Trade-off Analysis: An Extension of Threshold Pricing Analysis

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BACKGROUND

- Investment decisions are made on the basis of whether a new drug is expected to meet certain criteria specified in a target product profile (TPP).
- Such decisions assume a target price, which is used in calculations of return-on-investment.
- Assuming a payer cost-effectiveness threshold, threshold pricing models are used to estimate the maximum value-based price of a new drug that achieves its TPP, and to estimate the minimum value-based efficacy, safety, and tolerability required to support a target price.
- To assess the effects of uncertainty, one-way and probabilistic sensitivity analyses may be tailored to apply to threshold pricing models.
- However, to assess the overall value of a new drug when it fails to achieve a particular criterion, it is essential to understand the relationships among the criteria listed in the TPP.

OBJECTIVE

- To explore trade-off analysis as an extension of value-based threshold pricing analysis.

METHODS

- Using a hypothetical new product early in clinical development, we developed a threshold pricing model that produced an estimate of the maximum value-based price associated with the base-case TPP and intended product indication and comparator.
- We examined the influence of product attributes on the estimated maximum value-based price to assess the missed price opportunity.
- We developed trade-off analyses to examine the relationship among product attributes when estimating maximum value-based price.

The Hypothetical Threshold Model

- We developed a simple decision-analytic model (Figure 1 and Table 1).
  - A hypothetical cohort of patients takes either standard of care (SOC) or a new product to treat a hypothetical condition.
  - The new product is expected to reduce the probability of hospitalization, the probability of in-hospital mortality, and the length of stay over the course of a 1-year timeframe.

Figure 1. Decision Tree

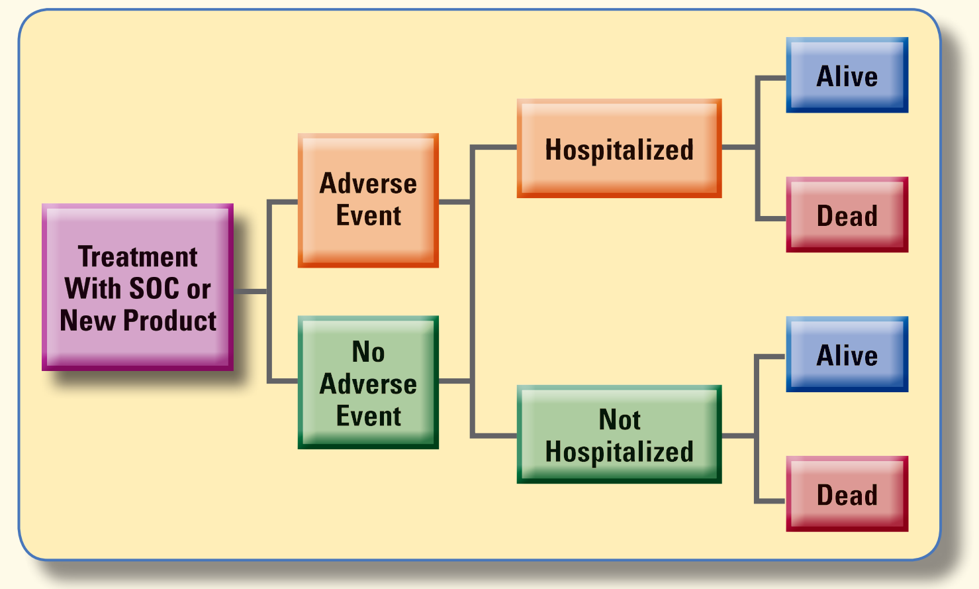


Table 1. Hypothetical Model Inputs and New Product TPP[a]

Input	SOC	New Product	
		TPP	Resulting Value
Probability of hospitalization	13.14%	25% better than SOC	9.86%
Probability of in-hospital mortality	1.92%	5% better than SOC	1.82%
Probability of adverse event	16.00%	Same as SOC	16.00%
Probability of mortality for patients not hospitalized	0.00%	Same as SOC	0.00%
Hospital length of stay	4.60 days	0.25% better than SOC	4.59 days
Cost inputs			
Daily price of SOC	$17.50		
Daily price of new product	$20.00		
Cost per day in hospital	$1,994.13		
Cost to treat adverse event	$175.00		
Health utility inputs			
Utility for hospitalization	0.60		
Utility for nonhospitalization	1.00		
Disutility for adverse event per day	0.15		
Duration of disutility for adverse event	15 days		

[a] All mathematical values are for illustrative purposes only.

