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QALYs When Health Varies Over Time: An Analysis of Model Identification and Parameter Estimation from Time Trade-Off and Standard Gamble Scores

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QALYS WHEN HEALTH VARIES OVER TIME: AN ANALYSIS OF MODEL IDENTIFICATION AND PARAMETER ESTIMATION FROM TIME TRADE-OFF AND STANDARD GAMBLE SCORES

KRISTIAN SCHULTZ HANSEN AND LARS PETER ØSTERDAL

ABSTRACT. In the first part of the paper, we consider various QALY (quality-adjusted life year) models in situations where health varies over time, and provide a theoretical analysis of model identification and parameter estimation from time trade-off and standard gamble scores. We investigate deterministic and probabilistic models, and consider five different families of discount factors in all. The second part of the paper contains a discussion of some recurrent themes from related literature. Among other things, we question the standard gamble method as a 'gold standard' in health preference measurement, re-examine the role of constant-proportional trade-off, and discuss so-called double discounting of QALYs. We also argue that it is not a matter of choosing between time trade-off and standard gamble procedures, since both types of scores are generally needed in order to be able to disentagle risk aversion from discounting. More broadly, we find that conclusions drawn from the analysis of models involving chronic health states only may not necesssarily apply to situations where health varies over time. One reason is that risk aversion and discounting may collapse to the same thing when all health states are chronic.

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Key words and phrases. Medical decision making, QALYs, varying health, double discounting, standard gamble, time trade-off.

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1. Introduction

Quality-adjusted life years (QALYs) have been developed to measure health related aspects of a person's well-being. In much of the literature on QALY measurement, in particular the theoretically oriented, attention has been restricted to chronic health states (e.g. Pliskin al., 1980; Gafni and Torrance, 1984; Miyamoto and Eraker 1985, 1988; Johannesson et al. 1994; Bleichrodt et al., 1997; Cairns and van der Pol, 1997; Miyamoto et al., 1998; Miyamoto 1999; Bleichrodt, 2002; Østerdal 2002).

Restricting attention to chronic health states is indeed very powerful: For instance, elegant axiomatic characterizations of QALY models can be established under expected utility or rank-dependent utility assumptions (Miyamoto et al. 1998, Miyamoto 1999), and it is a useful simplification for an axiomatic approach to justice in health care resource allocation (Østerdal, 2002).

For some empirical applications, models where health states are assumed to be chronic may be sufficiently rich. This is the case in situations where we aim to assess the value of a health care service that remedies a permanent handicap, or if we aim to assess the value of prolonging life at some fixed state of well-being. In practice, however, we often consider medical conditions where health states vary over time.

In recent years, a number of papers have explicitly addressed health preference measurement in situations where health varies over time. Among others, Lipscomb (1989), Stiggelbout et al. (1994), Richardson et al. (1996), Cher et al. (1997), Kuppermann et al. (1997), Krabbe and Bonsel (1998), Treadwell (1998), MacKeigan et al. (2003) and Spencer (2003) consider non-chronic health profiles. Among the many different issues analyzed in these papers, a common theme has been to test the validity of the additivity assumption over time, which is usually assumed in QALY models, using stated preference experiments. The present paper is closely related to the above-mentioned contributions, but our focus is different.

The purpose of this paper is twofold. In the first part of the paper (Sections 2 and 3), we present a unified approach to health preference measurement in situations where health states not necessarily are chronic. This serves as an overview of QALY models that we also hope could useful for future empirical work. We distinguish between deterministic models and models where uncertainty is explicit, and consider four different types of discounting (five in all with a special variant discussed in Section 3.5). In each case we specify the type of empirical

information that is necessary (and sufficient) for estimating the parameters in the model. We focus on procedures using either standard gamble (SG) scores, time trade-off (TTO) scores or a combination; the type of empirical data usually collected in this type of health economic assessments.

In Section 2, we consider four deterministic models with exponential, polynomial, proportional and hyperbolic discounting respectively, and describe how parameters can be estimated with TTO techniques (Sections 2.1-2.4).

In Section 3, we go on to models where uncertainty is explicit and describe how parameters can be estimated with a combination of TTO and SG scores for each of the discounting models (Sections 3.1-3.4). In Subsection 3.5 we also consider a fifth type of discounting related to work by Johannesson et al. (1994). In this case, we initially restrict attention to chronic health states and then discuss possible generalizations of the model to situations with non-chronic health states.

Knowing the theoretical relationship between TTO and SG scores and between the time horizon and TTO scores, the models can, in principle, be identified from plots of the empirical relationship between these figures. We derive such theoretical relationships, and provide some numerical examples suggesting that, even assuming that one of the above-mentioned discounting models is "true", although it theoretically is possible to identify the model from TTO and/or SG scores only, in practice it is likely to be extremely difficult.

The second part of the paper (Section 4) contains a discussion based on the above-mentioned findings, and challenge some conclusions obtained in previous literature. Among other things, we question the SG method as a 'gold standard' for parameter estimation, re-examine the role of constant-proportional trade-off, and discuss so-called 'double discounting of QALYs'.

Overall, we argue that results drawn from theoretical analysis of models involving only chronic health states may not necessarily apply to situations where health is allowed to vary over time, hence restricting attention to chronic health states may blur some important aspects of QALY modeling. One important difference, among others, is that although risk aversion and discounting generally are distinct phenomena, these two effects cannot be disentangled in some of the most widely used models involving only chronic health states; a point which, to our knowledge, has received little attention (if any) in the literature.

Section 5 mentions two important limitations of our analysis, and in relation to this speculates on directions for future research.

2. QALY AS UTILITY OF DETERMINISTIC HEALTH PROFILES

In this section we consider deterministic QALY models. Let A denote a collection of possible *health states* with typical elements a and a'. The health state of an individual may be described by a variety of information on physical and mental well-being, for example the ability to walk, see, hear, ability to solve puzzles etc. We assume that A contains a health state a^* called 'perfect health' and a health state a^0 called 'dead'.

