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A COMPARISON OF STANDARD GAMBLE, TIME TRADE-OFF, AND ADJUSTED TIME TRADE-OFF SCORES

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Abstract

Objective: To adjust patients' time trade-off (TTO) scores using information on their utility functions for survival time to derive a measure of health state utility equivalent to the standard gamble (SG).
Methods: A sample of 199 cardiovascular patients were asked three TTO and SG questions (to assess their own health state), and three certainty equivalent questions (to assess their utility function for survival time) in an interview.
Results: Patients' utility functions for time were increasingly concave, but being unable to model this successfully, a constant function with an averaged level of concavity was used. The raw TTO scores were significantly higher than SG scores, while the adjusted TTO scores were equivalent to the SG.
Conclusions: Raw time trade-off scores will give biased estimates of health state utility when patients' utility functions for time are not linear, but these can be adjusted to yield true utilities. The constant proportional risk-posture assumption of the conventional QALY model, on which previous attempts to adjust time trade-offs have been based, was not supported by the data.

Keywords: Quality of life, Quality-adjusted life-years, Decision support techniques, Heart diseases

Quality-adjusted life-years (or QALYs) attempt to provide a single index for measuring the impact of treatment or disease on quality and quantity of life simultaneously. QALYs are calculated by adjusting an observed survival period by some

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weight that reflects the desirability of the health state experienced relative to full health and death. Full health and death are conventionally assigned weights of 1 and 0, respectively. If the weight used to adjust survival time is measured on a utility scale and a number of other (fairly demanding) assumptions are met, the QALY model proposed by Pliskin et al. (13) and Miyamoto and Eraker (11) will itself have utility properties. This is attractive because it establishes a theoretical link between QALYs and a formal method of decision making based on expected utility theory.

A variety of methods have been used to estimate health state utilities for calculating QALYs, including the standard gamble and the time trade-off. The standard gamble could be considered the theoretically optimal method because of its foundation in expected utility theory (21). The time trade-off approach was developed as a supposedly simpler alternative but typically gives lower estimates (15;19). This is likely due to a violation of the assumption that all future years of life have the same marginal utility (i.e., utility function for time is linear). The trend for time trade-off to systematically underestimate utilities suggests that people's utility functions for time are concave rather than linear.

The two graphs in Figure 1 illustrate this hypothesis. In both graphs the true utility of the health state with symptoms is 0.85. When future years of life have a constant marginal utility (as shown in the upper graph in Figure 1), 15% of remaining survival time will need to be traded to reflect a health state utility of 0.85. When future years of life have a decreasing marginal utility (as shown in the lower graph in Figure 1), a greater proportion of remaining survival time will need to be traded (around 38% in this example) to reflect the same utility. Applying the conventional interpretation to the trade-off represented in the lower graph to estimate the utility of health state with symptoms gives an underestimate of 0.63. The shape of an individual's utility function for time has implications for the way utilities are estimated from responses to time trade-off questions.

It is possible to explore the shape of utility functions for survival time using certainty equivalence questions (6;10). The task requires an individual to state the amount of survival time for sure (the certainty equivalent) that would be equally preferable to a gamble between some upper and lower survival period (e.g., 0 and 10 years). Certainty equivalents that are less than, equal to, or greater than the expected outcome of the gamble indicate a concave function, a linear function, or a convex function, respectively.

Gafni and Torrance (4) provide a good explanation of how a person's utility function for time can be influenced by three distinct effects: a gambling effect, a quantity effect, and a time preference effect (e.g., discounting). For example, an aversion to gambling will tend to make the sure outcome presented in the certainty equivalence task more attractive than a gamble with an equivalent expected outcome. This effect will tend to make the utility function for survival time concave. The quantity effect refers to the relative desirability of additional units of a particular good. A decreasing marginal value for money implies that the relative desirability of the 102nd dollar will be less than that for the second dollar. A person's marginal value for additional survival may decrease in the same way and tend to make the utility function for survival time concave. Time preference refers to the observation that the value assigned to an outcome will be influenced by *when* it will be obtained. People tend to have a positive time preference and prefer valued outcomes sooner rather than later. Assuming that the marginal value of additional survival time is constant, additional years of life could appear to have a decreasing marginal value