- Traditional cost-effectiveness model results:
  - Incremental average per-person cost of the new product compared with SOC = $604.16
  - Incremental average per-person quality-adjusted life-year (QALY) of the new product compared with SOC = 0.033
  - Incremental cost per QALY gained = $18,606.
- Threshold analysis results:
  - Assuming a $50,000 willingness-to-pay threshold for incremental cost per QALY gained, the resulting maximum value-based price for the new product is estimated to be $22.82.
  - With a target price of $20.00, there is a missed price opportunity of $2.82.
  - Figures 2 through 4 show the influence of three attributes of the new product (probability of hospitalization, length of stay, and probability of an adverse event) on the estimated value-based price.

Figure 2. Influence of Probability of Hospitalization on Value-Based Price of New Product

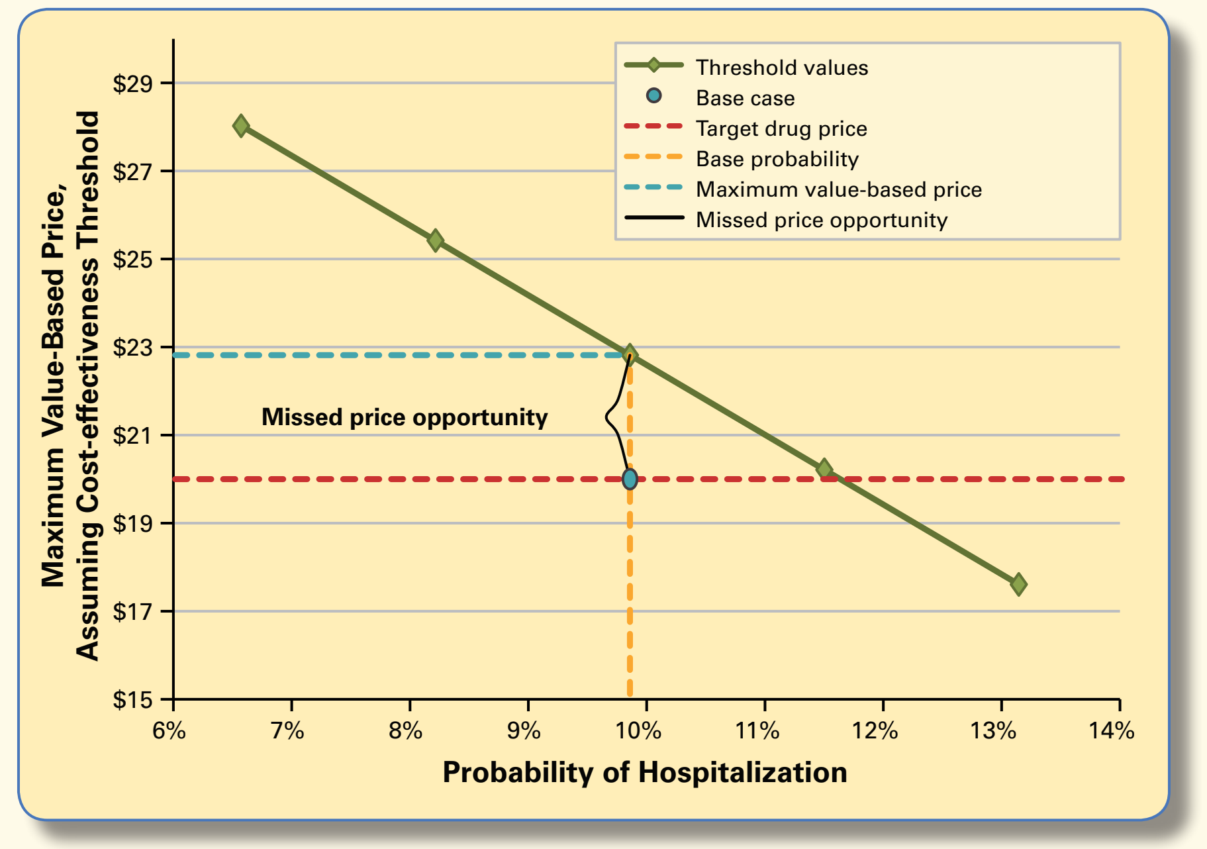


Figure 3. Influence of Length of Stay on Value-Based Price of New Product

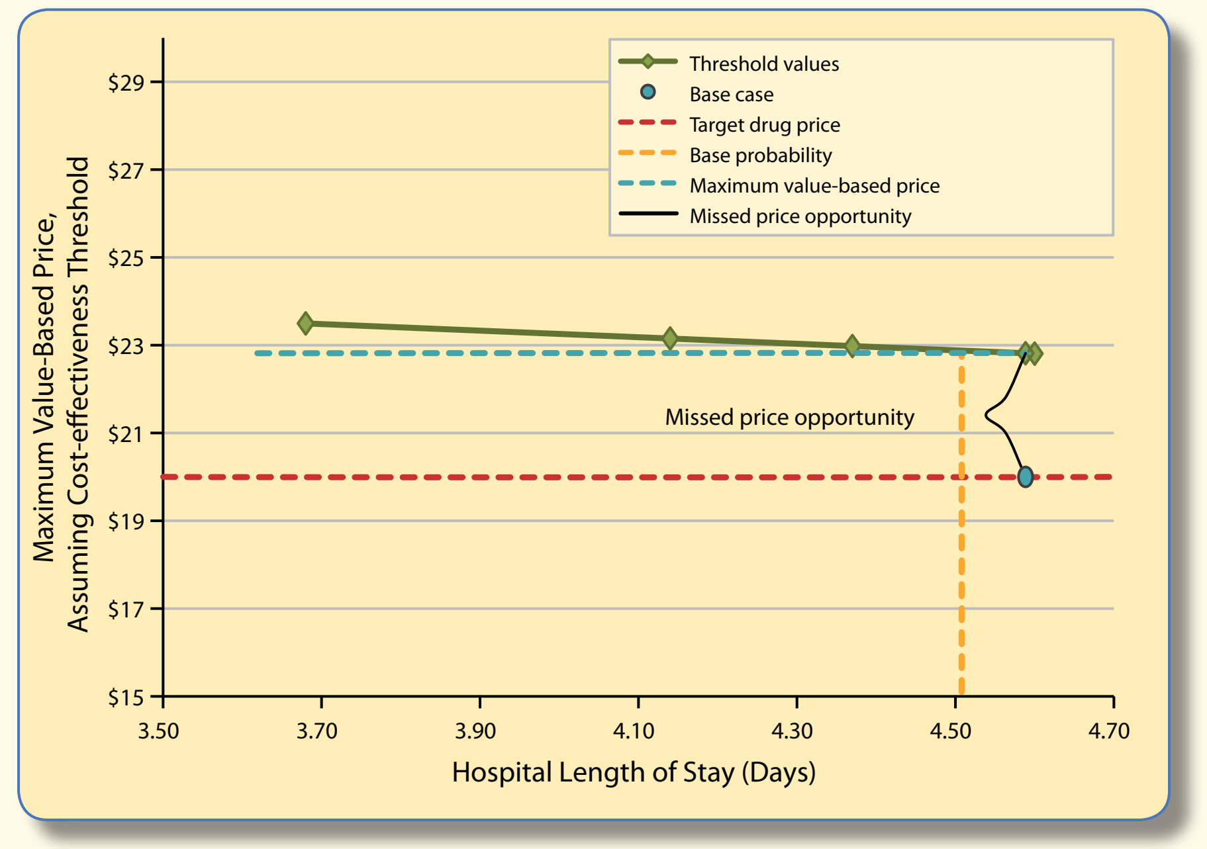
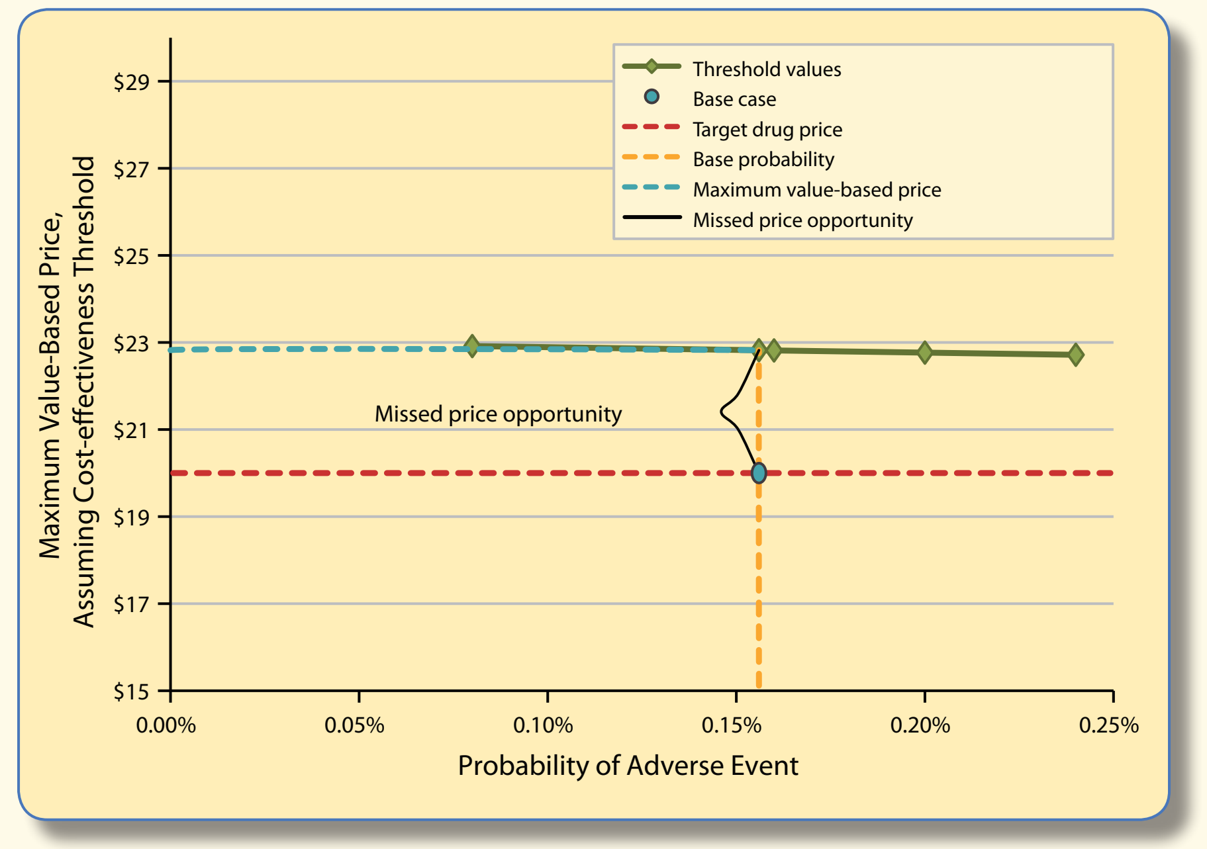


