Incorporating Risk Attitude into Markov-process Decision Models: Importance for Individual Decision Making

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Most decision models published in the medical literature take a risk-neutral perspective. Under risk neutrality, the utility of a gamble is equivalent to its expected value and the marginal utility of living a given unit of time is the same regardless of when it occurs. Most patients, however, are not risk-neutral. Not only does risk aversion affect decision analyses when tradeoffs between short- and long-term survival are involved, it also affects the interpretation of time-tradeoff measures of health-state utility. The proportional time tradeoff under- or overestimates the disutility of an inferior health state, depending on whether the patient is risk-seeking or risk-averse (it is unbiased if the patient is risk-neutral). The authors review how risk attitude with respect to gambles for survival duration can be incorporated into decision models using the framework of risk-adjusted quality-adjusted life years (RA-QALYs). Using a previously published Markov-process model of surgical vs expectant treatment for benign prostatic hypertrophy (BPH), they show how attitude towards risk affects the expected number of QALYs calculated by the model. In this model, under risk neutrality, surgery was the preferred option. Under mild risk aversion, expectant treatment was the preferred option. Risk attitude is an important aspect of preferences that should be incorporated into decision models where one treatment option has upfront risks of morbidity or mortality. Key words: risk attitude; Markov models; patient preferences; quality-adjusted life years. (Med Decis Making 1997;17:340-350)

Patient preferences for quality of life are a well-recognized component of medical decision modeling. The concept of quality-adjusted life years (QALYs), routinely used in decision modeling in the medical domain, attempts to take into account an individual's values regarding both survival duration and quality of life. Risk attitude, a third component of decision making, is not routinely accounted for in the current decision-making literature. All medical decisions are made under the condition of uncertainty and involve risks. Therefore, it seems reasonable to include attitude towards risk in medical decision models. There is evidence that attitude towards risk regarding gambles for length of life in perfect and poor health should play an important role in patients' clinical decision making. Failure to include attitude towards risk in decision models may result in recommendations that are mathematically optimal but simply do not "make sense at the bedside."

Depending on the method used to assess health-state utilities, decision models can either incorporate or ignore nonlinearity in risk attitudes towards survival duration. To explain this point, we must first review briefly the role of risk aversion in QALY utility models. The standard QALY model assumes a risk-neutral perspective with respect to survival duration.* Specifically, the utility of surviving T years in health state Q is assumed to satisfy the formula:

\[ U(Q, T) = \left( \frac{T}{T^*} \right) \cdot H(Q) \]  

(1)

where \( H(Q) \) is the utility of health state \( Q \) scaled on a range from 0 for death to 1.0 for full health, and \( T^* \) is the maximum that a patient can expect to live. We divide the survival duration \( T \) by \( T^* \) in order to
scale the utility of survival duration from 0.0 to 1.0. As is evident, this QALY model asserts a linear utility function for survival duration.

In their original analysis of the QALY model, Pliskin, Shepard, and Weinstein proposed several more general QALY utility models that incorporate nonlinear risk attitude towards survival duration. Miyamoto and Eraker noticed that one of these models could be expressed in a particularly simple form, namely,

\[ U(Q, T) = \left( \frac{T}{T^*} \right)^\beta \cdot H(Q) \]  

where \( \beta \) is a parameter representing risk attitude. The case of \( \beta = 1 \) is the standard QALY model that assumes risk neutrality; when \( \beta > 1 \), risk-seeking preferences are assumed; when \( \beta < 1 \), risk-averse preferences are assumed. From a clinical standpoint, a risk-averse individual achieves greatest utility during future time periods that are closest to the present, and hence, is less willing to risk morbidity or mortality in the short term even if the risk carries a potential benefit in the long term. We refer to the model of equation 2 as a risk-adjusted QALY (RA-QALY) model because the model takes into account risk attitude towards survival duration as well as tradeoffs between duration and quality of survival. Below we introduce another RA-QALY model.

It has been clear for some time that risk aversion with respect to survival duration is important in decisions involving choices between treatments that differ in the chances for short- and long-term survival. What has not been widely appreciated is that nonlinearities in the utilities of survival duration also affect the measurement of health-state utilities, i.e., the measurement of \( H(Q) \) in equation 2 [6,7]. To see this point, suppose that a patient judges 15 years in full health to be equal in preference to 25 years in an inferior health state \( Q \). For this patient, the proportional time tradeoff (TT0) is 15/25. We consider how this TT0 should be interpreted under assumptions of linear and nonlinear utilities for survival duration. The left panel of figure 1 depicts the linear utility assumptions of the standard QALY model (equation 1). The line connecting (0, 0) to point A is the utility function for full health, and the line connecting (0, 0) to point B is the utility function for survival duration in health state \( Q \). Points B and C are at the same height, indicating that the utility of 25 years in health state \( Q \) is equal to the utility of 15 years in full health. \( H(Q) \) is the ratio of the utility of (25 years, health state \( Q \)) to the utility of (25 years, full health), i.e., the ratio \( B/A \).

