Proposed Methods for Conducting Sensitivity Analyses on Threshold-Derived Estimates of Value-Based Price and Product Profiles of Early Stage Drugs

Deirdre Mladsi,[1] Stephanie Earnshaw,[1] Naoko Akashi-Ronquest,[1] Michael Keith[2]

[1] RTI Health Solutions, Research Triangle Park, NC, United States; [2] Shire Pharmaceuticals, Wayne, PA, United States

BACKGROUND

- Established methods exist for evaluating the effects of uncertainty around model structure and parameters on the results generated by traditional cost-effectiveness analyses (CEAs).
- These methods include, for example, one-way and probabilistic sensitivity analyses (PSAs).
- In a related poster,[1] we described value-based threshold pricing analysis, which permits a manufacturer to consider the potential value of a new drug, prior to making key pricing and development decisions, across the full spectrum of possible:
  - Indications
  - Positions in the treatment pathway
  - Potential comparators
  - Patient subgroups.
- In contrast to the primary outcome of a traditional CEA—the incremental cost-effectiveness ratio (ICER)—the primary outcomes of a value-based threshold pricing analysis conducted for a product early in development include:
  - Value-based price opportunity given a hypothetical or target product profile
  - Magnitude of effect required to justify the target price.
- To confirm assessments based on value-based threshold pricing analyses for early product development decisions, new methods of sensitivity analyses (SAs) should be explored to examine the robustness of this type of analysis.

OBJECTIVE

To explore new methods and applications of SA as it applies to value-based threshold pricing analysis.

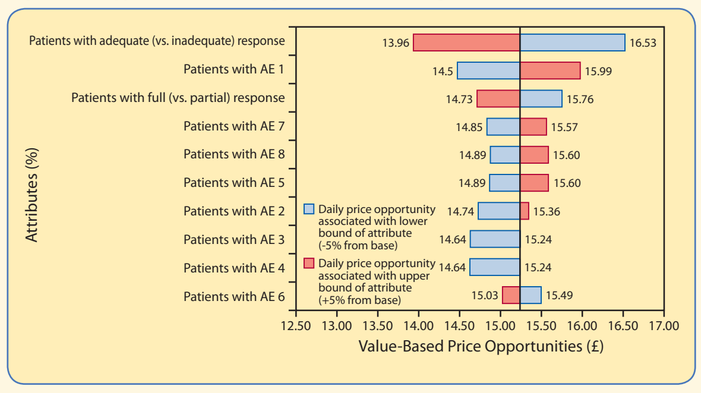
METHODS

- For this presentation, we based our examples on a hypothetical new product early in clinical development.
- We developed a threshold pricing model that produced estimates of, among other things, value-based price associated with the base-case target product profile and intended product indication, line of therapy, and comparator. (See the related poster[1] for details on the threshold pricing model and analysis approach.)
- We developed example one-way and PSA approaches for threshold pricing analyses and highlighted differences in objectives and interpretations of these new SA approaches compared with SAs as they would be applied in traditional CEA.
- We developed a one-way SA approach to examine the relationship between price (value-based and target) and individual product attributes, and we explored the use of PSA to evaluate the influence of uncertainty in all model inputs.

Pricing Contribution Diagram

- The purpose of one-way SA for a traditional CEA is to examine known uncertainty associated with model inputs on the ICER.
  - The primary outcome of a traditional CEA is the ICER.
  - Typically a tornado diagram presents a one-way SA that depicts the range over which the ICER may vary given the plausible range of values for each of the most influential model inputs.
- In contrast, the goal of a one-way SA for a value-based threshold pricing analysis is to examine the potential effects of the product attributes, so that we may understand their relative importance to achieving value-based price.
  - Figure 1 presents a hypothetical pricing contribution diagram (PCD), which characterizes the extent to which each product attribute (e.g., efficacy, safety, tolerability, quality of life, position in care pathway) influences the value-based price opportunity.
  - The anchor is a maximum value-based price opportunity (instead of an ICER).
  - The PCD examines only the potential effects of product attributes.
  - Because of the early stage of product development, there is limited product-specific information available; therefore, we varied all base product attribute values according to the same absolute changes (in this case, ±5 percentage points from baseline).
- In this hypothetical case, each baseline attribute was expressed as a percentage of patients experiencing each attribute (e.g., percentage of patients experiencing full response, percentage of patients experiencing Adverse Event 1).
- For each 1 percentage point change from baseline (i.e., for each 1 additional person out of 100 experiencing the attribute-event), the PCD shows the potential increase or decrease in value-based price that would be supported.

