_i) \) at their base case value.
3. Vary the values of \( \theta_i \) and record the cost-effectiveness.
4. The parameter threshold value \( \theta_i^* \) is: \[ \theta_i^* = \{ \theta_i| \theta_i \neq \theta_i, (\text{Value}_i - \text{Cost}_i) = \text{Max} \} \]

2-level Monte Carlo approach

1. Outer level: Sample value from \( \theta_i \), obtaining \( \theta_i^{(k)} \), with k=1,...,K.
2. Inner level: Obtain NB for each decision d.
   a) Sample value from \( \theta_i \), obtaining \( \theta_i^{(k)} \), with j=1,...,J
   b) Evaluate \( NB_{\theta_i^{(k)}}(\theta_i^{(k)},d) \) for each d
   c) Repeat a) and b) J times
3. Outer level: 
   a) For each k and d, determine \( NB_{\theta_i^{(k)}}(\theta_i^{(k)},d) \) with the highest expected net benefit (\( d^* = \max_{d} NB_{\theta_i^{(k)}}(\theta_i^{(k)},d) \)) 
   b) For each \( \theta_i \), determine the threshold value in the 
   c) Repeat the outer level K times
4. When \( d^* \) is obtained for all \( \theta_i^{(k)} \), determine \( \theta_i^* \).

Generalized additive model

 Generally, a generalized additive model (GAM) looks as follows:

\[ NB_{\theta_i}(\theta_i^{(k)}) = \beta_d(\theta_i^{(k)}) + \epsilon \]

1. Define a set of S samples from the joint distribution of the model input parameters (also known as the PSA sample).
2. For each decision \( d \), we fit a GAM: \( \beta_d(\theta_i) = \beta_d(\theta_i^{(k)}) \)
3. Obtain the fitted values, \( NB_{\theta_i}(\theta_i) \), for each \( \theta_i \).
4. The parameter threshold value is \( \theta_i^* \).

95% bootstrap CI are calculated to provide a measure of accuracy of the threshold value in the presence of possible model violations. Only the bootstrap samples that produce the same number of threshold values as the original PSA are used to calculate the 95% CI (Beff, out of 1000).

SUMMARY

1. GAM performs better than the deterministic threshold analysis.
2. GAM is faster in determining the threshold value compared to the other approaches.
3. Further research needs to be done on how to improve the precision of GAM.

REFERENCES