An individual is born at time zero and lives for a finite number of years $t \geq 0$. A *health profile* is a map l on the non-negative reals taking values in A where $l(s) \neq a^0$ for all $s < t$ and $l(s) = a^0$ for all $s \geq t$.

Let L be a collection of possible health profiles, and let $\succsim$ be preference relation (a complete and transitive binary relation) on L representing individual preference for health profiles. A real-valued function q on L is a representation of the preference relation $\succsim$ on health profiles if

$$l \succsim l' \Leftrightarrow q(l) \geq q(l'), \tag{2.1}$$

for all $l, l' \in L$. Let u be a real-valued *health state index* on A. In QALY models, it is assumed that preferences are separable over time[1] and that there exists a real-valued function v on $A \times \mathbb{R}$ such that

$$q(l) = \int_0^t v(l(s), s)ds.^2 \tag{2.2}$$

Suppose that $v(a, s) = u(a)\delta(s)$ for some functions u and δ, where $0 \leq u \leq 1$ and $0 < \delta \leq 1$.[3] In addition, assume that $u(a^0) \leq u(a) \leq u(a^*)$ for all a and $u(a^0) < u(a^*)$. Without loss of generality we normalize u such that $u(a^0) = 0$ and $u(a^*) = 1$. Then for any life time t and health state a there is exactly one non-negative real number $h(t, a)$ between zero and t such that

$$\int_0^{h(t,a)} u(a^*)\delta(s)ds = \int_0^t u(a)\delta(s)ds.$$

[1]The reasonableness of this assumption depends on the interpretation of the health states. For empirical tests and discussions, see the papers cited in the Introduction.

[2]The integrals we consider in this paper are well-defined under mild technical assumptions, see Grodal (2003, ch. 12 and 13).

[3]For a characterization of this class of functions in terms of conditions on the preference relation, see Grodal (2003, section 13.3).

In words, $h(t, a)$ is the number of years at a^* (perfect health) that gives the same utility as t years at health state a, and is referred to as the *time trade-off index* defined for chronic health states.

We focus on the most commonly used discounting functions; exponential discounting: $\delta(s) = c^s$, $0 < c < 1$ (Section 2.1), polynomial discounting: $\delta(s) = s^z$, $-1 < z < 0$ (Section 2.2), proportional discounting: $\delta(s) = \frac{1}{1+vs}$, $0 < v$ (Section 2.3), and hyperbolic discounting: $\delta(s) = (1 + vs)^{-w/v}$, $0 < v, w$ (Section 2.4).

In Figure 1, examples of each type of discounting is given where parameters have been selected such that the curves intersect at $s = 10$. We have $\delta(s) = 0.9^s$ (black curve), $\delta(s) = s^{-0.4576}$ (gray curve), $\delta(s) = (1 + 0.1868s)^{-1}$ (dashed curve) and $\delta(s) = (1 + 4s)^{-1.1349/4}$ (dotted curve).

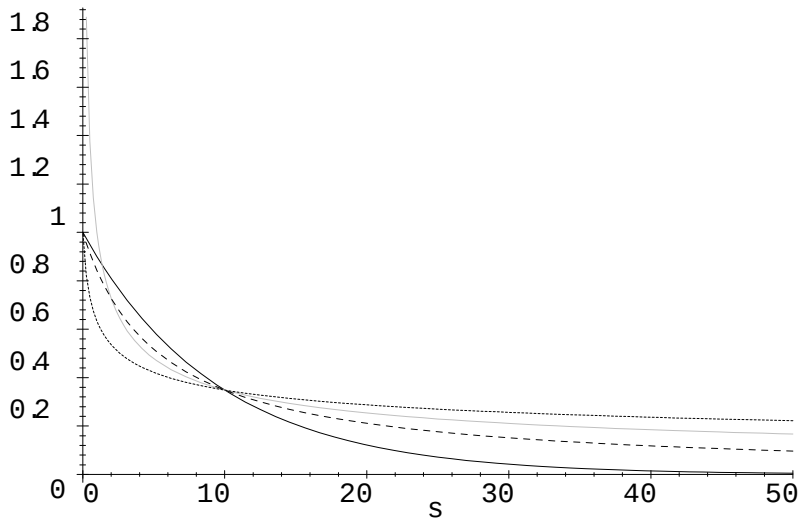

FIGURE 1. Four types of discounting.

The plausibility of various structural forms can be assessed by evaluating underlying axioms which in certain combinations give rise to different functional forms of individual health related utility (e.g. Miyamoto and Eraker, 1989; Bleichrodt and Johannesson, 2001). However this line of analysis is beyond the scope of the present paper. In the following, our focus is parameter estimation and model identification directly from TTO scores.

2.1. **Exponential discounting.** With exponential discounting the QALY has the form

$$q(l) = \int u(l(s))c^s ds, \tag{2.3}$$

for some health state index u and $0 < c < 1$. The question is how to estimate the function u and the discounting parameter c from empirical data. We may estimate the discounting parameter c using TTO scores (involving only chronic health states). Let a be a health state such that $0 < h(t,a) < t$. We then have the following relation

$$\int_0^{h(t,a)} c^s ds = \int_0^t u(a)c^s ds,$$

where $u(a)$ and c are unknown. This equation reduces to

$$\left[c^{h(t,a)} - 1\right] = u(a)\left[c^t - 1\right]. \tag{2.4}$$

For $0 < t < t'$ we obtain by substitution

$$\left[c^{h(t,a)} - 1\right]\left[c^{t'} - 1\right] = \left[c^{h(t',a)} - 1\right]\left[c^t - 1\right].$$

From two empirical estimates $\widehat{h}(t,a)$ and $\widehat{h}(t',a)$ we may then determine c numerically. For example if $\widehat{h}(1,a) = 0.5$ and $\widehat{h}(2,a) = 0.9$ then $\widehat{c} \cong 0.67$.

