

Multiattribute Structure for QALYs

Gordon Hazen

IEMS Department

Northwestern University

January 2003

Abstract

Health status is inherently a multi-attribute construct. We examine multiattribute utility decompositions for the *quality-adjusted life year* (QALY) utility model commonly employed in medical decision and cost-effectiveness analyses. We consider several independence conditions on preference, including the classical notions of preferential independence and utility independence, as well as new related notions of *standard-gamble independence* and *time-tradeoff independence*. The latter conditions are helpful in simplifying standard-gamble utility assessment procedures and time-tradeoff assessment procedures in the presence of multiple health attributes.

Introduction

Methods for evaluating health quality are central to medical decision analyses and cost-effectiveness analyses. The most important such method is the quality-adjusted life year (or QALY) model, in which a patient's survival duration is given weight proportional to the quality of health the patient experiences. The recommendation of the Panel on Cost Effectiveness in Health and Medicine (Gold *et al.* 1996) is that medical cost-effectiveness studies should incorporate morbidity and mortality consequences into a single measure using QALYs. QALYs have indeed become ubiquitous in these and other analyses: A *Medline* search on *Quality-Adjusted Life Years* for the 5-year period ending December 2002 produced 1070 articles. Assumptions under which quality-adjusted lifetime constitutes a von Neuman-Morgenstern utility function over health pathways are given by Pliskin *et al.* (1980), Miyamoto *et al.* (1998), and Miyamoto (1999). Under such assumptions, the utility $U(y,t)$ assigned to a duration- t sojourn in health state y is given by

$$U(y,t) = u(y) \cdot m(t). \tag{1}$$

Here $u(y)$ represents the health quality or health utility associated with state y .

In practice, methods for assessing the QALY utility function $U(y,t)$ take $m(t)$ to be determined exogenously (e.g., the linear function $m(t) = t$), and focus on eliciting the health utility $u(y)$ by subjectively querying patients, physicians, or community members. A variety of methods are available for this purpose (e.g., Gold *et al.* 1996, Hunink *et al.* 2001). Listed in order of increasing level of cognitive burden for subjects, these include rating scale, time-tradeoff, standard gamble, and multiattribute health indexes such as the Health Utilities Index (HUI, e.g., Feeny *et al.* 1995) or the EuroQol (e.g., Dolan 1997).

Eliciting a multiattribute health index is too challenging to be done for individual decision or cost-effectiveness analyses. However, analysts may obtain health utilities $u(y)$ from in-depth studies in which utilities are carefully assessed over combinations of attributes representing most morbidities encountered in medical interventions. For example, the HUI Mark III (Feeny et al 2002) is an eight-attribute system with attributes describing 5 to 6 levels each of vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain. The EuroQol is a 5-attribute system with 3 levels each describing mobility, self-care, usual activity, pain/discomfort, anxiety/depression. Nevertheless, for some analyses, these attributes are not specific enough to address important issues, and analysts must assess health utilities directly.

Direct elicitation of health utilities is often hampered by the natural multiattribute structure of health status. A multiattribute description of health status is cognitively complex and can yield more health status combinations than can be feasibly elicited. One expedient is to apply time-tradeoff or standard gamble techniques along each health attribute separately, and then combine the results in some fashion. The first contribution of the present paper is to indicate for what forms of utility function $u(y)$ this strategy is valid.

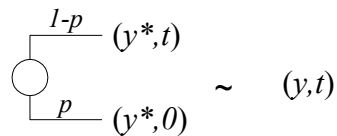
A second common expedient is to *multiply* single-attribute health utilities, however elicited, in order to obtain overall health utility. For example, Roach *et al.* (1988) obtain an overall utility of 0.30 for the simultaneous presence of AIDS and metastatic cancer by multiplying the utility 0.50 for AIDS by the utility 0.60 for metastatic cancer. The same strategy is used by Sonnenberg and Pauker (1986), Plante et al. (1987), Fleming et al. (1988), and Eckman et al. (2002). The second contribution of

the present paper is to indicate what preference assumptions are required to justify this procedure.

This paper is organized as follows. In Section 1 we discuss single-attribute versus multiattribute elicitation using time-tradeoff and standard gamble procedures. Basic results involving single-attribute elicitation using standard-gamble and time-tradeoff are given in Section 2. In Section 3 we delineate relationships of the assumptions we introduce to other conditions such as preferential independence and utility independence. The appendix contains proofs of these and related results under a general utility structure.

1 Single-attribute versus multiattribute elicitation

The standard gamble procedure is a specific form of the traditional probability-equivalent approach for utility assessment (e.g., Clemen 1996). In this approach, a subject is asked to specify the largest chance p of immediate death she would be willing to incur in order to raise her health status from a given state y to full health y^* . In other words, the subject must be indifferent between duration t in health state y , and a gamble yielding immediate death with probability p and duration t in full health y^* with probability $1-p$:



Here the symbol \sim denotes indifference, and immediate death is represented by $(y^*, 0)$.

Equating expected utilities gives

$$(1-p)u(y^*)m(t) = u(y)m(t)$$

and using $u(y^*) = 1$ gives the desired utility $u(y) = 1 - p$.

In the time-tradeoff procedure, a subject is asked what reduced survival duration she would accept to improve her health from y to y^* . In other words, the subject is asked what duration t' should be so that

$$(y^*, t') \sim (y, t).$$

Under the linear QALY model, equating utilities gives

$$u(y^*) \cdot t' = u(y) \cdot t$$

from which the desired utility $u(y) = t'/t$ can be obtained.

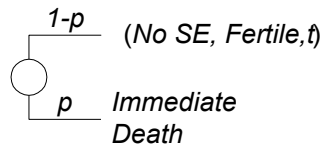
In this paper we are interested in multiattribute health states $y = (y_1, \dots, y_n)$. It has long been recognized that directly assessing a utility function over multi-attribute outcomes can be a daunting task, due both to a subject's potential cognitive overload in thinking about multiattribute health states, or to the sheer number of indifference responses required. Consider, for example, a health state y that might be appropriate for an analysis of screening or treatment options for ovarian cancer. Treatment outcomes include side effects due to radiation therapy, and infertility should ovaries be surgically removed. A health-state descriptor incorporating these issue might be $y = (y_1, y_2)$, where

y_1 = radiation side-effects (None, mild or severe¹)

y_2 = fertility (fertile or infertile)

¹ In practice, each level of side effects would be described in detail

The state $(y_1, y_2) = (No\ side\ effects, Fertile)$ corresponds to full health and would be assigned utility one. There remain five combinations (y_1, y_2) to assess. The standard gamble approach would require subjects to choose five probabilities p under which the gamble



is respectively indifferent to the five health scenarios

$(No\ SE, Infertile, t)$

$(Mild\ SE, Fertile, t)$

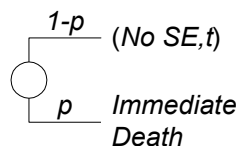
$(Mild\ SE, Infertile, t)$

$(Severe\ SE, Fertile, t)$

$(Severe\ SE, Infertile, t)$

Such assessments would require potentially complex cognitive tradeoffs between level of side effects, fertility, and chance of death.