Figure 4. Influence of Probability of an Adverse Event on Value-Based Price of New Product



The Trade-off Analysis

- Using trade-off analysis, it is possible to estimate the improvement required in one attribute to offset the failure of the new drug to achieve the expected effect in one or more attributes and retain the maximum value-based price.
- As in the threshold pricing model, the following incremental cost-effectiveness ratio (ICER) equation must be solved for the applicable unknown. However, the individual components that determine the total cost and QALYs for the new product must be expanded further to solve for the minimum value-based levels of individual attributes.

Equation 1. ICER Equation, Assuming Threshold ICER

Possible unknown

$$\mathrm{ICER}_T = \frac{\boxed{\text{Total Cost}_{NP}} - \text{Total Cost}_{SOC}}{\boxed{\text{Total QALY}_{NP}} - \text{Total QALY}_{SOC}}$$

Alternative unknown

NP = new product.

- Equation 2 depicts the ICER equation but highlights the approach of solving the equation for an attribute when another attribute varies and the maximum value-based price is maintained.
- In this example equation, the target reduction in mortality is not reached and the reduction in hospitalization needed to maintain the maximum value-based price is the unknown.
- The terms of this equation are as follows:
  - **ICER_T**: the threshold ICER
  - **$\text{Total Drug Cost}_{NP\text{-}MVP}$**: the total drug cost over the 1-year time horizon for the new product given that the maximum value-based price is used (duration of use is adjusted for mortality)
  - **$\%\ \text{Hospitalized}_{NP\text{-}TO}$**: the unknown representing the required percentage (trade-off) of hospitalization needed for the new product to maintain the maximum value-based price (one minus this term gives the percentage not hospitalized)
  - **$\text{Cost Per Stay}_{NP}$**: the cost if a patient taking the new product is hospitalized (i.e., cost per day times the length of stay for a patient who takes the new product)
  - **$\text{Cost of Adverse Event}_{NP}$**: the amount it costs to treat the adverse event if a patient taking the new product gets the adverse event (i.e., cost to treat adverse event times the percentage of patients receiving the new product that get the adverse event)
  - **Total Cost_{SOC}**: unchanged from Equation 1, the total cost for a patient who is receiving SOC (i.e., drug cost plus hospitalization cost plus adverse event cost)
  - **$\text{QALY}_{NP\text{-}Hospital}$**: the QALYs associated with a patient who is taking the new product and is hospitalized
  - **$\text{QALY}_{NP\text{-}Nonhospital}$**: the QALYs associated with a patient who is taking the new product and is not hospitalized
  - **Total QALY_{SOC}**: unchanged from Equation 1, the total QALYs (hospitalized and nonhospitalized patients) associated with a patient taking SOC