Because the utility functions are linear, \( B/A \) equals 15/25, hence, \( H(Q) = 0.6 \). Now consider risk-averse utility functions as in the right panel of figure 1. According to the RA-QALY model (equation 2), the health-state utility \( H(Q) \) equals the ratio of the utility of (25 years, health state \( Q \)) to the utility of (25 years, full health), i.e., the ratio \( B'/A' \). Because the utility functions are risk-averse, \( B'/A' \) does not equal 15/25. Rather \( B'/A' = H(Q) > 15/25 \), and it should be clear that this relationship holds for any risk-averse utility function. A similar argument shows that if the utility functions are risk-seeking, the proportional time tradeoff overestimates the health-state utility.

The preceding arguments show that risk aversion affects the utility analysis of treatment selection in two ways. First, it implies greater utility increases in the short term than in the long term, thereby favoring treatments that offer greater chances of superior health states in the short term. Second, it implies that proportional time tradeoffs underestimate the utilities of inferior health states. The primary focus of the present study was to examine how these two implications of risk aversion affect the utility analysis of treatment selection in a Markov-process model for benign prostatic hypertrophy.

Before examining this problem, however, we should briefly discuss whether biases in the measurement of health-state utilities could be avoided if the utilities were measured with standard gambles.
(SGs) rather than time tradeoffs. Because the SG procedure requires that patients trade off probability rather than time, would not the SG procedure avoid the biasing effects of risk attitude? The answer is that the SG procedure does indeed avoid the biasing effect of risk attitude, but it does so at the price of introducing a different bias due to nonlinear probability weighting. Under expected-utility assumptions, if a patient is indifferent between 25 years in health state Q and a p chance of 25 years in full health and a 1 - p chance of death, then the health state utility H(Q) = p. This holds true regardless of whether the utility of survival duration is linear or nonlinear.*

Unfortunately, the inference that H(Q) = p is invalid if the psychological weight of a probability is a nonlinear function of the probability.† Specifically, if the psychological process maps the probability p nonlinearly to a probability weight w(p), as postulated in cumulative prospect theory and rank-dependent utility theory, then H(Q) = w(p), not H(Q) = p.† To the extent that the probability-weighting function is nonlinear, and w(p) ≠ p, the SG probability p is a biased measure of health-state utility. In this paper, we explain how a Markov decision process is altered when time tradeoffs are corrected for the biasing effects of risk attitude. We leave it to future investigations to determine how the Markov decision process would be altered if health-state utilities were measured by SGs and the biasing effects of nonlinear probability weighting were taken into account.

In this paper we study two classes of RA-QALY models. The first, the power QALY model, is stated formally in equation 2. The second, the exponential family of utility models, is defined by the equation:

$$U(Q, T) = \frac{1}{1 - e^{-\lambda Q}} H(Q)$$  (3)

Equation 3 differs from equation 2 only in that the utility of survival duration is now described by an exponential function rather than a power function. In the model of equation 3, the patient is risk-averse if \( \lambda > 0 \), and risk-seeking if \( \lambda < 0 \). In the risk-neutral case (\( \lambda = 0 \)), we replace the exponential function with the linear function, \( U(Q, T) = (T/T^*) \cdot H(Q) \), or equation 1. Thus, the standard risk-neutral QALY model (equation 1) is contained as a special case of both the power and exponential QALY models (equations 2 and 3).

The power and exponential QALY models are themselves special cases of a more general class of models, the multiplicative utility model for survival duration and health quality, that was introduced by Miyamoto and Eraker. According to this model, \( U(Q, T) = F(T) \cdot H(Q) \) for some utility functions F and H. The power and exponential QALY models are single-parameter classes of models, whereas the multiplicative utility model would allow the utility of survival duration, F, to be described by more parameters, or even to have a form that is not describable by a parametric model. One reason for considering the multiplicative utility model as a generalization of the power and exponential QALY models is that it is possible to test the predictions that derive from the multiplicative form of the utility functions, as well as predictions that derive from the specific parametric forms.

It is likely that single-parameter models of risk attitude, such as those represented by equations 2 and 3, are oversimplifications. Miyamoto and Eraker tested axioms for the power and exponential utility functions for survival duration in a sample of 38 student subjects. The axiom for the power functions was violated by 92% of the subjects at the 0.05 level of significance. The axiom for the exponential functions was violated by 74% of the subjects at the 0.05 level of significance. Nevertheless, we would argue that the RA-QALY models (equations 2 and 3) are useful approximations because they allow one to summarize the degree of risk aversion or risk seeking in a single-parameter value. Furthermore, if a single-parameter representation of risk attitude is an oversimplification, the assumption of risk neutrality in the standard QALY model is an even grosser oversimplification. Risk neutrality was violated by 92% of Miyamoto and Eraker’s subjects, and comparisons of goodness of fit show that the power and exponential models of risk attitude are clearly superior to the risk-neutral utility model.

RA-QALY models have lain fallow for many years because in their published form, they apply only to decision-tree representations of decision models. This form of representation has largely been eclipsed by Markov-process modeling. In this paper we describe simple extensions of the RA-QALY models that allow the incorporation of risk preferences into Markov-process decision models. We then illustrate, using a well-known decision model for a domain thought to be sensitive to preferences for quality of life, how variations in attitudes towards risk can dominate other aspects of preferences in the calculation of the optimal treatment strategy.