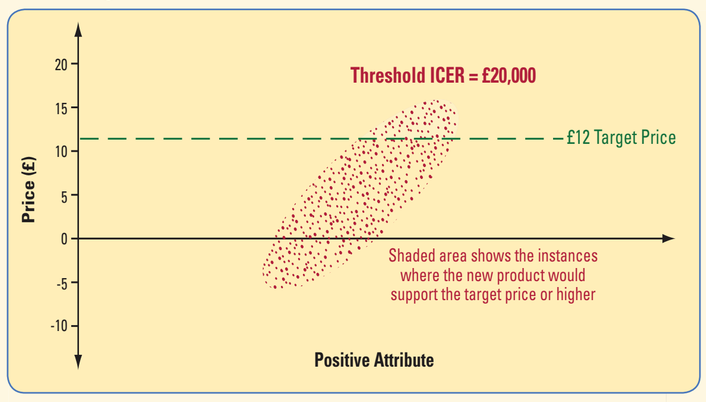
Figure 1. Hypothetical Pricing Contribution Diagram



Value-Based Price Opportunity Plane

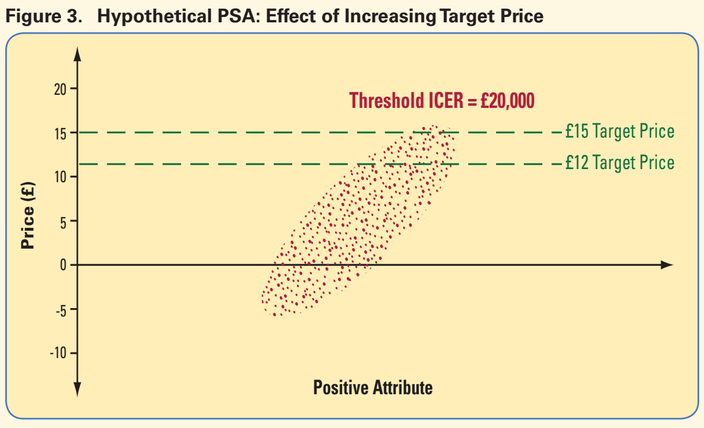
- PSA also must be approached differently in a value-based threshold pricing model. In our PSA approach, we include quantified or assumed uncertainty in any type of variable (attributes and other input parameters), as we would in a PSA of an ICER in the traditional CEA.
- Simulations, as in a traditional PSA, are run in which all variables (attributes and other inputs) are varied according to predefined distributions while the ICER threshold is held constant.
- Instead of the PSA being depicted in a cost-effectiveness plane, the PSA for a value-based threshold pricing model is depicted in the "value-based price opportunity" plane.
- A "value-based price opportunity" plane is represented with a product attribute on the x-axis and a target price on the y-axis (Figure 2).
- At every point in the plane, the hypothetical new drug is cost-effective at the threshold ICER (e.g., £20,000).
- The PSA visually depicts the number of model simulations in which the target price for the new product would be economically justifiable (i.e., that it would be a value-based price).
- The percentage of value-based prices that fall at or above the target price represents the probability that the new product will be able to support the target price (or higher) from an economic (i.e., value-based) standpoint.
- In contrast to the scenario associated with the PCD in Figure 1, the hypothetical scenario used to examine the application of PSA to threshold pricing analysis is one in which the value-based price is negative is some simulations.

Figure 2. Hypothetical PSA, Depicted in the Value-Based Price Opportunity Plane Using a Positive Attribute



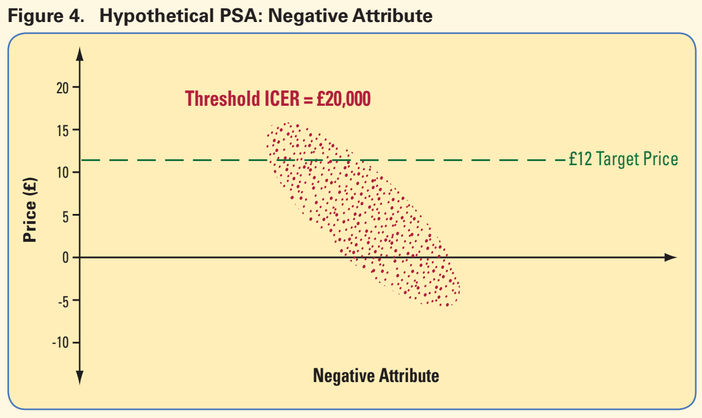
- As the target price increases, the probability that it will be value-based, all else being equal, gets smaller (Figure 3).