Equation 2. ICER Equation, Assuming Mortality Reduction Target is Not Met

Unknown

$$\mathrm{ICER}_T = \frac{[\text{Total Drug Cost}_{NP\text{-}MVP} + (\boxed{\%\ \text{Hospitalized}_{NP\text{-}TO}} \bullet \text{Cost Per Stay}_{NP}) + \text{Cost of Adverse Event}_{NP}] - \text{Total Cost}_{SOC}}{[\boxed{\%\ \text{Hospitalized}_{NP\text{-}TO}} \bullet \text{QALY}_{NP\text{-}Hospital} + (1 - \boxed{\%\ \text{Hospitalized}_{NP\text{-}TO}}) \bullet \text{QALY}_{NP\text{-}Nonhospital}] - \text{Total QALY}_{SOC}}$$

Unknown *Unknown*

TO = trade-off.

- Equation 2 must be solved for the new reduction in hospitalization needed for the new product, given a reduction of mortality that did not reach the target (which also may be accomplished using the Goal Seek function in Microsoft Excel). The resulting equation is shown in Equation 3.

Equation 3. Trade-off Equation

$$\%\ \text{Hospitalized}_{NP\text{-}TO} = \frac{(\text{Total Drug Price}_{NP\text{-}MVP} + \text{Cost of Adverse Event}_{NP}) - \text{Total Cost}_{SOC} + \mathrm{ICER}_T \bullet (\text{Total QALY}_{SOC} - \text{QALY}_{NP\text{-}Nonhospital})}{\mathrm{ICER}_T \bullet (\text{QALY}_{NP\text{-}Hospital} - \text{QALY}_{NP\text{-}Nonhospital}) - \text{Cost Per Stay}_{NP}}$$

- Using the threshold value-based pricing model, it is possible to estimate improvements required in other attributes, such as improved reduction in length of stay or reduction in hospitalization, to offset potential failure for the mortality attribute to reach or exceed expectations. Table 2 presents these hypothetical trade-offs for the new product's attributes.

Table 2. Attribute Trade-offs When Target Improvement in Mortality is Not Reached

Reduction in Probability of In-Hospital Mortality for the New Product	Reduction in Length of Stay Needed to Offset the Change in Probability of In-Hospital Mortality and to Continue to Meet the Maximum Value-Based Price ($22.82)	Reduction in Probability of Hospitalization Needed to Offset the Change in Probability of In-Hospital Mortality and to Continue to Meet the Maximum Value-Based Price ($22.82)
0.00%[a]	3.21%	25.50%
2.50%	1.73%	25.24%
3.70%	1.00%	25.13%
5.00%[b]	0.25%[b]	25.00%[b]
7.50%	-1.23%[c]	24.76%
10.00%	-2.71%[c]	24.51%

[a] New product's probability of in-hospital mortality is the same as SOC.

[b] TPP values for new product (base case).