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*Indeed, for the derivation to be valid, one need only assume that \( U(T, Q) = F(T) \cdot H(Q) \) for some function F. The QALY model (equation 1) and the RA-QALY model (equation 2) are special cases of this more general assumption.

†This claim is valid within the cumulative prospect-theory framework provided that the reference level for survival duration is 0, i.e., current age is the status quo. If the reference level is greater than zero, the interpretation of SG utilities is even more complicated.
Methods

HEALTH-STATE UTILITIES IN A RISK-ADJUSTED QALY MODEL

Here we present the calculation of health-state utilities in BA-QALY models. Consider first the power QALY model defined by equation 2. Our method for determining health-state utilities follows that of Miyamoto and Eraker.\(^6\) Let \(T^*\) represent the maximum duration that a patient might expect to live in the given decision problem, and let \(Q^*\) represent full health. Suppose that a patient is asked to provide a time-tradeoff judgment, and judges \(X\) years in full health \(Q^*\) to be equal in preference to \(Y\) years in health state \(Q\). In utility terms, the patient has made the judgment. \(U(X, Q^*) = U(Y, Q)\). Equation 2 implies that \((X/T^*)^\beta \cdot H(Q^*) = (Y/T^*)^\gamma \cdot H(Q)\). Therefore

\[
H(Q) = (X/Y)^\beta
\]

since \(H(Q^*) = 1.0\). Equation 4 can be used to infer the value of \(H(Q)\) from TTO values under the assumptions of the power QALY model (equation 2).

Equation 4 has two important implications. First, it shows that if risk attitude towards survival duration is nonlinear, as described in equation 2, the proportional time-tradeoff \(X/Y\) misrepresents the utility of the health state \(Q\). The bias in the proportional time tradeoff is removed by raising \(X/Y\) to the power \(\beta\), the parameter in equation 2 that represents the degree of curvature of the utility function for survival duration. Equation 4 gives algebraic confirmation to a point made in our discussion of the geometry of figure 1, namely, that if the utility function is risk-averse, then \(\beta < 1\), and \(H(Q) = (X/Y)^\beta > X/Y\). Conversely, if the utility function is risk-seeking, then \(r > 1\) and \(H(Q) = (X/Y)^\beta < X/Y\). Thus, the proportional time tradeoff overestimates or underestimates the utility of health state \(Q\), depending on whether the utility function is risk-seeking or risk-averse. Second, the power QALY model (equation 2) implies that time tradeoffs must satisfy the property of constant proportional time tradeoff. In other words, there exists a constant \(K_Q\) such that for any \(Y\) years in health state \(Q\) is equal in preference to \(K_Q\cdot Y\) years in full health \(Q^*\). This implication follows immediately from equation 4 since \(H(Q)\) is a function of the ratio of values \(X/Y\), and therefore this ratio must be the same for any \(X\) and \(Y\) that stand in a TTO relation. Indeed, equation 4 shows that \(K_Q\), the constant of proportionality, must have the value \(K_Q = H(Q)^\beta\). We can easily verify that for any \(Y\), \(K_Q\cdot Y\) years in health state \(Q^*\) is equal in preference to \(Y\) years in health state \(Q\), i.e., \(U(K_Q\cdot Y, Q^*) = K_Q\cdot Y/T^*)^\beta \cdot H(Q^*) = H(Q)(Y/T^*)^\beta = U(Y, Q)\).

Next we develop a formula for \(H(Q)\) in the exponential QALY model (equation 3). Suppose a subject judges \(X\) years in full health to be equal in preference to \(Y\) years in health state \(Q\). Then \(U(Q^*, X) = U(Q, Y)\). By equation 3, we have

\[
\frac{1 - e^{-\lambda X/T^*}}{1 - e^{-\lambda Y/T^*}} \cdot H(Q^*) = \frac{1 - e^{-\lambda Y/T^*}}{1 - e^{-\lambda X/T^*}} \cdot H(Q)
\]

\[
H(Q) = \frac{1 - e^{-\lambda X/T^*}}{1 - e^{-\lambda Y/T^*}}
\]

Equation 5 can be used to infer the value of \(H(Q)\) from TTO values under the assumptions of equation 3. Equation 5 shows that the exponential family of QALY models does not satisfy constant proportional time tradeoff because in this family, \(H(Q)\) is not a function of the ratio \(X/Y\).

We may summarize the results for the power and exponential families of QALY models. Let \(X\) and \(Y\) be any durations such that \(X\) years in full health are judged to be equal in preference to \(Y\) years in health state \(Q\). Substituting the formula for \(H(Q)\) in equation 4 into equation 2, we have a characterization of the power family of QALY models.

\[
U(Q, T) = \left( \frac{T}{T^*} \right)^\beta \cdot \left( \frac{X}{Y} \right)^\beta
\]

Similarly, substituting the formula for \(H(Q)\) in equation 5 into equation 3, we have a characterization of the exponential family of QALY models:

\[
U(Q, T) = \left[ \frac{1 - e^{-\lambda Y/T^*}}{1 - e^{-\lambda X/T^*}} \right] \cdot \left[ \frac{1 - e^{-\lambda X/T^*}}{1 - e^{-\lambda Y/T^*}} \right]
\]

Equations 6 and 7 are the full specification of the two RA-QALY models that we consider in this paper.