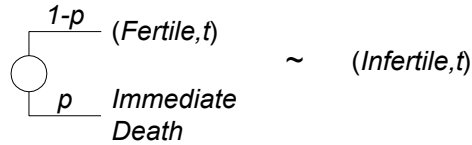
On the other hand, if preferences for side-effect severity are somehow *independent* of fertility, then one could perform standard gamble assessments on side-effect severity without reference to fertility. The subject would need to provide two probabilities p under which the gamble



is respectively indifferent to the two health scenarios

(Mild SE,t) (Severe SE,t).

Similarly, if preferences for fertility are somehow independent of side-effect severity, then the subject would need to provide a single probability p yielding the indifference



Here we have only three cognitively simpler indifference responses required, trading off side-effect severity against chance of death, or fertility against chance of death. Of course, questions remain: When (if ever) is it valid to proceed in this way? How can one recover overall utilities $u(y_1, y_2)$ from these single-attribute assessments, and what additional information (if any) is needed to do so? In the next section we answer these questions for the standard gamble procedure and also for the corresponding single-attribute time-tradeoff procedure.

Those familiar with multiattribute utility theory may suspect that what is required here is some form of *utility independence*, and that the utility function $u(y_1, y_2)$ must have the additive form with multiplicative interaction terms

$$u(y_1, y_2) = k_1 u_1(y_1) + k_2 u_2(y_2) + k_1 k_2 u_1(y_1) u_2(y_2)$$

specified by Keeney and Raiffa (1976). Indeed, the additive/ multiplicative utility function has been employed by Torrance, Feeny, and their colleagues to evaluate health states arising in their HUI models (Torrance et al. 1982, Torrance et al. 1996, Feeny et al. 2002). Utility independence is in fact one version of the required condition, as we will discuss further below. However, due to the special multiplicative structure of the QALY

model (1), the additive/ multiplicative form collapses to the special *purely multiplicative* instance

$$u(y_1, y_2) = u_1(y_1)u_2(y_2).$$

For this simpler form, *no assessments* are required to obtain attribute weights k_i or interaction parameter k . We elaborate on these points in the following sections.

2 Standard-gamble and time-tradeoff independence for nonlinear-QALY preferences

We assume preference over gambles involving state-duration pairs (y, t) is represented by a von Neuman-Morgenstern utility function $U(y, t)$ having the *nonlinear QALY* form (1), where $t \geq 0$ and the health descriptor y is contained in some set Y of possible health states. We assume the function $m(t)$ is a continuous, increasing² function of $t \geq 0$, with $m(0) = 0$. We assign maximum utility $u(y^*) = 1$ to the state y^* of *full health*, as defined by problem context. The quantity $m(t)$ is the utility associated with a duration- t sojourn in y^* , anchored by $m(0) = 0$. In the simplest version of this model, it is assumed that $m(t) = t$. Known as the *linear QALY* model, this represents the case in which there is no time discounting, and preferences for survival duration are risk-neutral. The more general nonlinear QALY model (1) allows time discounting and/or risk-averse preferences for survival duration. For example, the function

$$m(t) = \int_0^t e^{-\alpha s} ds = \frac{1}{\alpha}(1 - e^{-\alpha t}) \quad (\alpha > 0)$$

² Throughout this paper, *increasing* is meant in the strict sense, that is $m(t_1) < m(t_2)$ whenever $t_1 < t_2$.

can account for constant risk aversion with coefficient of risk aversion equal to α (e.g., see Pratt (1964), Keeney and Raiffa (1976, Ch. 4), Clemen (1996, Ch. 13)), or time discounting at rate α .

The set Y of possible health states y need not include a *death* state, as that is accounted for by duration $t = 0$. However, the nonlinear QALY model does allow states y to be *worse than death* ($u(y) < 0$) or *equivalent to death* ($u(y) = 0$). We will discuss such possibilities later. For the present, we note that results in this paper assume that all states $y \in Y$ are better than death ($u(y) > 0$).

We consider the case in which Y has multiattribute structure, that is, $Y \subset Y_1 \times \dots \times Y_n$ for sets Y_i of health attributes. If $y \in Y$, we write $y = (y_1, \dots, y_n)$. If we wish to focus on component i of y , then we may write $y = (y_i, z_i)$ where $z_i = (y_1, \dots, y_{i-1}, y_{i+1}, \dots, y_n)$ is the vector of complementary components to y_i , and we let $Z_i = Y_1 \times \dots \times Y_{i-1} \times Y_{i+1} \times \dots \times Y_n$ be the set of all such z_i . We assume the most preferred state $y^* = (y_i^*, z_i^*) \in Y$ has the *partial closure* property:

$$(y_i, z_i) \in Y \text{ implies } (y_i^*, z_i) \in Y \text{ and } (y_i, z_i^*) \in Y \quad \text{for all } i.$$

Following Keeney and Raiffa (1976), we abuse notation slightly and use $u(y_i)$ to mean $u(y_i, z_i^*)$, and similarly, $u(z_i)$ to mean $u(y_i^*, z_i)$. Because $u(y^*) = 1$, it follows that $u(y_i^*) = 1$ and $u(z_i^*) = 1$.

Standard-gamble independence

We now formalize the independence notion discussed above in the context of standard-gamble assessment. We say that Y_i is *standard-gamble independent of Z_i* if for all $t > 0$, whenever the standard-gamble indifference

$$\begin{array}{c} \text{---} \frac{1-p}{\text{---}} (y_i^*, z_p, t) \\ | \\ \text{---} \frac{p}{\text{---}} (y_i^*, z_p, 0) \end{array} \sim (y_p, z_p, t)$$

holds for one pair $(y_b, z_i) \in Y$, it holds for *all* values of z_i with $(y_b, z_i) \in Y$. Under the nonlinear QALY model, this standard-gamble indifference becomes

$$(1-p)u(z_i)m(t) = u(y_b, z_i)m(t).$$

Suppose that health quality $u(y_b, z_i)$ decomposes into the *purely multiplicative form*

$$u(y_b, z_i) = u(y_b)u(z_i).$$

Then the standard-gamble indifference is equivalent to

$$(1-p)u(z_i)m(t) = u(y_b)u(z_i)m(t)$$

The quantities $u(z_i)$ and $m(t)$ are positive and may be cancelled. Therefore the last equality is equivalent to

$$1-p = u(y_b).$$

Therefore, under the purely multiplicative form $u(y_b, z_i) = u(y_b)u(z_i)$, the standard-gamble equivalence above determines the single-attribute utility $u(y_b)$, *independently* of the health state z_i . It follows that Y_i is standard-gamble independent of Z_i . The converse holds as well, as we shall see below.

Time-tradeoff independence

In this section we show how a similar notion of independence for time tradeoffs also leads to the purely multiplicative utility form. First, we give some additional comments on the time-tradeoff procedure.