It remains to estimate the health state index $u(a)$. From (2.4),

$$u(a) = \frac{1 - c^{h(1,a)}}{1 - c},$$

so in our example, $\widehat{u}(a) \cong 0.55$. The derivation above is similar to those offered by Olsen (1994), Cher et al. (1997) and Martin et al. (2000) and also applied in recent studies by Gyrd-Hansen (2002) and Stavem et al. (2002).

Solving (2.4) for $h(t,a)$ gives

$$h(t,a) = \frac{\ln\left(1 + u(a)(c^t - 1)\right)}{\ln c}.$$

Clearly we have $u(a)t > h(t,a)$ for any $0 < c < 1$ and $u(a)t \to h(t,a)$ for $c \to 1$. In fact for $0 < u < 1$, $h(t,a)$ is strictly concave in t, since

$$h'_t(t,a) = u\frac{c^t}{1 + u(c^t - 1)},$$

is positive and

$$h''_{tt}(t,a) = -uc^t (\ln c) \frac{-1+u}{(1+uc^t-u)^2},$$

is negative. Plots of $h(t,a)$ against t are depicted in Appendix A for selected values of u (and different types of discounting, see below). We comment on the figures in the last part of Section 2.4.

2.2. **Polynomial discounting.** With polynomial discounting the QALY function has the form

$$q(l) = \int u(l(s))s^z ds, \tag{2.5}$$

where $-1 < z < 0$.

Polynomial discounting has been studied by Harvey (1986) in discrete time. This utility structure satisfies a generalized form of constant proportional trade-off. Given a health profile l and $d > 0$ let l_d be the health profile obtained from stretching out or contracting l such that the health state obtained at time s in l is obtained at time ds in l_d, i.e. $l_d(s) = l(ds)$, $s \geq 0$. The ranking of two lives does not depend on the unit measuring life years: $l \succsim l'$ if and only if $l_d \succsim l'_d$ for all $d > 0$.

For a health state a we have

$$\int_0^{h(t,a)} s^z ds = \int_0^t u(a)s^z ds,$$

which reduces to

$$\frac{1}{z+1}(h(t,a))^{z+1} = \frac{1}{z+1}u(a)t^{z+1},$$

or

$$h(t,a) = u(a)^{\frac{1}{z+1}}t. \tag{2.6}$$

We therefore have $h(t,a) = h(1,a)t$, or $u(a) = (h(1,a))^{z+1}$.

Since $h(t,a)$ is linear in t it is not possible to extract information on discounting from estimates of $h(t,a)$ for varying t. In other words, *the parameter z cannot be derived from time-trade off scores involving only chronic health states.* For the purpose of estimating z, we can make use of non-chronic health profiles. A parameter estimation technique is the following: Let a be an arbitrary health state for which $0 < h(1,a) < 1$, and let l be the health profile composed of one year in health a^* followed by one year in health state a. In addition, let l^w be the health profile

with w life years in health state a followed by $2-w$ life years at health state a^*. Now, if w is such that $l^w \sim l$ then

$$\int_0^1 s^z 1 ds + \int_1^2 s^z (h(1,a))^{z+1} ds = \int_0^w s^z (h(1,a))^{z+1} ds + \int_w^2 s^z 1 ds,$$

which after some calculations reduces to

$$1 + (h(1,a))^{z+1}\left[2^{z+1} - 1\right] = (h(1,a))^{z+1} w^{z+1} + \left[2^{z+1} - w^{z+1}\right], \tag{2.7}$$

where z is the unknown parameter. If the number w that satisfies $l^w \sim l$ and $h(1,a)$ are determined empirically, the solution to (2.7) can then be found numerically. For example if $\widehat{h}(1,a) = \frac{1}{2}$ and $\widehat{w} = 0.75$ then $\widehat{z} \cong -0.16$ and $\widehat{u}(a) \cong 0.56$.

As it will be clear in the following sections, the case of polynomial discounting is the only discounting model we examine where the function h is not strictly concave in t - see Appendix A. (We comment further on this in Section 2.4).

2.3. **Proportional discounting.** Proportional discounting has been used by for instance by Herrnstein (1981) and Mazur (1987). See Harvey (1994) for a characterization. In this case the utility of a health profile l is

$$q(l) = \int u(l(s))(1+vs)^{-1} ds,$$

where $v > 0$. For a health state a we have

$$\int_0^{h(t,a)} (1+vs)^{-1} ds = \int_0^t u(a)(1+vs)^{-1} ds,$$

which reduces to

$$\ln(vh(t,a)+1) = u \ln(tv+1). \tag{2.8}$$

We may elicit v from two estimates $h(t,a)$ and $h(t',a)$. By (2.8) we have

$$\ln(vh(t,a)+1) = u(a)\ln(tv+1),$$

and

$$\ln(vh(t',a)+1) = u(a)\ln(t'v+1).$$

Thus

$$\frac{\ln(vh(t,a)+1)}{\ln(tv+1)} = \frac{\ln(vh(t',a)+1)}{\ln(t'v+1)}.$$

For example, if $\widehat{h}(1,a) = 0.5$ and $\widehat{h}(2,a) = 0.9$ then by solving the equation numerically we get $\widehat{v} \cong 1.04$ and then $\widehat{u}(a) \cong 0.59$.

Solving (2.8) for $h(t,a)$ yields

$$h(t,a) = \frac{(tv+1)^u - 1}{v},$$

which is strictly concave in t.