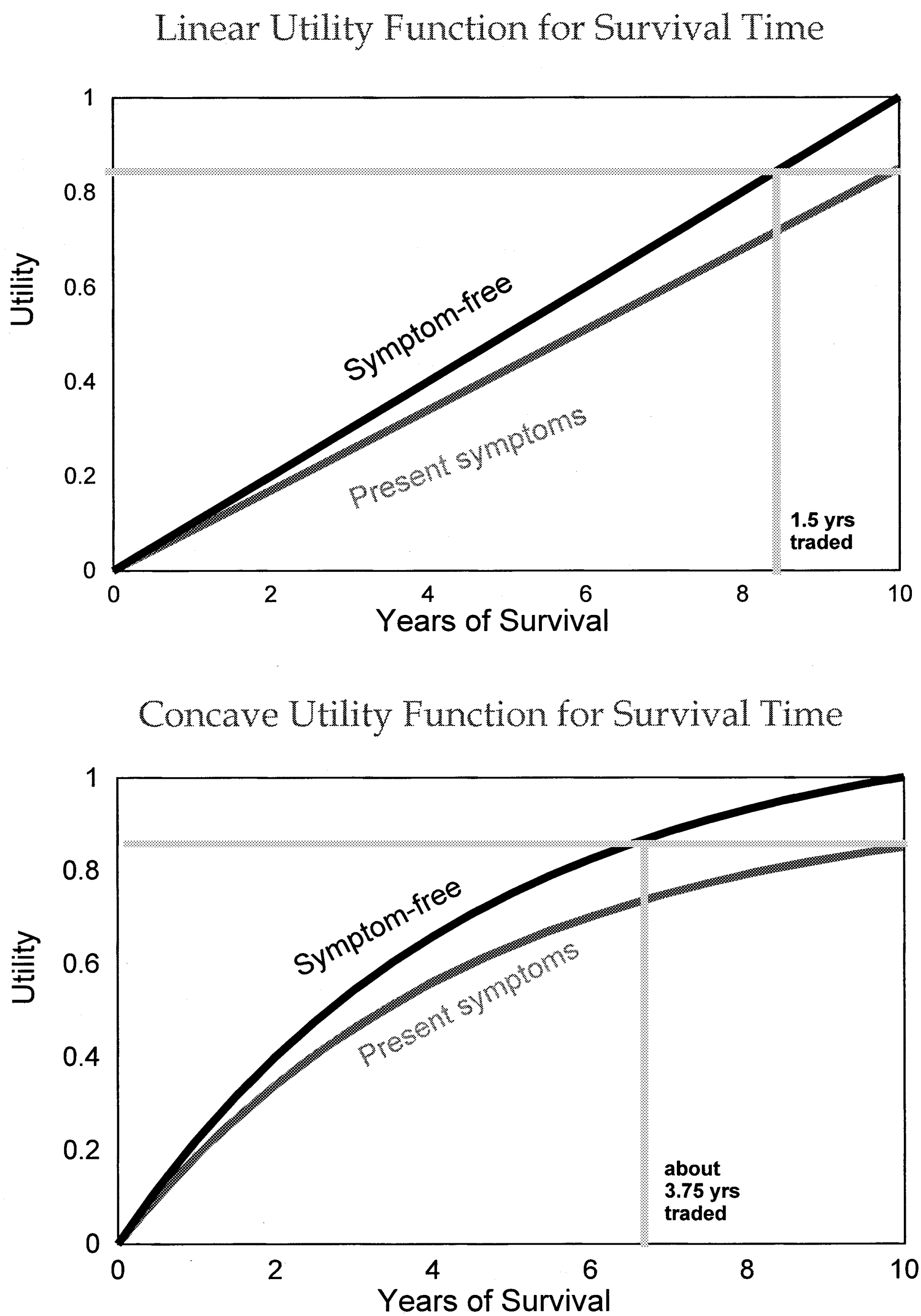

Figure 1. Time trade-offs and shape of utility function for time. In both graphs the true utility of the health state with symptoms is 0.85, but the shape of the utility function for time in each differs. Applying the conventional interpretation to the time trade-off response illustrated in the second graph gives an underestimate of about 0.63.

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because the present value of those future years are eroded due to our positive time preference. This effect (discounting) will again tend to make the utility function for survival time concave.