In the time-tradeoff procedure, a subject is given a health state y and a duration t , and is asked to provide a survival duration t' so that the indifference

$$(y^*, t') \sim (y, t).$$

holds. In practice, this task may be difficult for subjects. To ease the cognitive burden, strict preferences $(y^*, s) \succ (y, t)$ or $(y^*, s) \prec (y, t)$ may be elicited for various durations s until the desired indifference is obtained for some $s = t'$. For the multiple-attribute case $y = (y_i, z_i)$, we require that these intermediate preferences as well as the final indifference not depend on z_i . In particular, we say that Y_I is *time-tradeoff independent*³ of Z_i provided that for all $s, t > 0$, whenever

$$(y_i, z_i, t) \succeq (y_i^*, z_i, s)$$

holds for one pair $(y_i, z_i) \in Y$, it holds for all y_2 with $(y_1, y_2) \in Y$. Note that for the purely multiplicative utility form $u(y_i, z_i) = u(y_i)u(z_i)$, the latter time tradeoff is equivalent to

$$u(y_i)u(z_i)m(t) \geq u(z_i)m(s).$$

Because $u(z_i) > 0$, the latter is equivalent to

$$u(y_i)m(t) \geq m(s),$$

³ Not to be confused with *constant proportional tradeoffs* as discussed by Pliskin *et al.* (1980).

a statement that is independent of z_i . Therefore Y_i is time-tradeoff independent of the complementary attributes Z_i under the multiplicative form $u(y_i, z_i) = u(y_i)u(z_i)$. The converse of this assertion holds as well, as we shall see next.

Multiplicative decomposition

We have seen that the purely multiplicative form for $u(y)$ implies both standard gamble independence and time-tradeoff independence. In fact, these conditions are equivalent to each other and to the purely multiplicative form, as the next result states.

Theorem 1: Suppose the nonlinear QALY model holds over $Y \subset Y_1 \times \dots \times Y_n$. Then the following statements are equivalent:

- (a) Y_i is standard-gamble independent of the complementary attributes $Z_i = (Y_1, \dots, Y_{i-1}, Y_{i+1}, \dots, Y_n)$
- (b) The complementary attributes Z_i are standard-gamble independent of Y_i .
- (c) Y_i is time-tradeoff independent of the complementary attributes Z_i .
- (d) The complementary attributes Z_i are time-tradeoff independent of Y_i .
- (e) The purely multiplicative model

$$u(y_i, z_i) = u(y_i)u(z_i).$$

holds over $(y_i, z_i) \in Y$.

A surprising and nonobvious part of this result is that Y_i standard-gamble independent (or time-tradeoff independent) of Z_i implies, under the nonlinear QALY model, that Z_i is standard-gamble independent (or time-tradeoff independent) of Y_i . The

proof of this and all subsequent results may be found in the appendix, where this result follows from Theorem 6 and Corollary 8a. The following result gives necessary and sufficient conditions for a complete multiplicative decomposition over all attributes Y_1, \dots, Y_n . This combines Theorem 7 and Corollary 9a in the appendix.

Theorem 2: Suppose the nonlinear QALY model holds over $Y \subset Y_1 \times \dots \times Y_n$. Then the following statements are equivalent.

(a) Y_i is standard-gamble independent over Y of the complementary attributes $Z_i = (Y_1, \dots, Y_{i-1}, Y_{i+1}, \dots, Y_n)$ for at least $n-1$ of the n attributes Y_i .

(b) Y_i is time-tradeoff independent of the complementary attributes Z_i for at least $n-1$ of the n attributes Y_i .

(c) The purely multiplicative model

$$u(y) = u(y_1)u(y_2)\dots u(y_n).$$

holds over $y = (y_1, \dots, y_n) \in Y$.

(d) Y_i is standard-gamble independent over Y of the complementary attributes Z_i for $i = 1, \dots, n$.

(e) Y_i is time-tradeoff independent of the complementary attributes Z_i for $i = 1, \dots, n$.

3 Relationship to other utility models

There is a close relationship between the notions of standard-gamble independence and time-tradeoff independence that we have introduced here, and the

traditional concepts of preferential independence and utility independence found in the literature (e.g., Keeney and Raiffa 1976). In this section we discuss and clarify these relationships.

Preferential independence and utility independence

Let $T = [0, \infty)$ be the time attribute of the utility function $U(y, t)$, and let $T^+ = \{t \mid t > 0\}$ be the set of positive times. $Y_i T^+$ is said to be *preferentially independent of the complementary attributes* Z_i provided for all positive t, t' , whenever

$$(y_i, z_i, t) \succeq (y_i', z_i, t')$$

holds for one value of z_i with $(y_i, z_i), (y_i', z_i) \in Y$, it holds for all such z_i . The following result holds without any restriction on the utility model (see Theorem 5 in the appendix).

Theorem 3: Y_i is time-tradeoff independent of the complementary attributes Z_i if and only if $Y_i T^+$ is preferentially independent of Z_i .

$Y_i T^+$ is said to be *utility independent* of the complementary attributes Z_i provided for all nonnegative, nonzero random durations \tilde{s}, \tilde{t} , whenever

$$(\tilde{y}_i, z_i, \tilde{t}) \succeq (\tilde{y}_i', z_i, \tilde{s})$$

holds for one value of z_i with $(\tilde{y}_i, z_i), (\tilde{y}_i', z_i) \in Y$, it holds for all such z_i . Here $(\tilde{y}_i, z_i, \tilde{t})$ and $(\tilde{y}_i', z_i, \tilde{s})$ are gambles in which there may be joint uncertainty involving both Y_i and T .

Even without any assumptions on the utility model, it is easy to see that $Y_i T^+$ utility independent of Z_i implies that Y_i is standard-gamble independent of Z_i over Y : Simply take (\tilde{y}_i, \tilde{t}) to be the gamble giving a $1-p$ chance at (y_i^*, t) and a p chance at $(y_i^*, t = 0)$, and $(\tilde{y}'_i, \tilde{s})$ equal to (y_i, t) to obtain the standard-gamble indifference

$$(y_i^*, z_i, \tilde{t}) \sim (y_i, z_i, t).$$

Then $Y_i T^+$ utility independent of Z_i implies that this indifference holds for all values of z_i if it holds for one, which is precisely the statement that Y_i is standard-gamble independent of Z_i . Therefore $Y_i T^+$ utility independent of Z_i over Y implies that Y_i is standard-gamble independent of Z_i . Moreover, under the nonlinear QALY model, the two notions are equivalent to each other and to both time-tradeoff independence and preferential independence. The following result follows from the corollaries to Theorems 8 and 10 in the appendix.

Theorem 4: Suppose the nonlinear QALY model holds. Then the following are equivalent.

- (a) $Y_i T^+$ is utility independent of Z_i .
- (b) Y_i is standard-gamble independent of Z_i .
- (c) $Y_i T^+$ is preferentially independent of Z_i .
- (d) Y_i is time-tradeoff independent of Z_i .