Pliskin et al. provided axioms for a more general version of the power QALY model in their seminal paper. Their version was more general than the present power QALY model (equation 6) because it allowed for negative powers and logarithmic functions for the utility of survival duration. We exclude these functional forms because they imply that the utility of death is \(-\infty\), and therefore the patient should be unwilling to undergo any risk of death no matter how small for a potential prolongation of life. One cannot drive to a clinic to visit one’s doctor with such a utility function. A number of more recent papers have suggested simplifications, improvements, or generalizations of the Pliskin et al. axiomatization.\(^{10-14}\) Equation 4, the formula for estimating \(H(Q)\) from a TTO value under assumptions of a power QALY model, was derived by Miyamoto.
and Eraker. Stiggelbout et al. found that application of equation 4 to TTO data largely eliminated the discrepancy between TTO and SG measures of health-state utility. We know of no published axiomatizations of the exponential QALY model (equation 3). Therefore, we present an original set of axioms for this model in an appendix to this paper. Equation 5, the formula for estimating \( H(Q) \) from a TTO value under the assumptions of an exponential QALY model, is also new to this paper, and, of course, has not previously been applied to TTO data.

Let \( U(Q, T) \) be given by either the power QALY model (equation 6) or the exponential QALY model (equation 7). The expected utility for a standard decision tree of a prospect in RA-QALYs can be calculated as:

\[
EU = \sum_{i=1}^{\text{numstates}} U(Q_i, T_i) \cdot p(Q_i, T) = \sum_{i=1}^{\text{numstates}} [U(Q^*, T)H(Q_i)] \cdot p(Q_i, T) \quad (8)
\]

In other words, the expected utility (EU) is the sum over all health states of the utility of living time \( T \) in a health state times the probability of being in that health state. Using these formulas, the difference (in RA-QALYs) in the expected utilities of prospects can be compared across a range of attitudes towards risk.

Up to now, our analysis has assumed that a single health state \( Q_i \), is experienced throughout the duration of survival, i.e., health states are assumed to be chronic or unchanging. The next section generalizes the EU analysis to a discrete Markov decision process, and thus allows for changing health states.

### Extensions for Markov-Process Models

In order to adapt the RA-QALY model for discrete Markov processes, we derived a formula for the gain in utility per cycle (marginal utility) of the process. During each cycle, a theoretical subject gains a “risk-adjusted” utility closely approximated by the first derivative of the utility function times the cycle length:

\[
\text{Marginal RA-QALY} = (\frac{d}{dt} U(Q, T)) \cdot c
\]

where \( t \) denotes the time corresponding to the midpoint of the cycle, and \( c \) denotes the cycle length. The sum of the product of probabilities and marginal RA-QALYs for each cycle over both time and

### Table 1 Example of Marginal Utility Calculations in Risk-adjusted QALY Model for Living

<table>
<thead>
<tr>
<th>Month</th>
<th>No Adjustment</th>
<th>Discounting at 3% per Year</th>
<th>Power Utility Curve, ( \beta = 0.5 )</th>
<th>Exponential Utility Curve, ( \lambda = 3 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.80</td>
<td>0.80</td>
<td>8.93</td>
<td>3.00</td>
</tr>
<tr>
<td>2</td>
<td>0.80</td>
<td>0.80</td>
<td>5.37</td>
<td>2.97</td>
</tr>
<tr>
<td>3</td>
<td>0.80</td>
<td>0.79</td>
<td>4.54</td>
<td>2.95</td>
</tr>
<tr>
<td>4</td>
<td>0.80</td>
<td>0.79</td>
<td>4.00</td>
<td>2.92</td>
</tr>
<tr>
<td>5</td>
<td>0.80</td>
<td>0.79</td>
<td>3.82</td>
<td>2.90</td>
</tr>
<tr>
<td>Subtotal</td>
<td>4.0 RN-QALMs</td>
<td>3.97 RN-QALMs (discounted)</td>
<td>24.45 RA-QALMs</td>
<td>4.73 RA-QALMs</td>
</tr>
<tr>
<td>356</td>
<td>0.80</td>
<td>0.33</td>
<td>0.45</td>
<td>0.16</td>
</tr>
<tr>
<td>357</td>
<td>0.80</td>
<td>0.33</td>
<td>0.45</td>
<td>0.15</td>
</tr>
<tr>
<td>358</td>
<td>0.80</td>
<td>0.33</td>
<td>0.45</td>
<td>0.15</td>
</tr>
<tr>
<td>359</td>
<td>0.80</td>
<td>0.33</td>
<td>0.45</td>
<td>0.15</td>
</tr>
<tr>
<td>360</td>
<td>0.80</td>
<td>0.33</td>
<td>0.45</td>
<td>0.15</td>
</tr>
<tr>
<td>Subtotal</td>
<td>4.0 RN-QALMs</td>
<td>1.66 RN-QALMs (discounted)</td>
<td>2.24 RA-QALMs</td>
<td>0.76 RA-QALMs</td>
</tr>
</tbody>
</table>