Time trade-off scores that are adjusted to account for people's nonlinear utility function for time should theoretically have true utility properties. This has been attempted in three small studies (11;13;19), only one of which compared the adjusted time trade-off against a standard gamble (19). Each also modeled utility for time using a function with constant proportional properties, which assumes that an individual would be willing to forfeit a constant proportion of any survival time for a fixed quality of life improvement. The validity of this assumption was not thoroughly assessed in these studies and has been shown to be violated elsewhere (17;20).

We undertook a study with a sample of 201 cardiovascular patients that aimed to: a) examine the appropriateness of a utility function for survival time with constant proportional shape; b) calculate adjusted time trade-off scores using information on patients' utility functions; and c) compare the adjusted time trade-off scores with the standard gamble.

METHODS

Patients and Procedures

The 201 cardiovascular disease patients were selected from 322 patients taking part in a project to investigate the reliability and validity of a quality-of-life questionnaire (9). The mean age of the patients interviewed was 61 (SD, 9.3) and 26% were female. Thirty-nine percent of patients had no symptoms of angina or dyspnea at all, 19% had symptoms on strenuous exertion, 19% had symptoms on normal exertion, 10% had symptoms on mild exertion, and 13% had symptoms at rest. Nine percent reported their health was excellent, 44% reported their health was good, 40% reported their health was fair, and 8% reported their health was poor. Two of the 201 patients were unable to answer any of the utility questions, one due to insufficient English and the other because of cognitive/emotional problems.

The 45-minute interviews were performed by a single interviewer (AM). Three time trade-off questions were asked with 10-, 5-, and 15-year hypothetical survival time frames, followed by three standard gamble questions with the same time frames to obtain information on patients' *own* health state utility. The time trade-off and standard gamble questions were asked in this order to minimize framing effects (8). Three certainty equivalence questions were asked to model patients' utility functions for survival time: one for a 50:50 gamble between 1 and 10 years, one for a 50:50 gamble between 5 and 15 years, and one for a 50:50 gamble between 10 and 20 years. The time frames of the gambles were chosen to be minimally threatening while providing data needed to model patients' utility functions for survival time over different intervals.

Analyses

The certainty equivalence data were used to model patients' utility functions for time. The appropriateness of a constant proportional model was examined as well as a less restrictive constant model. The constant proportional model took the form: utility of time = time^r, where $r < 1$ is concave, and $r > 1$ is convex. The constant model took the form: utility of time = $1 - e^{-c \times \text{time}}$ with $c > 0$ for a concave function, and utility of time = $e^{-c \times \text{time}}$ $c < 0$ for a convex function. An estimate of the

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Table 1. Standard Gamble Scores for Patients' Own Health State

Time frame (yrs)	All patients[a]		Patients with mean standard gamble score <1.00[a]	
	n	Mean (SD)	n	Mean (SD)
5	199	0.920 (0.17)	93	0.828 (0.21)
10	199	0.915 (0.17)	93	0.818 (0.21)
15	198	0.914 (0.17)	93	0.816 (0.21)

[a] Scores decreasing with time frame (p = .003).

parameter c for a constant concave model can be calculated by solving the following equation:

$$1 - e^{(-c \times \text{certainty equivalent})} = \frac{\left[1 - e^{(-c \times \text{best outcome of gamble})}\right] + \left[1 - e^{(-c \times \text{worst outcome of gamble})}\right]}{2} \qquad \textbf{(1)}$$

An estimate of the parameter r in the constant proportional model can be found in an analogous way. Solutions to these equations were obtained using the bisection method (14) for each of the three certainty equivalence questions asked of every patient.

The raw time trade-off data were adjusted using information on patients' utility functions for time. Equation 2 demonstrates how this was accomplished using a constant concave function as an example.

$$\text{Adjusted time trade-off score} = \frac{\text{utility of time}_i}{\text{utility of time}_j} = \frac{1 - e^{(-c \times \text{time}_i)}}{1 - e^{(-c \times \text{time}_j)}}; \qquad \textbf{(2)}$$

where j is the amount of time spent in patients' present health state that was rated as equally preferable to the lesser amount of time i spent in full health in the time trade-off question.