Conditional utility independence

What then is the relationship between the purely multiplicative utility decompositions discussed in this paper and the Keeney/Raiffa additive/ multiplicative decomposition for $u(y)$ employed by Torrance, Feeny and their colleagues in the Health Utility Index? We address this question in this subsection. The validity of the additive/ multiplicative decomposition for health utility depends on a weaker form of utility independence, which we now introduce.

We say that Y_i is *conditionally utility independent* of Z_i given T^+ provided for each $t > 0$, and all lotteries $\tilde{y}_i, \tilde{y}'_i$, if

$$(\tilde{y}_i, z_i, t) \succeq (\tilde{y}'_i, z_i, t)$$

holds for one value of z_i with $(\tilde{y}_i, z_i), (\tilde{y}'_i, z_i) \in Y$, then it holds for all such z_i .

Conditional utility independence of Y_i from Z_i given T^+ is a weaker assumption than utility independence of $Y_i T^+$ from Z_i , as the latter implies the former.

When there are n health attributes Y_1, \dots, Y_n , the assumption that every subset $\{Y_i \mid i \in I\}$ of attributes is conditionally utility independent of the complementary set given T^+ is known as *mutual* conditional utility independence given T^+ . Under this assumption, we can invoke Keeney and Raiffa in the following way: Let y^0 be a “least desirable” health state, and for each $t > 0$, let $U^0(y|t)$ be the positive linear transformation of $U(y, t) = u(y)m(t)$ having $U^0(y^0, t) = 0$, $U^0(y^*, t) = 1$. We have

$$U^0(y|t) = \frac{U(y, t) - U(y^0, t)}{U(y^*, t) - U(y^0, t)} = \frac{u(y) - u(y^0)}{u(y^*) - u(y^0)} = \frac{u(y) - u(y^0)}{1 - u(y^0)} \equiv u^0(y),$$

that is, $U^0(y|t)$ equals $u^0(y)$ and is therefore independent of t . Mutual utility independence holds for the utility function $u^0(y)$, and we may invoke Keeney and Raiffa's fundamental Theorem 6.1 (1976) to obtain the additive/multiplicative form

$$u^0(y) = \frac{1}{k} \left(-1 + \prod_{i=1}^n (1 + k k_i u_i(y_i)) \right)$$

Overall, using the definition of $u^0(y)$, we have $U(y,t) = (u_0 + (1-u_0)u^0(y))m(t)$, where $u_0 = u(y^0)$. This derivation of the additive/ multiplicative form of multiattribute utility from mutual conditional utility independence is new, as far as we know.

Torrance et al. use the disutility form of this model,

$$\bar{u}^0(y) = \frac{1}{c} \left(-1 + \prod_{i=1}^n (1 + c c_i \bar{u}_i(y_i)) \right) \quad (2)$$

where the disutility $\bar{u}^0(y)$ relates to the nonlinear-QALY utility $u(y)$ by

$$\bar{u}^0(y) = 1 - u^0(y) = \frac{1 - u(y)}{\bar{u}_0}, \quad \bar{u}_0 = 1 - u(y^0). \quad (3)$$

Moreover, the c_i are the disutilities of the complementary corner points,

$$c_i = \bar{u}^0(y_1^*, \dots, y_{i-1}^*, y_i^0, y_{i+1}^*, \dots, y_n^*) = \bar{u}^0(y_i^0)$$

and $\bar{u}_i(y_i)$ is $\bar{u}^0(y_i)$ normalized so that $\bar{u}_i(y_i^0) = 1$:

$$\bar{u}_i(y_i) = \frac{\bar{u}^0(y_i)}{\bar{u}^0(y_i^0)} = \frac{\bar{u}^0(y_i)}{c_i}. \quad (4)$$

Note that we may invert (3) to obtain

$$u(y) = 1 - \bar{u}_0 \bar{u}^0(y) \quad (5)$$

from which we conclude, using (2)

$$u(y) = 1 - \frac{\bar{u}_0}{c} \left(-1 + \prod_{i=1}^n (1 + c c_i \bar{u}_i(y_i)) \right) \quad (u\text{CUI})$$

This is the form of u implied by mutual conditional utility independence given T^+ .

To compare this with the purely multiplicative form $u(y) = \prod_{i=1}^n u(y_i)$ implied by standard-gamble independence or time-tradeoff independence, we need an expression for the factors $u(y_i)$. We have, from (5) and (4),

$$u(y_i) = 1 - \bar{u}_0 \bar{u}^0(y_i) = 1 - \bar{u}_0 c_i \bar{u}_i(y_i).$$

Substitute this to obtain

$$u(y) = \prod_{i=1}^n (1 - \bar{u}_0 c_i \bar{u}_i(y_i)) \quad (u\text{SGI})$$

This is the form of u implied by mutual standard-gamble independence.

Comparing (uCUI) with (uSGI), we note that the former is obtained from the latter by setting $c = -\bar{u}_0$. Therefore, one measure of the similarity of specific instances of the two forms is the difference between the quantities c and $-\bar{u}_0$. The values obtained by Torrance *et al* (1996) for their Health Utilities Index Mark II were $c = -0.967$ and $\bar{u}_0 = 1.03$ for the utility function formed from mean subject responses. For their Health Utilities Index Mark III (Feeny *et al.* 2002), the values were $c = -0.991$, $\bar{u}_0 = 1.36$. Thus the Mark-II utility $u(\cdot)$ is very nearly our purely multiplicative form, whereas the Mark-III $u(\cdot)$ is not. Note, however, that the utility (uCUI) can be defined over worse-than-

death states y as well as better-than-death states, whereas the utility (u_{SGI}) is defined only over better-than-death states. This is an advantage of the conditional utility independence assumption compared to standard-gamble independence or time-tradeoff independence.

4 Conclusion

The results of this paper provide answers to two questions concerning the nonlinear QALY model $U(y,t) = u(y)m(t)$ when the health state $y = (y_1, \dots, y_n)$ has multiattribute structure. First, for what functions $u(\cdot)$ is it valid to apply the standard-gamble or time-tradeoff techniques one attribute at a time to elicit health utilities? That is, when are standard-gamble independence and time-tradeoff independence valid? The answer is that $u(y)$ must have the purely multiplicative form $u(y) = u(y_1) \dots u(y_n)$. It is only under the purely multiplicative form that one can consistently use standard-gamble assessments or time-tradeoff assessments over single health attributes. For example, under the Keeney-Raiffa additive/ multiplicative form used in the Health Utilities Index, it is not valid to attempt to assess the single-attribute utility functions via standard-gamble or time-tradeoff procedures.

Second, when is the common practice of obtaining overall health utility $u(y)$ by *multiplying* single-attribute health utilities valid? The answer is that this procedure is valid when and only when for each i the combination $Y_i T^+$ of attribute i and durations T^+ is *preferentially independent* (or equivalently, *utility independent*) of the complementary attributes $Z_i = (Y_1, \dots, Y_{i-1}, Y_{i+1}, \dots, Y_n)$.