*In this example, the time-tradeoff (TTO) rating for life in poor health is \( 0.6 \beta = 0.5 \) for the power utility curve, and \( \lambda = 3 \) for the exponential utility curve, representing mild to moderate risk aversion. The first column shows the month of the Markov cycle. The second and third columns show the risk-neutral marginal utilities of living for an additional month in poor health either non-discounted or discounted at 3% per year. The fourth and fifth columns show the risk-averse marginal utilities of living an additional month for the power and exponential utility functions, respectively. Values in the fourth and fifth columns have been multiplied by 360 such that \( U(Q^*, T^*) \), the utility of \( T^* \) years in perfect health, is 360 months (30 years). In this example, \( H(Q) \), the risk-adjusted quality weight for the RA-QALY model, is 0.69 for the fourth column and 0.96 for the fifth column. RN-QALM means risk-neutral quality-adjusted life months; RA-QALM means risk-adjusted quality-adjusted life months.
health states is the "risk-adjusted" expected utility in RA-QALYs of a Markov process:

\[ EU = \sum_{k=1}^{T^*} \sum_{i=1}^{\text{states}} \left( \frac{d}{dt} U(Q^*i, H(Q^*i)) \right) \cdot c \cdot p(Q_o, i) \cdot (Q^*i) \cdot \sum_{j=1}^{\text{states}} \left( \frac{d}{dt} U(Q^*j, H(Q^*j)) \right) \cdot c \cdot p(Q_o, i) \] (10)

For a power utility curve with risk parameter \( \beta \), the EU of a Markov process is approximated by:

\[ EU = \sum_{k=1}^{T^*} \sum_{i=1}^{\text{states}} \beta \left( \frac{\bar{t}_k}{T^*} \right)^{\beta-1} \cdot [K_o]^{\beta} \cdot c \cdot p(Q_o, i) \] (11)

For an exponential utility curve with risk parameter, \( A \), the EU of a Markov process is:

\[ EU = \sum_{k=1}^{T^*} \sum_{i=1}^{\text{states}} \left[ \frac{\lambda e^{-\lambda \bar{t}_k/T^*}}{T^* \cdot \left(1 - e^{-\lambda T^*}\right)} \right] \cdot \left[ \frac{1 - e^{-\lambda \bar{t}_k}}{1 - e^{-\lambda T^*}} \right] \cdot c \cdot p(Q_o, i) \] (12)

If the value chosen for \( Y \) in the TTO task is equal to \( T^* \), then equation 12 reduces to:

\[ EU = \sum_{k=1}^{T^*} \sum_{i=1}^{\text{states}} \left[ \frac{\lambda e^{-\lambda \bar{t}_k/T^*}}{T^* \cdot \left(1 - e^{-\lambda T^*}\right)} \right] \cdot \left[ \frac{1 - e^{-\lambda \bar{t}_k}}{1 - e^{-\lambda T^*}} \right] \cdot c \cdot p(Q_o, i) \] (13)

where \( K_o \) is the proportional time tradeoff with respect to \( T^* \) years in health state \( Q \).

An example of the accruement of utility in a QALY framework for both the power and exponential utility curves is given in table 1 for living five months in a poor health state. As can be seen, the per-cycle gain in utility in the RA-QALY models is much different from that in the simple temporal-discounting model.

ESTIMATES FOR RISK COEFFICIENTS

In order to estimate the sensitivity of one particular Markov-process decision model to risk attitude, we reviewed the literature to determine a reasonable range of risk-attitude coefficients for medical decisions. For reference, sample exponential and power utility curves with various risk coefficients are shown in figure 2.

Studies of attitudes towards risk among healthy and sick subjects suggest there is a wide range of risk attitudes. Constructing utility curves for survival durations for older patients with lung cancer, McNeil et al. found \( CE_{50\%} \) (certain equivalents in years for 50-50 gamble of 25 years of full health vs immediate death) ranging from 12.5 years to less than 1 year. The median \( CE_{50\%} \) was 3.5 years and the mean 5 years (mild to moderate risk-averse preferences). For \( \beta \), the risk coefficient for the power utility curve, these figures correspond to median 0.35 and mean 0.43 (range 0.22 to 1.01. For \( \lambda \), the risk coefficient of the exponential utility curve, these \( CE_{50\%} \) correspond to median 4.88 and mean 3.27 (range 0 to 17.31. Hospitalized patients with angina showed a wide range of risk coefficients with geometric mean \( \beta \) 1.0 (range 0.25 [very risk-averse] to about 12 [very risk-seeking]). Based upon \( CE_{50\%} \), the corresponding range for \( \lambda \) would be -11 to 12. Only a small proportion of this group was risk-neutral.
Table 2 • “Utilities” for a Decision Model for Treatment of Benign Prostatic Hypertrophy*

<table>
<thead>
<tr>
<th>Health State</th>
<th>TTO Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asymptomatic after surgery (TUR)</td>
<td>1.0</td>
</tr>
<tr>
<td>Asymptomatic (spontaneous remission)</td>
<td>0.97</td>
</tr>
<tr>
<td>Moderate symptoms after surgery</td>
<td>0.69</td>
</tr>
<tr>
<td>Severe symptoms after surgery</td>
<td>0.7</td>
</tr>
<tr>
<td>Mild incontinence after surgery</td>
<td>0.95</td>
</tr>
<tr>
<td>Impotence after surgery</td>
<td>0.9</td>
</tr>
<tr>
<td>Urinary tract infection, total incontinence after surgery</td>
<td>0.5</td>
</tr>
<tr>
<td>Urinary retention and subsequent surgery (TUR)</td>
<td>0.25</td>
</tr>
<tr>
<td>Dead</td>
<td>0.0</td>
</tr>
</tbody>
</table>

*Notice that for this analysis, we assumed that the values listed represented values obtained from a time-tradeoff (TTO) task.