2.4. **Hyperbolic discounting.** With hyperbolic discounting the QALYs are given by

$$q(l) = \int u(l(s))(1+vs)^{-w/v} ds,$$

where $v, w > 0$. The special case $v = w$ is proportional discounting (cf. Section 2.3). As with polynomial discounting, hyperbolic discounting entails discount rates that decline over time (see Loewenstein and Prelec, 1992, for an axiomatic study). Note that if v tends to zero, the discounting function converges to exponential discounting with discount rate w, i.e. $\lim_{v\to 0}(1+vs)^{-w/v} = e^{-wt}$.

For a health state a we have

$$\int_0^{h(t,a)} (1+vs)^{-w/v} ds = \int_0^t u(a)(1+vs)^{-w/v} ds,$$

which for $w/v \neq 1$ after some calculations[4] reduces to

$$\left[(1+vh(t,a))^{(-w/v+1)} - 1\right] = u(a)\left[(1+tv)^{(-w/v+1)} - 1\right]. \tag{2.9}$$

We may elicit v and w from three estimates $h(t,a)$, $h(t',a)$ and $h(t'',a)$. From the equation system

$$\begin{aligned}
\left[(1+vh(t,a))^{(-w/v+1)} - 1\right] &= u(a)\left[(1+tv)^{(-w/v+1)} - 1\right], \\
\left[(1+vh(t',a))^{(-w/v+1)} - 1\right] &= u(a)\left[(1+t'v)^{(-w/v+1)} - 1\right], \\
\left[(1+vh(t'',a))^{(-w/v+1)} - 1\right] &= u(a)\left[(1+t''v)^{(-w/v+1)} - 1\right],
\end{aligned}$$

where $u(a), w$ and v are unknown we obtain by substitution

$$\left[(1+vh(t,a))^{(-w/v+1)} - 1\right] = \frac{\left[(1+vh(t'',a))^{(-w/v+1)} - 1\right]}{\left[(1+vt'')^{(-w/v+1)} - 1\right]}\left[(1+tv)^{(-w/v+1)} - 1\right],$$

and

$$\left[(1+vh(t',a))^{(-w/v+1)} - 1\right] = \frac{\left[(1+vh(t'',a))^{(-w/v+1)} - 1\right]}{\left[(1+vt'')^{(-w/v+1)} - 1\right]}\left[(1+t'v)^{(-w/v+1)} - 1\right].$$

For completeness, it remains to consider the special case $v = w$. In principle, if there is no solution to the above equation system for which $v \neq w$ we should test the data with the proportional discounting model (for this case, see Section 2.3). For example, assume that $\widehat{h}(1,a) = 0.40$,

[4]Note that $\int (1+vs)^{-w/v} ds = \frac{(1-vs)^{(-w/v+1)}}{(-w/v+1)v}$, $v \neq w$.

$\widehat{h}(2,a) = 0.75$ and $\widehat{h}(3,a) = 1.08$. Solving these equations numerically yields $\widehat{v} \cong 4$ and $\widehat{w} \cong 2$. From this we have $\widehat{u}(a) \cong 0.5$.[5]

For any pair v,w the TTO index $h(t,a)$ is strictly concave in t: solving (2.9) for $h(t,a)$ gives

$$h(t,a) = -\frac{1 - \left(1 + u\left(1+tv\right)^{\frac{-w+v}{v}} - u\right)^{\frac{v}{-w+v}}}{v}.$$

We have

$$h'_t(t,a) = \left(1 + u\left(1+tv\right)^{\frac{v-w}{v}} - u\right)^{\frac{w}{v-w}} u\left(1+tv\right)^{-\frac{w}{v}},$$

which is positive, and after some calculations we obtain

$$h''_{tt}(t,a) = \left(1 + u\left(1+tv\right)^{\frac{v-w}{v}} - u\right)^{\frac{2w-v}{v-w}} u\left(1+tv\right)^{-\frac{w+v}{v}} w\left(-1+u\right),$$

which is negative. In Figures 2-4 $h(t,a)$ appears to be linear in t. Indeed, if $w < v$ (as we have assumed in Figures 2-4) h is almost linear: the second order derivatives are small and converging to zero when t tends to infinity.[6] If $w > v$, $h(t,a)$ has an upper bound; however convergence may be extremely slow.[7]

For the purpose of identifying a suitable family of discounting functions for a given application, figures like those depicted in Appendix A can be useful. We give three examples that aim to illustrate the curvature of $h(\cdot,a)$ for different types of discounting. For example, if a plot of empirical estimates $\widehat{h}(t,a)$ for different values of t gives approximately a straight line, it may indicate that polynomial or hyperbolic discounting models are well suited. If $\widehat{h}(t,a)$ clearly shows a strictly concave relationship, we may wish to select exponential, proportional or hyperbolic discounting.

[5]It is relevant to note that there is a difficulty here using numerical procedures. Non-valid solutions to the above pair of equations for which $v = w$ are likely to appear, depending on the choice of initial guess values. It is beyond the scope of this paper to study general properties of this sort of equation systems; here we shall only notice that our experience with selected estimates has been that a solution for which $v = w$ is likely to appear using numerical methods to solve the equation system, at least if the initial guess value is far from the valid solution.

[6]For example if $u(a) = 0.5$, $v = 4$ and $w = 1.1349$ we have $h''_{tt}(1,a) \cong -0.023$, $h''_{tt}(10,a) \cong -0.00071$ and $h''_{tt}(100,a) \cong -0.000015$.

[7]For example if $u(a) = 0.5$, $v = 1$ and $w = 1.1$ then $h(t,a)$ converges toward 1023.0, but we have $h(10,a) \cong 2.0871$, $h(1000,a) \cong 16.624$, $h(10^{10},a) \cong 393.8$ and $h(10^{30},a) \cong 1012.8$ etc.