Should these independence assumptions be acceptable, the assessment burden for multiattribute health states is substantially eased – both the number of health states and their cognitive complexity are substantially less for single-attribute standard-gamble or time-tradeoff assessments as compared to direct multiattribute assessment. Moreover, because results from single-attribute assessment can be *directly combined by multiplying*, no importance weights for the attributes need be assessed.

Standard-gamble or time-tradeoff independence as we have defined them cannot, however, be invoked when there are both positive (better-than-death) and negative (worse-than-death) health states. The purely multiplicative form for health utility therefore is not a viable candidate for health classification systems such as the HUI, in which some combinations of health attributes are ranked worse than death by many subjects. Fortunately, most effectiveness and cost-effectiveness analyses examine health impacts along only some of the wide range of possible health attributes, and worse-than-death states are rare in these settings – for example, Bell *et al.* (2001) found *no* such states in 228 cost-utility analyses published from 1976 to 1997. The purely multiplicative form could be appropriate here, and in fact has already been used in this context, as we pointed out in the introduction.

Our standard-gamble independence condition is superficially similar to the *standard-gamble invariance* condition introduced by Miyamoto *et al.* (1998). The latter states that gambles over duration t are independent of health state y , and assumes no multiattribute structure for y , so the two conditions are not really comparable.

We note that we have previously provided formal conditions for the purely multiplicative form (Hazen 2000). However, the results in that paper apply only to the

two-attribute case and only to so-called *Markovian* utility, which includes the linear QALY model – but not the nonlinear QALY model – as a special case. Results in the appendix of this paper apply to utility functions more general than Markovian, however.

For utility structures $U(y,t)$ more general than nonlinear QALY, three of the four equivalent conditions we have treated above – time-tradeoff independence, standard gamble independence, preferential independence, and utility independence – do not remain equivalent. The appendix details their implications for utility structure in the absence of the nonlinear QALY model.

References

CM Bell, RH Chapman, PW Stone, EA Sandberg, PJ Neumann, “An off-the-shelf help list: A comprehensive catalog of preference scores from published cost-utility analyses”, *Medical Decision Making* **21** (2001) 4, 288-294.

RT Clemen, *Making Hard Decisions: An Introduction to Decision Analysis*, Duxbury Press, 1996.

P Dolan, “Modeling valuations for EuroQol health states,” *Medical Care* **35** (1997), 11, 1095-1108.

MH Eckman, SK Singh, JK Erban, G Kao, “Testing for factor V Leiden in patients with pulmonary or venous thromboembolism: a cost-effectiveness analysis,” *Medical Decision Making* **22** (2002) 2, 108-124.

D Feeny, W Furlong, M Boyle, and GW Torrance, “Multi-attribute health status classification systems: Health Utilities Index,” *Pharmacoeconomics* **7** (1995) 6, 490-502.

D Feeny, W Furlong, GW Torrance, CH Goldsmith, Z Zhu, S DePauw, M Denton, and M Boyle, “Multiattribute and single-attribute utility functions for the Health Utilities Index Mark 3 system,” *Medical Care* **40** (2002) 2, 113-128.

C Fleming, JB Wong, AJ Moskowitz, SG Pauker, "A peripartum neurologic event: Shooting from the hip," *Medical Decision Making* **8** (1988) 1, 55-71.

MR Gold, DL Patrick, GW Torrence, DG Fryback, DC Hadorn, MS Kamlet, N Daniels, MC Weinstein, "Identifying and Valuing Outcomes" in *Cost-Effectiveness in Health and Medicine*, MR Gold, JE Siegel, LB Russell, MC Weinstein (eds), Oxford University Press, 1996.

G.B. Hazen and J.M. Pellissier (1996), "Recursive Utility for Stochastic Trees," *Operations Research* **44**, 788-809.

G.B. Hazen, "Preference Factoring for Stochastic Trees," *Management Science* **46** (2000), 389-403.

M Hunink, P Glasziou, J Siegel, J Weeks, J Pliskin, A Elstein, M Weinstein, *Decision Making in Health and Medicine: Integrating Evidence and Values*, Cambridge University Press, 2001.

RL Keeney and H Raiffa, *Decisions with Multiple Objectives: Preferences and Value Trade-offs*, John Wiley and Sons 1976, and Cambridge University Press, 1993.

JM Miyamoto, "Quality-adjusted life years (QALY) utility models under expected utility and rank dependent utility assumptions," *Journal of Mathematical Psychology* **43** (1999) 201-237.

JM Miyamoto, PP Wakker, H Bleichrodt, HJM Peters, "The zero-condition: a simplifying assumption in QALY measurement and multiattribute utility," *Management Science* **44** (1998), 6, 839-849.

DA Plante, JF Piccirillo, RA Sofferman, "Decision analysis of treatment options in pyriform sinus carcinoma," *Medical Decision Making* **7** (1987) 2, 74-83.

JS Pliskin, DS Shepard and MC Weinstein, "Utility functions for life years and health status," *Operations Research* **28** (1980), 206-224.

JW Pratt, "Risk aversion in the small and in the large," *Econometrica* **32** (1964) 122-136.

PJ Roach, C Fleming, MD Hagen, SG Pauker, “Prostatic cancer in a patient with asymptomatic HIV infection: Are some lives more equal than others?”, *Medical Decision Making* **8** (1988) 2, 132-144.

FA Sonnenberg and SG Pauker, “Elective pericardiectomy for tuberculous pericarditis: Should the snappers be snipped?” *Medical Decision Making* **6** (1986) 2, 110-123.

J Tsevat, MH Eckman, RA McNutt, SG Pauker, “Warfarin for dilated cardiomyopathy: A bloody tough pill to swallow?” *Medical Decision Making* **9** (1989) 3, 162-169.

GW Torrance, MH Boyle, and SP Horwood, “Application of multi-attribute utility theory to measure social preferences for health states,” *Operations Research* **30** (1982) 6, 1043-1069.

GW Torrance, DH Feeny, WJ Furlong, RD Barr, Y Zhang, Q Wang, “Multiattribute utility function for a comprehensive health status classification system: Health Utilities Index Mark 2,” *Medical Care* **34** (1996) 7, 702-722.

Appendix: General results and proofs

If $I \subset \{1, \dots, n\}$ and $y \in Y$, then we let y_I be the vector $(y_i \mid i \in I)$ of components of y for $i \in I$, and we let Y_I be the set of all such y_I . Let \bar{I} be the complement of I in $\{1, \dots, n\}$. Then the complementary component Z_i used above is merely $Y_{\bar{I}}$. We shall use the two terms interchangeably.

Utility models

The proofs below are presented for the following general class of utility models which includes the nonlinear QALY case. We will assume that the von Neuman- Morgenstern utility function $U(y,t)$ has the following properties:

A1: $U(y,0) = 0$ for all states y (the zero condition).

A2: $U(y,t)$ is a continuous increasing function of t for all states y .

Miyamoto et al. (1998) discuss the zero condition. These assumptions imply that $U(y,t) > 0$ for all $t > 0$, that is, all states are preferred to death. Define

$$u(y) = U(y,1)$$

$$m(t|y) = U(y,t)/U(y,1).$$

Then we have for all y

$$U(y,t) = u(y)m(t|y).$$

Under the assumptions A1 and A2 above, the function $m(\cdot)$ has the following properties:

P1: $m(0|y) = 0$ for all states y .