Source: Barry et al.16

Stiggelbout et al.7 found mostly mild to moderate risk aversion in young men with testicular cancer (mean β 0.74, range 0.30 to 1.78). The corresponding figures for λ are mean 1.1, range -1.8 to 6. Verhoef et al.15 found that most healthy women were risk-seeking in the short term and risk-averse in the long term (s-shaped utility curves). Based upon CEopS, the mean β was 0.80 (range 0.3 to 1.61 and the mean λ was 0.65 (range -1.3 to 6.9). We believe that most older patients show risk-averse preferences regarding gambles for survival duration. We chose to study a “reasonable” range of risk coefficients extending from β = 1 (or λ = 0, risk-neutral) to β = 0.2 (λ = 8, moderately risk-averse).

APPLICATION IN A MARKOV DECISION MODEL

Using tables 2 through 5 of their original article, we reconstructed the Markov-process decision model published by Barry et al.16 for the decision between immediate transurethral resection (TUR) vs expectant “watchful waiting” (WW) for men with moderate symptoms of benign prostatic hyperplasia (BPH). WW is thought to represent a reasonable “treatment” option for men who are moderately bothered by symptoms of BPH, for two reasons: spontaneous remission can occur with expectant follow-up (watchful waiting) and surgery is associated with an immediate risk of death and complications such as postoperative mild and total urinary incontinence and impotence. The “down side” of watchful waiting is that symptoms of moderate BPH can progress to severe symptoms necessitating surgery at some later point in time when surgical risks might be higher. In addition, there are moderate risks of urinary retention and urinary tract infection given WW, risks that are substantially reduced (80% in Barry’s model) by surgery. Barry’s results were presented in a risk-neutral format with variable amounts of time discounting.

The Markov-chain simulation of Barry’s decision model was programmed in Excel 5.0 (Microsoft Corporation, Redmond, WA1 on a Power Macintosh personal computer. As in Barry’s model, the cycle length was one month and the Markov-process simulation was run for 360 months. Transition probabilities used were the same as those in Barry’s model. We fitted operative mortality to a logistic function using Barry’s reported data with age as the dependent variable using the I2-week figures. We used baseline death rates from 1988 vital statistics life tables.

“Utilities” for each health state are taken directly from Barry’s paper and are briefly summarized in table 2. Though these utility values were not derived from patient interviews, we assumed, in this analysis, that these quality weights were assessed using the TTO method. For each TTO value, H(Q) was calculated by the risk-adjustment method outlined above.

Results

Our base-case analysis, the same as in the Barry model, was for a risk-neutral (RN), healthy, sexually active 10-year-old man with moderate symptoms of BPH who has assigned a TTO utility of 0.89 to moderate symptoms of BPH. It was assumed that his TTO utility for moderate symptoms of BPH was 0.89. Expected utilities were calculated in units of quality-adjusted life months (QALMs); hence, this analysis compares RN-QALMs for WW and TUR. The expected number of RN-QALMs for WW calculated by the model was 110.3 and that for initial TUR was 113.4. Surgery therefore provided a net gain in expected utility of 3.54 RN-QALMs.

When the TTO value for moderate symptoms was raised to 0.95, the difference in RN-QALMs approached zero and the two options were of essentially equal utility. At TTO values above 0.95, the expected number of RN-QALMs for surgery was lower than that of WW, and WW was the preferred strategy. Discounting at 3% per year, the base-case difference in discounted RN-QALMs was 2.6 QALMs. Even raising the discount rate to 24%, TUR remained the preferred option (not shown). These results essentially replicate the findings of Barry et al. Rates of follow-up surgery calculated using our model nearly exactly replicated those of Barry’s model (not shown).

We then incorporated risk attitude into the decision model with the goal of calculating the difference in risk-adjusted quality-adjusted life months (RA-QALMs) provided by the same two treatment options as a function of attitude towards risk regarding survival duration in perfect and poor health according to the multiplicative utility model re-
viewed above. As did Barry, we assumed that a 70-year-old will live, at most, 360 months (30 years). We chose this value as the maximum life expectancy upon which to base the utility curves for QALMs. We also assumed that 30 years was the time frame under which the TTO values for health states were elicited. The resulting curves for the power utility and exponential utility curves are shown in figures 3a and 3b over a clinically reasonable range of risk tolerance (as discussed above). As risk aversion increased (increasing $\lambda$ or decreasing $\beta$), the net expected utility gain of surgery decreased, until, at $-\log_2(\beta) = 0.39$ ($\beta = 0.41$) or $\lambda = 2$, a mild to moderate amount of risk aversion, WW was the preferred option. This makes intuitive sense: as a patient becomes more risk-averse, the downside of surgery, with its chance of immediate death and other bad outcomes, predominates gains in quality of life.