It is also worth noticing that concavity of $h(\cdot, a)$ does not follow from discounting. For example, the discounting function

$$\delta(s) = \begin{cases} s^{-0.5}, & 0 \leq s \leq 1 \\ s^{-0.25}, & 1 < s \end{cases}$$

is continuous and strictly decreasing in s but the associated TTO index $h(\cdot, a)$ is *not* concave in t. Concavity of $h(\cdot, a)$ is therefore a special property shared by any of the discounting functions studied in this paper. Unfortunately, this shared feature makes it more difficult to identify a model from empirical TTO scores. Hence if empirical TTO scores seem to follow a strictly *convex* curve, neither of the standard families of discounting functions are likely to provide a good fit to the data, and some non-standard discounting function could be needed.

3. QALY as expected utility of health lotteries

In order to deal explicitly with uncertainty, we consider a *health lottery* which is a map p on L taking values in the unit interval, where $p(l) \neq 0$ for a finite number of health profiles l and where all probabilities sum to unity. Let P denote the set of all finite health lotteries on L. Thus we may view L as the set of degenerate health lotteries with unit probability attached to a single health profile.

In this section, let $\succsim_P$ be a preference relation on P representing individual preference for lotteries over health profiles.

Let $\text{supp}(p) = \{l \in L \mid p(l) \neq 0\}$ denote the *support* of p. Under expected utility assumptions (see Kreps, 1988, Theorem 5.15), there exists a real-valued function q on L and a real-valued function Q on P such that for any $p, p' \in P$,

$$p \succsim_P p' \Leftrightarrow Q(p) \geq Q(p'), \tag{3.1}$$

where

$$Q(p) = \sum_{l \in \text{supp}(p)} p(l)q(l), \tag{3.2}$$

and where q is unique up to a positive affine transformation. In words, this is an expected utility representation on health profiles. However, usually we are interested in more than that: expected utility on A (the set of health states), not L (the set of health profiles). More precisely, we may assume that there is a function v (or derive existence from assumptions imposed on $\succsim_P$) such that (3.2) holds with $q(l) =$

$\int v(l(s), s)ds$ which gives

$$Q(p) = \sum_{l \in \text{supp}(p)} p(l) \int v(l(s), s)ds \tag{3.3}$$

or equivalently

$$Q(p) = \int \sum_{a \in \text{supp}(\overline{p}(a|s))} \overline{p}(a|s) v(l(s), s)ds,$$

where $\overline{p}(a|s) = \sum_{l \in \text{supp}(p) | l(s)=a} p(l)$ is the probability of health state a at time s for health lottery p. In the following, we assume that preferences over health lotteries can be represented by a function Q of the form (3.3). This model can be interpreted as risk neutrality over discounted deterministic health profiles or short 'risk neutrality over QALYs'; see Subsection 3.5 and Section 4 for a discussion of this assumption. We have risk aversion over (discounted deterministic) QALYs if the expected utility increases from replacing a lottery over (discounted deterministic) QALYs by its expectation, i.e. there is a function v and a strictly concave function f such that (3.2) holds with

$$q(l) = f\left(\int v(l(s), s)ds\right). \tag{3.4}$$

Let $p[t, a, \pi]$ be a health lottery where, with probability π, health state a is experienced for t years followed by death and, with probability $1 - \pi$, immediate death occurs. A *standard gamble index* defined on chronic health states is then a map g on $\mathbb{R}_+ \times A$ taking values in the unit interval, such that $p[t, a^*, g(t, a)] \sim_P p[t, a, 1]$ for all a and t.

Suppose, as in Section 2, that there is u and δ such that $v(a, s) = u(a)\delta(s)$, where $0 < \delta \leq 1$ and $0 = u(a^0) \leq u(a) \leq u(a^*) = 1$. In this case, it is easy to verify that g is well-defined and uniquely determined (i.e. we can talk about *the* standard gamble index). In addition, we have $Q(p[t, a^*, g]) = g \int_0^t \delta(s)ds$ and $Q(p[t, a, 1]) = \int_0^t u(a)\delta(s)ds = u(a) \int_0^t \delta(s)ds$, i.e. $g(t, a) = u(a)$ for all t. In words, under the conditions outlined above, the SG estimate does not depend on the time horizon and is equal to the health state index. In the following we therefore leave out time as argument in the standard gamble function and write $g(a) \equiv g(1, a)$.

In this section, our interest is again the following special cases: exponential discounting (Section 3.1), polynomial discounting (Section 3.2), proportional discounting (Section 3.3) and hyperbolic discounting (Section 3.4). In addition, we consider a specific form of discounting

derived from an assumption of constant-proportional risk posture over exponentially discounted life years (Section 3.5).

3.1. **Exponential discounting.** We have (3.2) with $q(l) = \int u(l(s))c^s ds$. The discounting parameter c can be estimated using TTO information on deterministic life profiles as outlined in Section 2.1. Alternatively, the discounting parameter c can be elicited from a comparison of the time trade-off and standard gamble estimate. Let a be a health state and t a life time where $0 < g(a) < 1$ and $0 < h(t,a) < t$. Then from (2.4) and the fact that $g(a) = u(a)$ we have

$$\left[c^{h(t,a)} - 1\right] = g(a)\left[c^t - 1\right], \tag{3.5}$$

where c is the unknown.

For example if $\widehat{h}(1,a) = 0.5$ and $\widehat{g}(a) = 0.55$, we obtain $\widehat{c} \cong 0.67$. However, the first possibility contradicts $h(1,a) \neq g(a)$ and we therefore find that $\widehat{c} \cong 0.67$ is the discounting parameter. Thus, even a quite small difference between the SG and TTO score is an indication of substantial discounting. Or, the other way around, substantial discounting gives only rise to quite small differences in the SG and TTO scores.