P2: $m(1|y) = 1$ for all states y .

P3: $m(t|y)$ is a continuous increasing function of $t \geq 0$ which is positive for all $t > 0$ and all states y .

If the function $m(t|y)$ is independent of health state y , then we obtain the nonlinear QALY model $U(y,t) = u(y)m(t)$. If $m(t|y)$ takes the form $m(t|y) = e^{-a(y)t}$, then we obtain *Markovian utility* (Hazen and Pellissier 1996), and the utility independence results in this appendix generalize those for Markovian utility in Hazen (2000), which anyway apply to only two attributes. In the main part of this paper, we assumed that the special health state $y^* \in Y$ had $u(y^*) = 1$, but here we let $u(y^*) = u^*$ be an arbitrary positive quantity.

Time-tradeoff independence and preferential independence

Theorem 5: Y_i is time-tradeoff independent of Z_i if and only if $Y_i T^+$ is preferentially independent of Z_i .

Proof: Time-tradeoff independence is a special case of preferential independence, hence is implied by it. Conversely, suppose time-tradeoff independence holds. To show preferential independence holds, suppose we have pairs $(y_i, z_i), (y_i', z_i') \in Y$ for which $(y_i, z_i, t) \succeq (y_i', z_i', t)$. We wish to show for $(y_i, z_i), (y_i', z_i') \in Y$ that we have $(y_i, z_i, t) \succeq (y_i', z_i', t)$.

Because $(y_i, z_i) \in Y$, it follows by partial closure that $(y_i^*, z_i) \in Y$ also. Because of P3, we can find durations s, s' such that $(y_i, z_i, t) \sim (y_i^*, z_i, s)$ and $(y_i', z_i', t) \sim (y_i^*, z_i', s')$. Because $(y_i, z_i, t) \succeq (y_i', z_i', t)$, we have by transitivity $(y_i^*, z_i, s) \succeq (y_i^*, z_i', s')$. Then by time-tradeoff independence, the last three preference conclusions imply

$$(y_i, z_i, t) \sim (y_i^*, z_i, s), \quad (y_i', z_i', t) \sim (y_i^*, z_i', s'), \quad (y_i^*, z_i, s) \succeq (y_i^*, z_i', s').$$

Therefore by transitivity we have $(y_i, z_i, t) \succeq (y_i', z_i', t)$, which is the desired conclusion. \blacklozenge

Theorem 6: Suppose the nonlinear QALY model holds over $Y \subset Y_i \times Z_i$. Then the following are equivalent:

- (a) Y_i is time-tradeoff independent of Z_i .
- (b) Z_i is time-tradeoff independent of Y_i .
- (c) $u(y_i, z_i) = u(y_i)u(z_i)/u^*$ for all $(y_i, z_i) \in Y$.

Proof: (a) \Rightarrow (c). Let $Y_i(z_i)$ be the set of all y_i for which $(y_i, z_i) \in Y$. If $(y_i, z_i) \in Y$, then by partial closure $(y_i, z_i^*) \in Y$ also, so $Y_i(z_i) \subset Y_i(z_i^*)$. Therefore by the preferential independence assumption, for each z_i for

which $Y_i(z_i) \neq \emptyset$, the utility functions $U(y_i, z_i, t)$ and $U(y_i, z_i^*, t)$ are ordinally equivalent as functions over $Y_i(z_i) \times T^+$. Therefore there is a function $f(u, z_i)$ increasing in u with $f(u, z_i^*) = u$ such that

$$U(y_i, z_i, t) = f(U(y_i, z_i^*, t), z_i),$$

for all y_i, z_i, t with $(y_i, z_i) \in Y$. That is,

$$u(y_i, z_i)m(t) = f(u(y_i)m(t), z_i).$$

Then because

$$u(y_i, z_i) = u(y_i, z_i)m(I) = f(u(y_i)m(I), z_i) = f(u(y_i), z_i)$$

we have, substituting this into the last equation,

$$f(u(y_i), z_i)m(t) = f(u(y_i)m(t), z_i).$$

Set $y_i = y_i^*$ to get

$$f(u^*, z_i)m(t) = f(u^*m(t), z_i),$$

that is, quantities $m(t)$ may be factored from the first component of f . In the defining equation for f

$$u(y_i, z_i)m(t) = f(u(y_i)m(t), z_i)$$

let t' be such that $u(y_i)m(t) = u^*m(t')$. This is possible because $u(y_i) \leq u^*$ and by P3, $m(\cdot)$ is continuous, positive and increasing. Then the right side of the last equation becomes

$$f(u(y_i)m(t), z_i) = f(u^*m(t'), z_i) = m(t')f(u^*, z_i) = (u(y_i)m(t)/u^*)f(u^*, z_i)$$

Cancel the positive value $m(t)$ to get

$$u(y_i, z_i) = (u(y_i)/u^*)f(u^*, z_i).$$

Set $y_i = y_i^*$ to conclude $u(z_i) = f(u^*, z_i)$. Substitute this conclusion into the last equation to get $u(y_i, z_i) = u(y_i)u(z_i)/u^*$, as claimed in (c).

(c) \Rightarrow (a) Suppose (c) holds. Then for states $(y_i, z_i), (y_i, z_i') \in Y$,

$$U(y_i, z_i, t) = u(y_i)u(z_i)m(t)/u^*$$

$$U(y_i, z_i', t) = u(y_i)u(z_i')m(t)/u^*.$$

With respect to y_i both these utility functions are ordinally equivalent to $u(y_i)m(t)$. Hence Y_i is preferentially independent of Z_i , and therefore (a) holds, by Theorem 5.

The arguments above may be repeated with Y_i and Z_i interchanged to show that (b) and (c) are equivalent. Therefore all three statements are equivalent, and the theorem is proved. \blacklozenge

Theorem 7: Suppose the nonlinear QALY model holds over $Y \subset Y_1 \times \dots \times Y_n$. Then the following statements are equivalent:

(a) Y_i is time-tradeoff independent over Y of its complementary attributes $Y_{\bar{i}}$ for at least $n-1$ of the n attributes Y_i .

(b) For $y \in Y$,

$$\frac{u(y)}{u^*} = \prod_{i=1}^n \frac{u(y_i)}{u^*}.$$

(c) Y_i is time-tradeoff independent over Y of its complementary attributes $Y_{\bar{i}}$ for $i = 1, \dots, n$.