When the TTO value for life with moderate symptoms was increased to 0.95 (not much bother from urinary symptoms), WW was the preferred option in both utility models over all ranges of risk aversion; TUR became the preferred option only if risk-seeking values of $\beta$ or $\lambda$ were selected. At a TTO value of 0.95 and under the conditions of risk neutrality (Barry’s analysis), the difference between TUR and WW was almost nil, a “toss-up.” Under mild risk aversion, however, WW was preferred across the entire range of TTO values assigned to moderate symptoms of BPH (0.89 to 0.97; not shown). Thus, using Miyamoto and Eraker’s multiplicative utility model for calculating the expected value of this Markov-process decision model, WW was the preferred option for all patients who show mild to moderate risk aversion. These findings suggest that under certain circumstances, attitude towards risk may be a more important determinant in medical decision making than preferences for varying levels of quality of life.

For patients who are risk-seeking (not shown in figure 3a), TUR was always the preferred option except for patients who were hardly bothered by symptoms of BPH.

How are these findings explained? As risk aversion increases, the values for $H(Q)$, the risk-adjusted quality weights for living in poor health, are compressed towards 1. As well, under conditions of risk-averse preferences regarding gambles for survival duration, the marginal utility of survival is higher for the near future than for the distant future. The risk-averse patient therefore gains more utility from being alive no matter how poor his health is. The downside of surgery, with its chance of immediate death and other bad outcomes, predominates gains in quality of life. Whkn a patient shows risk-seeking preferences regarding gambles for survival duration, the values for $H(Q)$ are depressed, amplifying the effects of poor quality of life in expected-utility calculations.

Discussion

The concept of risk adjustment has been described by several authors, but it is not current practice to report the effects of risk attitude on the optimal decision strategy. Decision analyses that use TTO values for expected-utility calculations inherently assume that the subject is risk-neutral. Most
studies of patient preferences, however, suggest that most patients are not risk-neutral regarding gambles for survival duration.

The multiplicative model for utilities described by Miyamoto and Eraker implies that $H(Q)$, the risk-adjusted quality weight for life in poor health, will be higher than the TTO value for patients who are risk-averse. Many investigators have found that SG values for poor health are greater than TTO values. Because of nonlinear weighting of probabilities, using the SG to estimate $H(Q)$ may be biased. Nevertheless, Stiggelbout et al. have confirmed that adjusting the TTO value by $\beta$, the risk coefficient derived from patients' utility curves for survival duration in perfect health, results in values closely approximating their SG values.7

These findings suggest that risk aversion (nonlinear utility curves) is a real phenomenon in individual patients. While a risk-neutral perspective might make sense from a societal perspective (based upon the assumption that societal preferences are, on average, risk-neutral), when a physician attempts to apply the results of a decision model to an individual patient, he or she needs to be aware that the optimal treatment for a patient, even under normative theory, may depend on that patient's attitude towards risk. Attitudes towards risk, as far as can be determined by experimental methods, are as real as preferences for quality of life. Failure to consider attitudes towards risk may result in recommendations from decision models that do not make sense "at the bedside."3

In this paper, we describe a simple method, derived from a multiplicative theory of utilities, for incorporating risk attitude into QALY calculations for decision models based upon Markov processes. Because they involve both time and health-state outcomes, Markov-process decision models are ideal candidates for risk attitude adjustment. We used this method to calculate the expected value of risk-adjusted QALYs provided by either initial transurethral resection (TUR) or "watchful waiting" (WW) for a 70-year-old sexually active man with moderate symptoms of benign prostatic hyperplasia (BPH) followed for 30 years: Not surprisingly, the gain in expected utility of TUR over WW varied markedly with changes in risk attitude. Under risk aversion, WW was preferred and the decision was not sensitive to changes in TTO values assigned to moderate symptoms of BPH or any other health state in the model. Patient preferences continued to be the key factor in determining the best treatment option; however, it was attitude towards risk that was important rather than preferences for quality of life.

Risk aversion will have more of an effect on expected-utility differences when one or more of the prospects contains the possibility of early, bad outcomes such as death or severe disability. As most older people are risk-averse, early bad outcomes will "count more" in expected value calculations based upon the RA-QALY model. Consequently, incorporating risk attitude into Markov-process models is likely to have important consequences in decisions to undergo initial surgical or medical treatments that have high rates of early complications.

Time discounting of QALYs in a decision model, while taking into account diminishing returns as time progresses, is an inadequate substitute for adjusting QALYs for risk because it does not yield a correction of TTO values for risk aversion. In our model for treatment decisions for BPH, discounting up to 24% resulted in no change in the preferred option.

Decision models that measure health-state utilities by means of TTO values implicitly assume that the patient has risk-neutral preferences for survival duration. The RA-QALY model provides the means by which TTO values can be adjusted to account for aversion to risk. Depending on the assumptions regarding empirical validity of constant proportional TTO, either the power or the exponential utility family of curves can be used to adjust TTO values to estimate $H(Q)$ in the RA-QALY model.