Statistical Tests

Three main types of statistical tests were used to analyze the data. The Wilcoxon signed rank-sum test was used for paired data that were not normally distributed. A stratified (by patient) Mantel-Haenszel test for trend was used to examine associations between ordinal variables collected from the same patient (1). Repeated measures were also analyzed using the generalized estimating equation methods (25).

RESULTS

Standard Gamble Scores

One patient found the standard gamble question with the 15-year time frame too unrealistic and answered "not applicable" to the question. The standard gamble scores were generally high (Table 1) with about half of the sample unwilling to accept a risk of death to be restored to full health. Seventy-seven percent of these patients had no symptoms of angina or dyspnea with normal or less strenuous effort. There was a slight, yet highly significant, trend for standard gamble scores to decrease with the increasing time frame of the question (GEE, β coefficient = −0.003, SE = 0.001, Z = 3.0, p = .003). Because this effect was diluted by the substantial proportion of patients with an average standard gamble score of 1.00,

Table 2. Certainty Equivalence Results

Time frame	n	Expected outcome of gamble	Certainty equivalents mean (SD)	Estimates of c mean (SD)[a]
50:50 1 and 10 yrs	196	5.5	4.88 (1.74)	0.09 (0.28)
50:50 5 and 15 yrs	194	10	8.83 (2.21)	0.15 (0.33)
50:50 10 and 20 yrs	187	15	13.66 (2.14)	0.18 (0.36)
Overall mean	—	—	—	0.14

[a] Scores increasing with time frame ($p = .001$).

we repeated the analysis for the subgroup of patients whose average standard gamble score was less than 1.00 and found the effect was still small in absolute terms but about twice as large as that for the entire sample (GEE, β coefficient = −0.006, SE = 0.002, Z = 3, $p = .003$).

Modeling Utility Functions for Time (Certainty Equivalence Data)

Two patients felt the 50:50 gamble between 5 and 15 years was too unrealistic for them, and seven patients felt similarly for the 50:50 gamble between 10 and 20 years. On average, patients gave certainty equivalents that were less than the expected outcome of the three gambles—indicative of a concave utility function (Table 2).

The proportion of patients with concave functions increased for certainty equivalence gambles with larger time frames (M−H $\chi_1^2 = 7.74$, $p = .005$). These results suggest that patients' utility functions for survival were increasingly concave, and hence that a constant proportional model (which has a declining degree of concavity) was inappropriate. Unfortunately, estimating the parameters of models with double exponential terms—typically used to model increasingly concave functions—is extremely difficult. Deterministic methods (e.g., solving an equation) give highly unstable estimates because they are unable to deal with measurement error. There are presently no practical statistical methods for directly estimating these parameters.

As a next best option, we chose to construct a utility function for each of the three time intervals using the less restrictive constant function. The last column in Table 2 shows the estimates of c increasing with expected outcome of the certainty equivalence questions. This positive trend was highly significant (GEE, β coefficient = 0.043, SE = 0.013, Z = 3.31, $p = .001$). Age was not a significant ($p = .18$) predictor of increasing concavity when fitted as a covariate in this analysis.

Time Trade-off Scores

Three patients found the time trade-off question with a 15-year time frame unrealistic to their own survival expectations and answered "not applicable" to the question. Table 3A shows the average time trade-off scores for each time frame. Many patients (47%) had an average score of 1.00, i.e., they would not trade-off any amount of time for full health. Seventy-nine percent of these patients had no symptoms of angina or dyspnea with normal or less strenuous effort, and 92% had also refused to risk survival time in response to the standard gamble questions. The tendency for time trade-off scores to decrease with increasing time frame was highly significant (GEE, β coefficient = −0.02, SE = 0.004, Z = 5.0, $p < .0001$). The trend was about twice as large in the subgroup of patients with an average

Table 3A. Time Trade-off Scores for All Patients

Time frame (yrs)	Raw time trade-off[a]		Individually adjusted time trade-off		Group-adjusted time trade-off	
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
5	199	0.901 (0.17)	197	0.923 (0.14)	199	0.921 (0.14)
10	198	0.883 (0.17)	196	0.930 (0.13)	198	0.929 (0.11)
15	196	0.863 (0.19)	194	0.924 (0.15)	196	0.933 (0.11)

[a] Scores decreasing with time frame $p < .0001$.

time trade-off score below 1.00 (GEE, β coefficient = −0.04, SE = 0.008, Z = 5.36, $p < .0001$). This subgroup was prepared to trade 21% of a 5-year survival period and 30% of a 15-year survival period to be restored to full health.