Proof: (b) implies (c) as in Theorem 6, and (c) implies (a) trivially. So it remains to show that (a) implies (b). Suppose Y_i is time-tradeoff independent of $Y_{\bar{i}}$ over Y for $i = 1, \dots, n-1$. Then by Theorem 6 we have $y \in Y$,

$$u(y) = u(y_i, y_{\bar{i}}) = u(y_i)u(y_{\bar{i}})/u^* \quad i = 1, \dots, n-1 \quad (6)$$

Consider the induction hypothesis

$$\frac{u(y)}{u^*} = \frac{u(y_{\bar{I}})}{u^*} \prod_{i=1}^k \frac{u(y_i)}{u^*} \quad I = \{1, \dots, k\}. \quad (7)$$

for $y \in Y$. By (6), we know this holds for $k = 1$. We suppose it holds for some $k < n$, and show that it then must hold for $k+1$. So suppose (7) holds. Then invoke (6) with $i = k+1$ and $y_i = y_{k+1}^*$ to get

$$u(y_{\bar{I}}) = u(y_{k+1})u(y_{\overline{I \cup (k+1)}})/u^*.$$

Substitute back into (7) to get for $y \in Y$,

$$\frac{u(y)}{u^*} = \frac{u(y_{k+1})}{u^*} \frac{u(y_{\overline{I \cup (k+1)}})}{u^*} \prod_{i=1}^k \frac{u(y_i)}{u^*} = \frac{u(y_{\overline{I \cup (k+1)}})}{u^*} \prod_{i=1}^{k+1} \frac{u(y_i)}{u^*} \quad I = \{1, \dots, k\}.$$

Therefore the induction hypothesis holds for $k+1$. By induction it holds for all $k = 1, \dots, n$, so (b) is proved.

◆

Standard gamble independence

Let $\langle p, (y, t) \rangle$ denote a gamble in which outcome (y, t) occurs with probability p and immediate death (that is, the state-duration pair $(y, 0)$) occurs with probability $1-p$. Using this notation, Y_i is standard gamble independent of Z_i if for all $t > 0$, and all y_i , whenever

$$\langle p, (y_i^*, z_i, t) \rangle \sim (y_i, z_i, t)$$

holds for one level z_i with $(y_i, z_i) \in Y$, then it holds for all such z_i .

Theorem 8: The following are equivalent:

- (a) Y_i is standard gamble independent of Z_i .
- (b) Z_i is standard gamble independent of Y_i .
- (c) For all $(y_b, z_b) \in Y$, we have

$$u(y_b, z_b) = u(y_b)u(z_b)/u^*$$

$$m(t|y_b, z_b) = m(t|y_b, z_b^*)m(t|y_i^*, z_b)/m(t|y_i^*, z_b^*).$$

Proof: (a) \Rightarrow (c). Suppose Y_i is standard gamble independent of Z_i . If p satisfies the standard gamble indifference $\langle p, (y_i^*, z_i, t) \rangle \sim (y_b, z_b, t)$ for some $(y_b, z_b) \in Y$, then we have

$$pu(z_b)m(t|y_i^*, z_b) = u(y_b, z_b)m(t|y_b, z_b)$$

and therefore

$$p = \frac{u(y_b, z_b)m(t|y_b, z_b)}{u(z_b)m(t|y_i^*, z_b)}.$$

Denote the right-hand side of this equality by $p(y_b, z_b, t)$. The hypothesized standard gamble independence asserts that for $(y_b, z_b) \in Y$, $p(y_b, z_b, t)$ does not depend on z_b . Therefore $p(y_b, z_b, t) = p(y_b, z_b^*, t)$, that is,

$$\frac{u(y_b, z_b)m(t|y_b, z_b)}{u(z_b)m(t|y_i^*, z_b)} = \frac{u(y_b)m(t|y_b, z_b^*)}{u^*m(t|y_i^*, z_b^*)}.$$

Set $t = I$ and rearrange to conclude $u(y_b, z_b) = u(y_b)u(z_b)/u^*$. Substitute this back into the last equality and cancel to obtain the second assertion in (c).

(c) \Rightarrow (a) Under (c), the quantity $p(y_b, z_b, t)$ defined above is given by

$$p(y_b, z_b, t) = \frac{u(y_b, z_b)m(t|y_b, z_b)}{u(z_b)m(t|y_i^*, z_b)} = \frac{u(y_b)m(t|y_b, z_b^*)}{u^*m(t|y_i^*, z_b^*)}.$$

for $(y_b, z_b) \in Y$. Because $p(y_b, z_b, t)$ does not depend on z_b , it follows that Y_i is standard gamble independent of Z_i .

The arguments above may be repeated with Y_i and Z_i interchanged to show that (b) and (c) are equivalent. Therefore all three statements are equivalent, and the theorem is proved. \blacklozenge

Corollary 8a: Suppose the nonlinear QALY model holds for all states $y \in Y$. Then the following are equivalent:

- (a) Y_i is standard gamble independent of Z_i .
- (b) Z_i is standard gamble independent of Y_i .

(c) For all $(y_i, z_i) \in Y$, we have

$$u(y_i, z_i) = u(y_i)u(z_i)/u^*.$$

Theorem 9: The following statements are equivalent.

(a) Y_i is standard-gamble independent of $Y_{\bar{i}}$ for at least $n-1$ of the n attributes Y_i .

(b) For all $y \in Y$,

$$\frac{u(y)}{u^*} = \prod_{i=1}^n \frac{u(y_i)}{u^*}$$

$$\frac{m(t|y)}{m(t|y^*)} = \prod_{i=1}^n \frac{m(t|y_i, y_{\bar{i}}^*)}{m(t|y^*)}.$$

(c) Y_i is standard-gamble independent over Y of $Y_{\bar{i}}$ for $i = 1, \dots, n$.

Proof: We show (b) \Rightarrow (c) \Rightarrow (a) \Rightarrow (b). First suppose (b) holds. If p satisfies the standard gamble indifference $\langle p, (y_i^*, y_{\bar{i}}, t) \rangle \sim (y, t)$ for some $y \in Y$, then under (b) we have

$$p = p_i(y, t) = \frac{u(y)m(t|y)}{u(y_i^*, y_{\bar{i}})m(t|y_i^*, y_{\bar{i}})} = \frac{u(y_i)m(t|y_i, y_{\bar{i}}^*)}{u^*m(t|y^*)}.$$

It follows that for $y \in Y$, $p_i(y, t)$ does not depend on $y_{\bar{i}}$. Therefore Y_i is standard-gamble independent of $Y_{\bar{i}}$ over Y , and (b) implies (c).