In Appendix B, plots of $h(t,a)$ against $u(a)$ are depicted for selected values of t. It is interesting to note that the relative distance between $h(t,a)$ and $u(a)t$ increases in t for all types of discounting except for polynomial discounting where the distance is unaffected by t (see Section 3.2 below).

3.2. **Polynomial discounting.** We have (3.2) with $q(l) = \int u(l(s))s^z ds$. The discounting parameter z can be estimated using TTO information on chronic life profiles as in Section 2.2. Alternatively, the discounting parameter z can be elicited from a comparison of TTO and SG scores. Let a be a health state and t a life time where $0 < g(a) < 1$ and $0 < h(t,a) < t$. Then from (2.6) and the fact that $g(a) = u(a)$ we have

$$h(t,a) = g(a)^{\frac{1}{z+1}} t, \tag{3.6}$$

where z is the unknown. Isolating z gives

$$z = \frac{\ln g(a)}{\ln h(1,a)} - 1.$$

For example, if $\widehat{h}(1,a) = 0.5$ and $\widehat{g}(a) = 0.55$ then $\widehat{z} \cong -0.14$.

Miyamoto and Eraker (1985) and Miyamoto (2000) show how the discounting parameter can be derived from information on 'certainty equivalents' which is the amount of life time in some (non-perfect)

health state a which is equally good as some lottery with fixed probabilities of either perfect health at some positive amount of time or immediate death. The certainty equivalence method has also been used by Stiggelbout et al. (1994) and by Martin et al. (2000) for both exponential and polynomial discounting.

3.3. **Proportional discounting.** With proportional discounting we have (3.2) with $q(l) = \int u(l(s))(1+vs)^{-1}ds$. The discounting parameter v can be estimated using TTO information on chronic life profiles as in Section 2.2. Alternatively, v can be elicited from a comparison of TTO and SG scores. Let a be a health state and t a life time where $0 < g(a) < 1$ and $0 < h(t,a) < t$. Then from (2.8) and the fact that $g(a) = u(a)$ we have

$$\ln(vh(t,a)+1) = g(a)\ln(tv+1), \tag{3.7}$$

which may be solved numerically for v. For example if $\widehat{h}(1,a) = 0.5$ and $\widehat{g}(a) = 0.55$ then $\widehat{v} \cong 0.50$.

3.4. **Hyperbolic discounting.** With the hyperbolic discounting family we have (3.2) with $q(l) = \int u(l(s))(1+vs)^{-w/v}ds$, where $v, w > 0$.

Again, the discounting parameters can be found as outlined in Section 2.4. We may also, slightly simpler, make use of both SG and TTO scores. Let a be a health state and t a life time where $0 < g(a) < 1$ and $0 < h(t,a) < t$. Then from (2.9) and the fact that $g(a) = u(a)$ for $v \neq w$ we have

$$\left[(1+vh(t,a))^{(-w/v+1)} - 1\right] = g(a)\left[(1+tv)^{(-w/v+1)} - 1\right],$$

where v and w are unknown parameters. For a health state a' where $0< g(a') < 1$ and $g(a') \neq g(a)$ we likewise have

$$\left[(1+vh(1,a'))^{(-w/v+1)} - 1\right] = g(a')\left[(1+v)^{(-w/v+1)} - 1\right],$$

which is sufficient to determine v and w numerically. For completeness, it remains to consider the special case $v = w$. In this case, discounting is proportional, see Section 3.3.

For example, assume that $\widehat{h}(1,a) = 0.5$, $\widehat{g}(a) = 0.55, \widehat{h}(1,a') = 0.77$ and $\widehat{g}(a') = 0.80$. Then

$$0.55\left[(1+v)^{(-w/v+1)} - 1\right] = \left[(1+0.5v)^{(-w/v+1)} - 1\right],$$

and

$$0.80\left[(1+v)^{(-w/v+1)} - 1\right] = \left[(1+0.77v)^{(-w/v+1)} - 1\right].$$

Solving the equations numerically yields $\widehat{v} \cong 7.03$ and $\widehat{w} \cong 1.56$. The equation system is simpler than that derived from TTO scores only (Section 2.4).[8]

3.5. **Constant-proportional risk posture over exponentially discounted life years.** Following Johannesson et al. (1994) we restrict attention to chronic health states and consider constant-proportional risk posture over exponentially discounted life years. We give a separate treatment of this form of discounting to give another illustration of the implications of restricting attention to chronic health states. We have (3.2) with

$$q(l) = \left(u(a)\int_0^t c^s ds\right)^r,$$

where $a = l(s), 0 \leq s \leq t$, and $0 < c, r < 1$. We then have

$$q(l) = (u(a))^r (\int_0^t c^s ds)^r. \tag{3.8}$$

or

$$q(l) = \widetilde{u}(a)(\int_0^t c^s ds)^r,$$

where $\widetilde{u}(a) = (u(a))^r$ for all a.

What is the underlying discounting factor? We look for a function $\delta(s)$ satisfying

$$\int_0^t \delta(s) ds = (\int_0^t c^s ds)^r.$$

for all $t > 0$ where c and r are fixed parameters. Since $(\int_0^t c^s ds)^r = (\frac{c^t - 1}{\ln c})^r$ and

$$\frac{\partial(\frac{c^s-1}{\ln c})^r}{\partial s} = r(\frac{c^t - 1}{\ln c})^{r-1} c^s,$$

we obtain

$$\delta(s) = r(\frac{c^s - 1}{\ln c})^{r-1} c^s.$$

When we restrict attention to chronic health states, this approach is therefore equivalent to the model (3.2) with a rather peculiar family of discounting functions.

[8] In this case there are also non-valid solutions to the equation system (for which $\widehat{v} = \widehat{w}$) that should be ruled out if obtained by a numerical procedure (see footnote 5).