We believe that incorporating risk attitude into decision analyses and describing the sensitivity of decisions to different risk postures may make it easier for physicians to use decision models in clinical practice. Clinicians have long recognized risk attitude as a fundamental part of patient values and in clinical practice often (implicitly) assess their patients' risk attitudes in considering whether a therapy is appropriate for an individual patient. Adding risk-attitude sensitivity to decision models provides a way to use this clinical impression to improve the quality of medical decision making.

Risk attitude may be important in societal-level health-resource-allocation decisions. Though societal values as a whole may be represented by a risk-neutral perspective, the individual members who make up society may, on average, have risk-averse preferences. Thus, an interesting variant on current methods for cost-effectiveness analysis might be to employ age- or time-horizon-adjusted risk coefficients in policy models. If younger patients are, on average, risk-seeking (especially in the setting of expected short time-horizons where all prospects may be viewed as losses), while older patients are risk-averse (as previous data suggest), age-adjusted population mean risk attitudes would favor heroic treatments (e.g., a small chance of success receives a high weight) in the young. An example of a heroic "risk-seeking" type of treatment might be bone-marrow transplantation for metastatic breast cancer. Adjusting for mean risk preferences might also favor
the use of consistent treatments (that is, those with little between-patient variability in outcomes) in the elderly. For example, angioplasty for coronary artery disease might be more highly valued in the elderly than coronary artery bypass surgery because of reduced “front” surgical mortality and morbidity. Using such a model would not represent bias against the aged. Rather it would be an optimization based upon known differences in preferences across age groups.

To summarize, the RA-QALY is a well-known method that is easily added to Markov decision models using the simple method described above. While there are limitations to the RA-QALY approach as described by Miyamoto and Eraker—the most notable being the assumption that utility curves can be described by a single risk parameter—examining the sensitivities of decision models’ recommendations to attitude towards risk may generate important insights, especially if the results of the model are intended to direct therapy for individual patients.

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References

APPENDIX

The problem posed and solved in this appendix is to find preference axioms that jointly imply the utility representation (equation 3). The axiomatization makes use of simplifications in QALY axioms that are discussed more fully by Miyamoto et al.14 We first require two definitions. We say that preferences satisfy the 0 condition if every health state is equally preferred when survival duration is 0. Formally, the 0 condition asserts that \((Q, 0) \simeq (Q', 0)\) for any health states \(Q\) and \(Q'\) where \(\simeq\) denotes indifference in preference. We say that preferences satisfy CE invariance if the certainty equivalents of lotteries for survival duration in a fixed health state \(Q\) are the same for every choice of \(Q\). Formally, CE invariance asserts that for any health states \(Q\) and \(Q'\) and durations, \(X_1, X_2, \ldots, X_n\), \(Y\),

\[
[(Q, X_1), p_1 \simeq (Q, X_2), p_2 \simeq \cdot \cdot \cdot \simeq (Q, X_n), p_n] \simeq (Q, Y)
\]

if and only if

\[
[(Q', X_1), p_1 \simeq (Q', X_2), p_2 \simeq \cdot \cdot \cdot \simeq (Q', X_n), p_n] \simeq (Q', Y)
\]

for some function \(H\) and some function \(F\) satisfying \(F(0) = 0\).

Theorem 1. Under the assumptions of expected-utility theory, the 0 condition and CE invariance imply that the utility function has the form

\[
U(Q, Y) = F(Y) \cdot H(Q)
\]

for some function \(H\) and some function \(F\) satisfying \(F(0) = 0\).

Theorem 1 is proved in Miyamoto et al.14 To complete the axiomatization of the model (equation 3), we add the well-known utility assumption of constant absolute risk aversion: For any health state \(Q\) of any duration, \(X_1, X_2, \ldots, X_n, Y\), and any positive constant \(c\) that is less than \(T^* = \max(X_1, \ldots, X_n, Y)\),

\[
[(Q, X_1), p_1 \simeq (Q, X_2), p_2 \simeq \cdot \cdot \cdot \simeq (Q, X_n), p_n] \simeq (Q, Y)
\]

if and only if

\[
[(Q, X_1 + c), p_1 \simeq (Q, X_2 + c), p_2 \simeq \cdot \cdot \cdot \simeq (Q, X_n + c), p_n] \simeq (Q, Y + c)
\]
The constant c is restricted to be less than $T^* \max(X^2, \ldots, X_n, Y)$, where $T^*$ is the maximum survival duration in the given domain, only because one does not want to assume that such equivalences have a meaning for arbitrarily large durations. It is well known that constant absolute risk aversion implies that a utility function is linear or exponential.

Theorem 2. Under the assumptions of expected utility theory, the 0 condition, CE invariance, and constant absolute risk aversion imply that the utility function has the form of equation 3.

The proof of theorem 2 is obvious. The 0 condition and CE invariance imply that the utility function has the multiplicative form (equation 12). Constant absolute risk aversion implies that the function $F$ in equation 12 is a linear or exponential function. The linear case is the standard QALY model. Combining the linear and exponential cases we have the exponential QALY model (equation 3), qed.