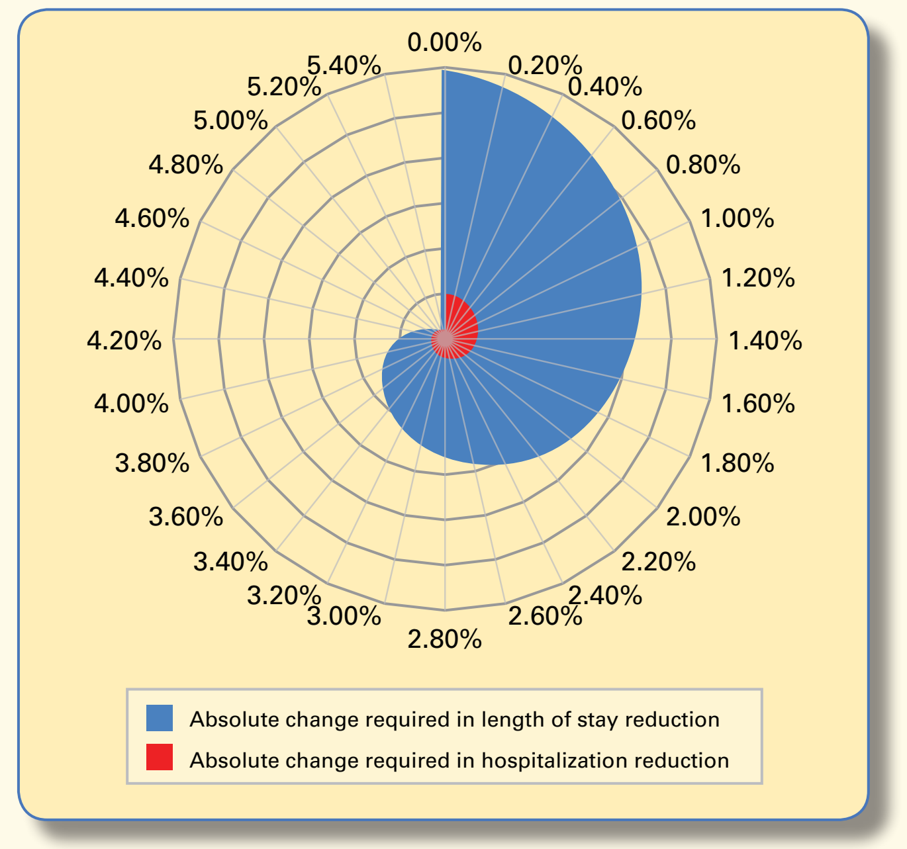
[c] Negative percentages indicate that as the mortality reduction increases, the length of stay can increase and the maximum value-based price can still be reached.

- The trade-off results show that if the new product fails to hit the target of 5.00% reduction in mortality and instead has a 3.70% reduction compared with SOC, then the relative reduction in hospital length of stay must quadruple (from 0.25% to 1.00%).
- The results also show that only small changes in the reduction of hospitalization are needed to offset the change in probability of in-hospital mortality.