We now turn to the case where health may vary over time. If we wish to preserve the property of constant-proportional risk posture (Pliskin et al., 1980) over exponentially discounted life years we have (3.2) with

$$q(l) = \int \widetilde{u}(l(s))r(\frac{c^s - 1}{\ln c})^{r-1}c^s ds, \tag{3.9}$$

for (not necessarily chronic) health profiles l. With (3.9) the SG index g can then be used as health utility index $\widetilde{u}$. Assume therefore that $\widetilde{u}$ is known in (3.9). We can then estimate r and c from a combination of SG and TTO scores. Let a be a health state where $0 < g(a) < 1$ and let $0 < h(t,a) < t$. Then

$$g(a)\int_0^t r(\frac{c^t - 1}{\ln c})^{r-1}c^s ds = \int_0^{h(t,a)} r(\frac{c^t - 1}{\ln c})^{r-1}c^s ds.$$

Which reduces to

$$g(a)(\frac{c^t - 1}{\ln c})^r = (\frac{c^{h(t,a)} - 1}{\ln c})^r,$$

or

$$r = \frac{\ln g(a)}{\ln(1 - c^{h(t,a)}) - \ln(1 - c^t)}.$$

For some health state $a' \neq a$ with $0 < h(t,a') < t$ we then have

$$\frac{\ln g(a)}{\ln(1 - c^{h(t,a)}) - \ln(1 - c^t)} = \frac{\ln g(a')}{\ln(1 - c^{h(t,a')}) - \ln(1 - c^t)}.$$

This equation may then be solved numerically. For example if $\widehat{h}(1,a) = 0.5$, $\widehat{g}(a) = 0.55, \widehat{h}(1,a') = 0.77$ and $\widehat{g}(a') = 0.80$ then $\widehat{c} \cong 0.88$ and $\widehat{r} \cong 0.90$.

We have

$$h(t,a) = \frac{\ln\left(1 + (g(a))^{\frac{1}{r}}c^t - (g(a))^{\frac{1}{r}}\right)}{\ln c},$$

which gives

$$h'_t(t,a) = (g(a))^{\frac{1}{r}}\frac{c^t}{1 + (g(a))^{\frac{1}{r}}c^t - (g(a))^{\frac{1}{r}}},$$

which is positive and after some calculations we obtain

$$h''_{tt}(t,a) = (\ln c)\, c^t \frac{(g(a))^{\frac{1}{r}} - (g(a))^{\frac{2}{r}}}{\left(1 + (g(a))^{\frac{1}{r}}c^t - (g(a))^{\frac{1}{r}}\right)^2},$$

which is negative. We therefore find that $h(t,a)$ is also strictly concave in t.

Another approach is to consider a model (3.2) with

$$q(l) = \left(\int \widetilde{u}(l(s))c^s ds \right)^r, \tag{3.10}$$

for (not necessarily chronic) health profiles l. In this case, we give up constant-proportional risk-posture over exponentially discounted life years, and obtain a model that is not of the form (3.3) but captures a (polynomial) form of risk aversion over (exponentially) discounted QALYs. We provide some further discussion of this type of models in the following Section 4.

4. Discussion of related literature

To avoid misunderstandings, we recall that *risk aversion* now relates to the curvature of the transformation f when we have a representation (3.4), whereas *discounting* relates to the functional form of δ in a model which can either of the type (3.3) or (3.4).[9]

4.1. **Is SG the gold standard?**

In the literature, some authors have claimed that QALYs are utilities while others have disputed this. In this paper, the QALY q (or Q) represents a preference relation on the space of (lotteries over) health profiles, and as such the QALY is by construction a utility in the health space.

In the literature, the SG method has often been referred to as the 'gold standard'. Drummond et al. (1997), for example, write in their book that "A utility, in our context, is a von Neumann-Morgenstern utility. So all QALYs that are formed from preferences measured in any other way other than with a standard gamble, by definition, can not be utilities." (p. 183). The authors do not explicitly formulate the model that underlies this conclusion, and it is interesting to elaborate on this using the framework in Section 3. First, suppose that the utility representation is of the form (3.3), a model with risk neutrality over QALYs. In this case, the utility function may be estimated fully with TTO scores only. Once the discounting factor has been determined (from TTO scores with varying time horizon) the health state index is not equal to the TTO score but uniquely determined by it which is sufficient for our purpose. In fact, contrary to the TTO score, the SG scores cannot be used for eliciting discount factors and as such they are

[9]Of course, even more complex models can be considered. However, for the present discussion these models are sufficiently rich to address the basic relationship between discounting and risk aversion.

typically less useful than TTO scores.[10] On the other hand, suppose that risk neutrality over QALYs is not necessarily assumed and the underlying model more generally is (3.4) for some strictly increasing concave function f.[11] Typically, it would then be assumed that f is a member of some parametric family with one of two free parameters that can be estimated with SG scores. However, the shape of the function v is not related to preferences over lotteries and possible risk aversion, and v is naturally estimated from TTO scores. To sum up, regardless of the exact form of the model, TTO scores are indeed relevant also in an expected utility framework.

4.2. **The role of constant proportional trade-off.** In a paper discussing the SG method, Gafni (1994) argues (p. 211) that the SG method requires constant proportional trade-off.[12] However, this claim seems be incorrect: In any model of the form (3.3) with $v(a,s) = u(a)\delta(s)$, a large family of models for which constant proportional trade-off not necessarily is satisfied, the SG scores can be substituted directly for the health state index. Generally, it is useful to distinguish between the underlying model and the particular method used for parameter estimation. The SG method can be useful for parameter estimation in *any* model, if SG scores otherwise are considered reliable and efficiently elicited (an empirical question to be answered case by case depending on the alternatives available). Of course, it may not be the case that the SG estimate can be used directly as a health state index, as for example in case of risk aversion over QALYs. This is also the case for the TTO scores which must be transformed depending on the specific family of discounting models used, but it is nevertheless an equally informative score.