Adjusted Time Trade-off Scores

The constant model more closely described patient utility functions for time than the constant proportional model and was consistent with patients trading an increasing proportion of remaining survival time in response to time trade-off questions with increasing time frames. It was therefore applied to adjust the time trade-off scores. Table 3A shows the utility estimates based on time trade-off scores that were adjusted using: a) patients' individual utility functions for survival time (individually adjusted time trade-off); and b) the group average utility function for survival time (group-adjusted time trade-off). The group and individually adjusted time trade-off data were similar, and not on average significantly different from each other (Wilcoxon signed rank-sum test, Z = 0.64, $p = .5$). The effect of time frame on the individually and group-adjusted time trade-off scores was not significant. For the subgroup with an average time trade-off below 1.00 (Table 3B), the effect of time frame on individually adjusted time trade-off scores was also not significant, but was approaching significance for the group-adjusted time trade-off scores ($p = .046$).

Comparison of the Standard Gamble and Time Trade-off Scores

The raw time trade-offs gave significantly lower estimates than the standard gamble (Wilcoxon signed rank-sum test, Z = 4.61, $p < .0001$). However, both the group and individually adjusted time trade-off data did not significantly differ from the standard gambles. The correlation between patients' average standard gamble score and their average group-adjusted time trade-off was 0.51, but was 0.64 for the individually adjusted data (Spearman's rank correlation was 0.8 for both). The corresponding intraclass reliability coefficients were 0.46 and 0.61, respectively.

DISCUSSION

A large proportion of the sample of cardiac patients (49%) did not trade/risk survival time for quality-of-life improvements. While somewhat surprising, other studies have obtained comparable results (5;12;20;22). There are several possible explanations for the tied utilities at unity. Patients may have valued survival over quality-of-life gains despite health deficits. Alternatively, they may have rounded up their utility estimates to 1.00 despite their diagnosis if they were asymptomatic or had only mild symptoms. This second explanation seems quite plausible given

Table 3B. Time Trade-off Scores for Patients with Average Time Trade-off Score Less Than 1.00

Time frame (yrs)	Raw time trade-off[a]		Individually adjusted time trade-off		Group-adjusted time trade-off[b]	
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
5	93	0.787 (0.19)	92	0.836 (0.17)	93	0.831 (0.16)
10	92	0.747 (0.17)	91	0.849 (0.16)	92	0.846 (0.12)
15	90	0.702 (0.19)	89	0.835 (0.19)	90	0.855 (0.13)

[a] Scores decreasing with time frame $p < .0001$.
[b] Scores increasing with time frame $p = .046$.

that 78% of patients with utility scores of 1.00 had no symptoms of angina or dyspnea, or symptoms only with strenuous effort, and 75% of them reported their health as being "excellent" or "good." It may have been possible to shift some of these patients from a utility of 1.00 by administering the standard gamble and time trade-off questions with very small gradations in probabilities (e.g., accept a 1/1,000 risk of death for a complementary probability of full health) or time frames (e.g., trade off 1 day of survival time in return for full health). Whether patients would find such tasks meaningful is questionable. Approaches for measuring utilities at the very upper end of the scale should nevertheless be pursued. Values in this range can be important from a public health perspective for weighing the benefits and disadvantages of mass screening campaigns or primary preventive programs that have the potential to confer only small absolute benefits and risks to individuals but appreciable benefits and risks at an aggregate level.

The certainty equivalence data showed that, on average, patients' utility functions were concave. The proportion of patients with concave functions was also found to increase, as did the average degree of concavity (as measured by the parameter c), for the certainty equivalence gambles with higher expected outcome.