Presentation Method for Trade-off Analyses

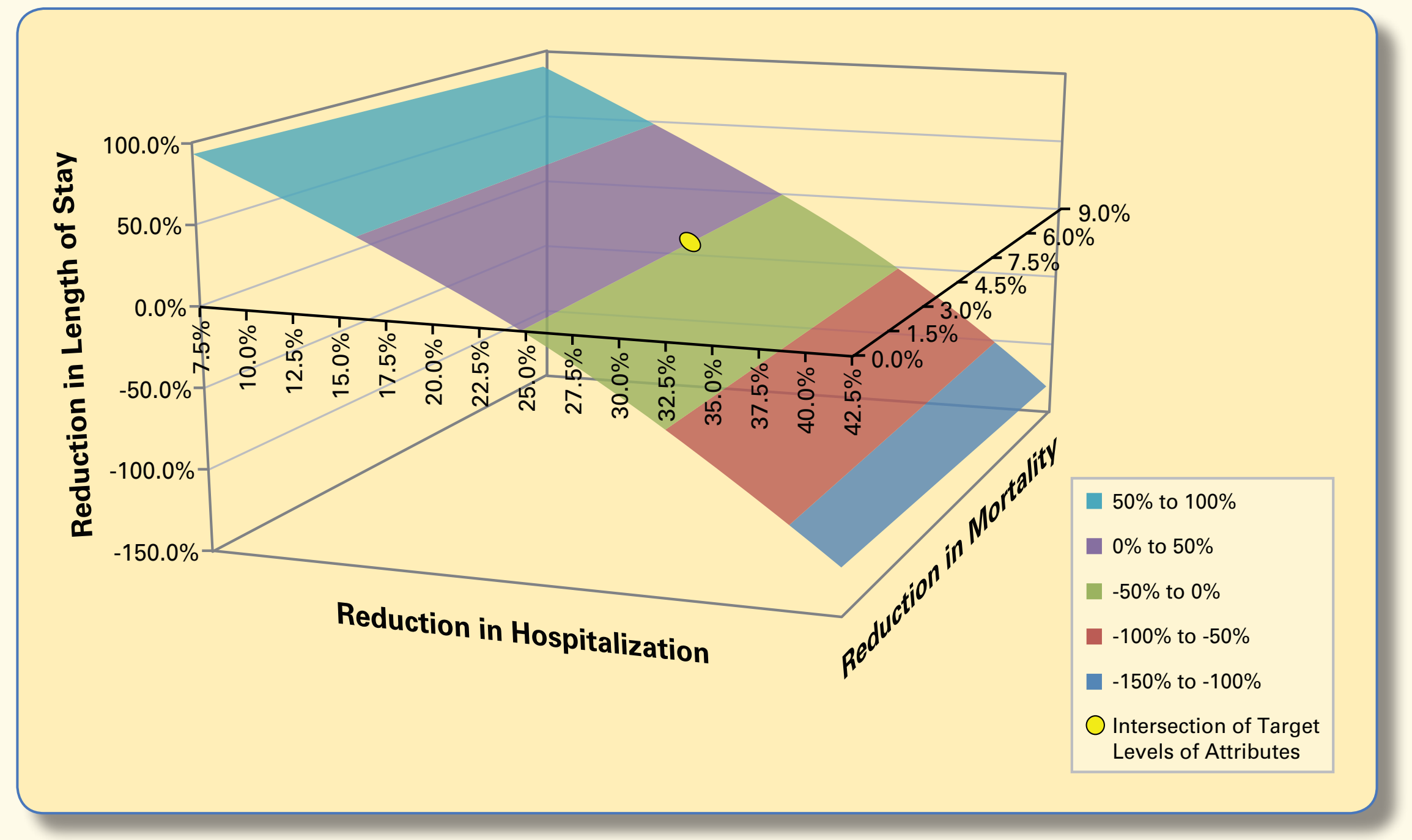
- Because it is important to understand the trade-offs among more than two attributes for one product, we explored tools to present such trade-offs visually.
- These graphical tools make it easier to visualize the magnitude of change required for an attribute when one or more attributes fail to achieve the targeted level.
- One way to visualize trade-off analysis is to graphically show a comparison of the trade-offs needed to maintain the maximum value-based price of two attributes when a third fails to reach the target level.
  - A "radar" chart can be used to create this visualization.
  - The chart helps to show what attributes may be easier to reach in order to maintain the maximum value-based price (i.e., ranks the attributes).
- Figure 5 presents an example of this concept based on the hypothetical model.
  - The percentages along the circle correspond to the reductions in the probability of in-hospital mortality, and the blue and red areas corresponding to each range of the mortality reduction represent the absolute change in the reduction of length of stay and the absolute change in the reduction of the probability of hospitalization with the new product that are necessary to offset the change in the probability of in-hospital mortality.
  - As the reduction in the probability of in-hospital mortality gets closer to 0.00% (probability equal to SOC), a greater reduction in both length of stay and probability of hospitalization are needed to offset the change compared with when the reduction in the probability of in-hospital mortality is closer to the targeted value (5.00% reduction).
  - Only small changes in the reduction in the probability of hospitalization are needed to offset changes to the probability of in-hospital mortality when compared with the reduction needed for length of stay.

Figure 5. Example Comparison of Trade-offs for Two Attributes as a Third Attribute Fails to Reach the Target Level



- An alternative tool is needed to visually analyze trade-offs when two attributes fail to reach the target levels.
- Figure 6 depicts the results of an analysis in which a reduction in length of stay is needed to offset missed targets in both the reduction in probability of hospitalization and in-hospital mortality.
- Figure 6 indicates that as both the reduction in probability of hospitalization and in-hospital mortality decrease, the reduction in length of stay must increase. The reduction approaches 100%; therefore, mean length of stay would have to be 0 days.
- Figure 6 also indicates that when the reduction in in-hospital mortality is close to the target but the reduction in probability of hospitalization is lower than the target, the reduction in length of stay must still be greater than the target.
- However, when the reduction in in-hospital mortality is not met but the reduction in probability of hospitalization is, then the reduction in length of stay does not have to be as great.
- Only small changes in hospitalization reduction can affect the results.

Figure 6. Trade-off Analysis Representation When the New Product Fails to Reach Target Levels of Two Attributes



CONCLUSIONS

- When applied to a threshold pricing model, trade-off analyses can make important contributions to value-based product development.
- The relationships between the product attributes given the maximum value-based price can be determined.
- Innovative graphical tools to analyze trade-offs among multiple attributes can facilitate the determination of key attributes for a product.

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