(c) implies (a) trivially. To show (a) implies (b), suppose (a) holds for attributes $i = 1, \dots, n-1$. By Theorem 8 we have for $i = 1, \dots, n-1$ and all $y \in Y$,

$$u(y) = u(y_i)u(y_{\bar{i}})/u^*$$

$$m(t|y) = m(t|y_i, y_{\bar{i}}^*)m(t|y_i^*, y_{\bar{i}})/m(t|y^*)$$

The first of these implies $\frac{u(y)}{u^*} = \prod_{i=1}^n \frac{u(y_i)}{u^*}$ for all $y \in Y$ just as in the proof of Theorem 7. Rewrite the second equality as

$$m^*(t|y) = m^*(t|y_i, y_{\bar{i}}^*)m^*(t|y_i^*, y_{\bar{i}}) \quad i = 1, \dots, n-1 \quad (8)$$

where $m^*(t|y) = m(t|y)/m(t|y^*)$. For $i = 1$ it follows that

$$m^*(t|y) = m^*(t|y_1, y_{\bar{1}}^*)m^*(t|y_1^*, y_{\bar{1}})$$

$$= m^*(t|y_1, y_{\bar{1}}^*)m^*(t|y_1^*, y_2, y_{\bar{2}}).$$

If $n = 2$, we are done. For $n > 2$, apply the $i = 2$ version of (8) to the last factor to get

$$m^*(t|y) = m(t | y_1, y_1^*)m^*(t | y_2, y_2^*)m^*(t | y_1^*, y_2^*, y_{12}^*)$$

For $n = 3$, we are done. If $n > 3$, then continue in this fashion, applying (8) for $i = 3, \dots, n-1$ to get

$$m^*(t | y) = \prod_{i=1}^n m^*(t | y_i, y_i^*)$$

for all $y \in Y$. Therefore (b) holds. \blacklozenge

Corollary 9a: Suppose the nonlinear QALY model holds. Then the following statements are equivalent.

(a) Y_i is standard-gamble independent of $Y_{\bar{i}}$ for at least $n-1$ of the n attributes Y_i .

(b) For all $y \in Y$,

$$\frac{u(y)}{u^*} = \prod_{i=1}^n \frac{u(y_i)}{u^*}$$

(c) Y_i is standard-gamble independent of $Y_{\bar{i}}$ for $i = 1, \dots, n$.

Utility independence

Theorem 10: $Y_i T^+$ is utility independent of Z_i if and only if

(i) $u(y_i, z_i) = u(y_i)u(z_i)/u^*$ for all $(y_i, z_i) \in Y$, and

(ii) for $(y_i, z_i) \in Y$, $m(t|y_i, z_i)$ does not depend on z_i .

Proof: (\Rightarrow) If $Y_i T^+$ is utility independent of Z_i then Y_i is standard-gamble independent of Z_i over Y , so by Theorem 8,

$$u(y_i, z_i) = u(y_i)u(z_i)/u^* \tag{9}$$

$$m(t|y_i, z_i) = m(t|y_i, z_i^*)m(t|y_i^*, z_i)/m(t|y_i^*, z_i^*). \tag{10}$$

The condition that $Y_i T^+$ is utility independent of Z_i means that for some $\alpha(z_i) > 0$, $\beta(z_i)$, we have

$$U(y_i, z_i, t) = \alpha(z_i)U(y_i, z_i^*, t) + \beta(z_i).$$

The zero condition forces $\beta(z_i) = 0$. Substitute $U(y_i, z_i, t) = u(y_i, z_i) m(t|y_i, z_i)$ and use (9) and (10) to obtain

$$\begin{aligned} u(y_i)u(z_i)/u^* m(t|y_i, z_i^*)m(t|y_i^*, z_i)/m(t|y_i^*, z_i^*) \\ = \alpha(z_i) u(y_i) m(t|y_i, z_i^*) \end{aligned}$$

Substitute $y_i = y_i^*$ and $t = 1$ to get

$$u(z_i) = \alpha(z_i) u^*$$

Substitute this into the penultimate equation and cancel to get

$$m(t|y_i^*, z_i)/m(t|y_i^*, z_i^*) = 1.$$

From this it follows using (10) that

$$m(t|y_i, z_i) = m(t|y_i, z_i^*).$$

Therefore, $m(t|y_i, z_i)$ does not depend on z_i . ♦

(\Leftarrow) Suppose conditions (i) and (ii) hold, and let $m(t|y_i) = m(t|y_i, z_i^*)$. Then for states $(y_i, z_i), (y_i, z_i') \in Y$,

$$U(y_i, z_i, t) = u(y_i)u(z_i)m(t|y_i)/u^*$$

$$U(y_i, z_i', t) = u(y_i)u(z_i')m(t|y_i)/u^*$$

Because $u(z_i)/u^* > 0$, $u(z_i')/u^* > 0$, both these utility functions are cardinally equivalent to $u(y_i)m(t|y_i)$.

Hence utility independence holds. ♦

Corollary 10a: The following are equivalent.

(a) $Y_i T^+$ is utility independent of Z_i and $Z_i T^+$ is utility independent of Y_i .

(b) The nonlinear QALY model holds for $y \in Y$, that is, for all $(y_i, z_i) \in Y$, $m(t|y_i, z_i)$ does not depend on (y_i, z_i) , and

$$u(y_i, z_i) = u(y_i)u(z_i)/u^*$$

Corollary 10b: Suppose the nonlinear QALY model holds for all states $y \in Y$. Then the following are equivalent:

(a) $Y_i T^+$ is utility independent of Z_i .

(b) $Z_i T^+$ is utility independent of Y_i .

(c) $u(y_i, z_i) = u(y_i)u(z_i)/u^*$ for all $(y_i, z_i) \in Y$.

Theorem 11: Suppose $n \geq 3$. Then the following statements are equivalent:

(a) $Y_i T^+$ is utility independent of the complementary attributes $Y_{\bar{i}}$ for at least $n-1$ of the n attributes Y_i .

(b) For $y \in Y$, the nonlinear QALY model holds with

$$\frac{u(y)}{u^*} = \prod_{i=1}^n \frac{u(y_i)}{u^*}.$$

(c) $Y_i T^+$ is utility independent over Y of the complementary attributes $Y_{\bar{i}}$ for $i = 1, \dots, n$.

Proof: The implications (b) \Rightarrow (c) \Rightarrow (a) are easily shown. It remains to demonstrate (a) \Rightarrow (b). So suppose (a) holds. Specifically, suppose $Y_i T^+$ is utility independent over Y of the complementary attributes $Y_{\bar{i}}$ for $i = 1, \dots, n-1$. Then by Theorem 10, $m(t|y)$ does not depend on $y_{\bar{i}}$ for $i = 1, \dots, n-1$, that is, $m(t|y)$ does not depend on $y_{\overline{1 \cup \dots \cup n-1}}$. But for $n \geq 3$, we have $\overline{1} \cup \dots \cup \overline{n-1} = \{1, \dots, n\}$, so we conclude that $m(t|y)$ does not depend on y . Therefore, the nonlinear QALY model holds. To show the remainder of (b), invoke Theorem 10(i) to get

$$u(y) = u(y_i, y_{\bar{i}}) = u(y_i)u(y_{\bar{i}})/u^* \quad i = 1, \dots, n-1.$$

Now proceed as in the proof of Theorem 7 to reach the desired conclusion. \blacklozenge

Corollary 11a: Suppose $n \geq 2$. Then under the nonlinear QALY model, the following statements are equivalent:

(a) $Y_i T^+$ is utility independent over Y of the complementary attributes $Y_{\bar{i}}$ for at least $n-1$ of the n attributes Y_i .

(b)
$$\frac{u(y)}{u^*} = \prod_{i=1}^n \frac{u(y_i)}{u^*}$$

(c) $Y_i T^+$ is utility independent over Y of the complementary attributes $Y_{\bar{i}}$ for $i = 1, \dots, n$.