Which of the three effects described by Gafni and Torrance (4) (time preference effect, a gambling effect, or a quantity effect) may best explain the increasing concavity observed? Evidence from other studies suggests that discount rates decrease with the length of delay for health outcomes (3;16), and so pure time preference is unlikely to explain the increasing concavity. Any gambling effect should not have varied between the certainty equivalence questions, because all were consistently posed as 50:50 gambles. Perhaps the more likely explanation is an accelerating decline in the marginal value of additional survival time (independent of pure time preference). This could have occurred if the longer time frames used far exceeded patients' survival expectations; however, age was not found to be a predictor of increasing concavity. An alternative explanation for the increasing concavity is that patients tend to anticipate future life-years with an acceleration in worsening health despite being asked to imagine health remains stable when answering the certainty equivalent questions.

Our certainty equivalence utility data for survival time, and others (23), are inconsistent with the constant proportional model used in previous studies that have attempted to adjusted time trade-off scores (11;13;19). We also observed a significant trend for patients to trade a greater proportion of time in time trade-off questions with increasing survival time frames as did Stiggelbout et al. (20).

This is additional evidence for the inappropriateness of a constant proportional model. We were unable to construct an increasingly concave function, but the constant function we chose more closely described the data than a constant proportional function. In the group as a whole there was no significant difference between the adjusted time trade-off estimates, and the means of the adjusted time trade-off and standard gamble scores were almost identical. The relatively modest correlation between patients' standard gamble and adjusted time trade-off scores may be explained by the imperfect reliability of both questions. If the time trade-off and standard gamble have a test-retest reliability of about 0.8, even a perfect linear relationship between their expected values would be diluted to a correlation on the order of 0.8. The prediction of group means would be much more accurate, as was observed for these data.

Expected utility theory provides the theoretical basis for preferring the standard gamble over the time trade-off as a criterion measure of utility. However, the status of expected utility theory has been questioned on the grounds of poor descriptive validity (18), and the standard gamble criticized for being internally inconsistent (7) and overly sensitive to the gambling effect (24). In practice the time trade-off is widely used, and the debate over whether the standard gamble is indeed optimal will continue. This study found that differences between standard gamble and time trade-off scores were successfully explained by drawing on the theory that underpins the standard gamble, as opposed to a strategy that implies some deficiency of the standard gamble or underlying theory. The results also suggest that raw time trade-off scores are not interpretable without information on the individual's utility function for survival time.

The results of this study have some implication for the validity of the assumptions that underlie the QALY model. Eighty-seven percent of patients gave identical standard gamble scores regardless of the time frame used to deliver the question. These responses are consistent with the mutual utility independence assumption (between quality of life and survival time) that underlies the QALY model (11;13). There was, nevertheless, a statistically significant, albeit very modest, inverse relationship between standard gamble scores and the time horizon used to deliver the question. The study was not designed to comprehensively explore the mutual utility independence assumption, and these results should be treated as an interesting observation. The study was designed to test the validity of the constant proportional trade-off assumption and found it was violated in two separate tasks (time trade-off and certainty equivalent). In contrast to our results and those of Stiggelbout et al. (20), a study by Bleichrodt and Johannesson (2) found some support for the constant proportional trade-off assumption. The discrepancy between the results of the studies may be explained in part by the differences in the characteristics of the two samples and differences in the nature of the evaluation tasks performed. The study population of Bleichrodt and Johannesson (2) comprised 172 undergraduate university students enrolled in economics, statistics, or health policy courses. In addition to being considerably younger, potentially more numerate, and healthier than our population, they rated a number of simplified health state descriptions as opposed to a health state with which they were very familiar. In the absence of a thorough appreciation of the health states placed before them, they may have found it simpler to accept the time trade-off task as a purely hypothetical exercise and given answers in accord with the constant proportional trade-off assumption as a logical response strategy. The health experiences of patients in the present study may have made it more difficult for them to accept the concept of their health remaining stable over each of the survival horizons used to deliver the utility questions. Patients may have associated additional survival with an acceleration in worsening health, thereby causing the increasing concavity in utility for time observed.

In conclusion, raw time trade-off scores will give biased estimates of health state utility when the individual's utility function for time is not linear. In such cases, the scores can be adjusted to allow for this to yield true utilities. The validity of the constant-proportional model that has previously been used to adjust time trade-off scores was not supported by the present study. Patients' utility functions for survival time were increasingly concave. We were unable to model this successfully, but found that adjusting time trade-off scores using a constant function with an averaged level of concavity gave scores that were not significantly different from standard gambles.

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