Figure 3. Hypothetical PSA: Effect of Increasing Target Price



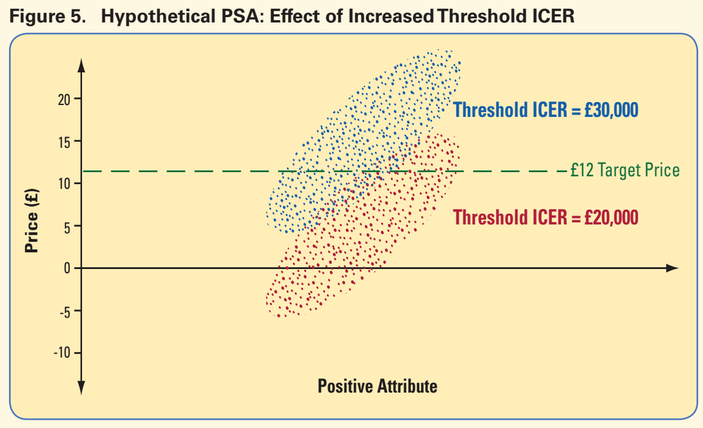
- As the rate of response to treatment with the hypothetical new drug (a "positive attribute") increases, so does the probability that the hypothetical new drug will be justifiable economically.
- The x-axis variable may be any product attribute. Selection of the product attribute would not affect the probability that the target price for the new product would be economically justifiable; it would only affect the shape of the PSA scatter.
- In contrast to Figures 2 and 3, which reflect a "positive" attribute (i.e., one that is positively correlated to value-based price), Figure 4 reflects a "negative" attribute.
- As the rate of Adverse Event 1 associated with the hypothetical new drug increases, the probability of justifying economically the target price decreases.

Figure 4. Hypothetical PSA: Negative Attribute



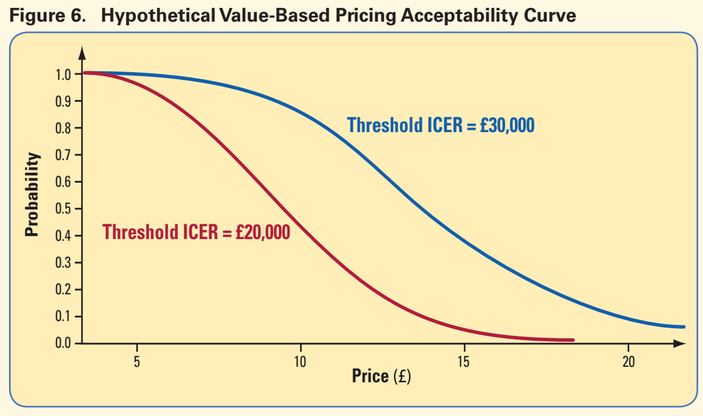
- Changing the definition of the value-threshold (e.g., from £20,000 per quality-adjusted life-year [QALY] gained to £30,000/QALY gained) serves to shift the entire PSA scatter up relative to the target price (Figure 5).
- Given a higher threshold ICER, it becomes more likely that the product profile will be able to support the target price from a cost-effectiveness standpoint.

Figure 5. Hypothetical PSA: Effect of Increased Threshold ICER



- The results of a PSA for a value-based threshold pricing analysis may be depicted in a manner similar to the cost-effectiveness acceptability curve (CEAC).
- In contrast to a CEAC, Figure 6 depicts the probability that the target price will be justifiable economically (i.e., the probability that it will be a value-based price).
- Various levels of the threshold ICER may be depicted.

Figure 6. Hypothetical Value-Based Pricing Acceptability Curve



CONCLUSIONS

- Traditional methods of conducting SA are insufficient when applied to the threshold application of CEA.
- The PCD offers a unique approach for understanding the relative potential contribution of individual attributes to supporting the target price, providing direction to data collection efforts.
- The value-based price opportunity plane provides a method for understanding–for a particular indication, line of therapy, comparator, and, patient subgroup scenario–the probability that the target price will be supported from a cost-effectiveness standpoint.
- SAs specific to threshold pricing models should be employed as a tool to inform decisions regarding early stage development.

REFERENCE

1. Mladsi D, Earnshaw S, Akashi N, Keith M. Threshold pricing model: Not just another cost-effectiveness model. Poster presented at the ISPOR 13th Annual European Conference; November 6-9, 2010. Prague, Czech Republic.

DISCLOSURE

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CONTACT INFORMATION

Deirdre Mladsi
Head, Health Economics and Market Access

RTI Health Solutions
200 Park Offices Drive
Research Triangle Park, NC 27709-2194

Phone: +1.919.541.7094
Fax: +1.919.541.7222
E-mail: dmladsi@rti.org

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