Broome (1993) claimed in a critique of the axioms introduced by Pliskin et al. (1980) that constant proportional trade-off rules out any discounting of future QALYs and is out of place at the level of a general theory. We do not wish to comment on the appropriate level of generality in health economic theory; it should be noted, however, that the constant proportional trade-off is consistent with the family of polynomial discounting functions, a property that might be useful in applications. Indeed, the constant-proportional trade-off axiom is

[10]However, the discounting factor can be derived from 'certainty equivalents' as those mentioned in section 3.2.

[11]Perhaps this more general model fits better with the discussion in their section 6.2.2.

[12]This conditions means that for each health state a there exists a number λ such that t years in a is equivalent to λt years in perfect health a^* for all $t > 0$.

powerful and has strong implications. On the other hand, it is rather easily understood and is simple to test in stated preference experiments. The family of polynomial discounting factors may be sufficiently rich for some purposes, but this clearly depends on expectations about the nature and quality of available empirical data.

4.3. **Double discounting of QALYs.** It was demonstrated in the previous sections that under discounting the ratio between the TTO score and the time horizon is not the same as the health state index, and the TTO score must be adjusted for in a way that depends on the type and degree of discounting. If an external discounting factor is used, but the TTO score/time horizon ratio nevertheless is used as a health state index, the values are underestimated for TTO scores strictly between zero and the time horizon. The number of QALYs is accordingly also lower relative to the situation where the same discounting and the correct health index is used. This phenomenon is referred to as 'double discounting of QALYs'.

Krahn and Gafni (1993) argue that discounting QALYs may result in double discounting both in case of the SG and the TTO method because time preference is already incorporated in utility assessment (p. 413-414). Since the SG score is not affected by discounting in models of the form (3.3) with $v(s,a) = u(a)\delta(s)$ (which usually underlies empirical work), in case of the SG method double discounting seems to refer to other types of biases unrelated to above-mentioned type of bias. For instance respondents may not act in accordance with expected utility. In this case, however, 'double discounting' is perhaps a misleading label to this phenomenon because the SG estimates are biased because of reasons that have nothing to do with the problem of discounting twice.

The problem with double discounting is not the use of an external discounting factor in conjunction with TTO based health indices, but the failure of adjusting the TTO score/time horizon ratio before using it as health index. In effect, not doing so would tend to underestimate bad health states and overestimate good health states because the *relative* distance between $h(t,a)$ and $u(a)t$ decreases in $u(a)$, as illustrated in Figures 5-7 in Appendix B. It makes little sense, however, to attempt adjusting for double discounting by reducing or even eliminating discounting, which seems to be the idea in a recent paper by MacKeigan et al. (2003).[13]

[13]In this study, the authors aim to determine the magnitude of the double discounting effect by comparing an undiscounted holistic TTO score (obtained from the evaluation of a non-chronic health profile) to composite scores (obtained from separate evaluations of chronic health states) explicitly discounted by 0%, 3% or

4.4. **TTO, SG, or both?** There is a large and growing literature examining the relative advantages of TTO and SG methods, usually taking departure in data gathered from questionnaire studies, with the aim of investigating which method is 'best'. For selected references, see Dolan (2000).

In a recent paper, for example, Gyrd-Hansen (2002) reports a study where time preferences were elicited through TTO scores and also with certainty equivalence scores. It was predicted, and richly confirmed experimentally, that the discount rate elicited through TTO scores would be lower than those elicited through the certainty equivalence scores, since the latter incorporate risk as opposed to the TTO method. From this it was concluded that the TTO method is the most troublesome (compared to the certainty equivalence method). We agree that the fact that the SG method may incorporate risk aversion with respect to discounted quality-adjusted life years is likely to explain the divergence between discount factors estimated from these two methods, but propose an alternative conclusion from this observation: We need *both* TTO and SG estimates to identify risk aversion and sort it out from discounting. If we allow for, and expect, risk aversion the TTO scores are not less useful than SG scores.

Broome (1993) also criticizes the SG method for not providing the right answer (to the health state index) in case of risk aversion over QALYs. In the example he provides, health state preferences are of the form (3.10), with $r = 0.5$ and with no discounting of deterministic health profiles. Johannesson (1995), on the other hand, argued in the comment to Broome's paper that the health state index and the parameter r can be derived from a combination of SG and TTO scores, and outlined a procedure similar to that in Section 3.2. However, Johannesson's argument relies on the assumption of chronic health states, using the fact that in this case the model can be restated in the form (3.8).

With non-chronic health there is an important difference between risk aversion and discounting, and typically neither the risk parameter r nor the discounting parameter(s) are known from the outset and must be estimated from observations as with the health state index. Again, we need both TTO and SG estimates: TTO scores can be used for estimating the discounting factor and the health state index, and SG estimates can be used to identify the risk parameter.

5%. The 0% discounted composite scores were closest to the undiscounted holistic score, but, contrary to what seems to be the messsage by the authors, this has not much to do with double discounting. (It is, for example, the expected outcome when health states are relatively similar and discounting is not too large.)

When all health states are chronic, risk aversion and discounting may be exactly the same thing. One illustration was given in Section 3.5. However, to the best of our knowledge, it has not been fully recognized in the literature that this is only a special feature of models with chronic health states that does not carry over to models where health is allowed to vary over time.

5. Final remarks

In this paper, we have outlined an overview of QALY models and derived procedures for parameter estimation from the most commonly used type of data in QALY studies. The models deal with varying health states, but with one exception (Section 2.2), procedures involving only comparisons of certain health profiles with chronic health states can be devised. In relation to this, some considerations about model identification were also provided.

Of course, the choice of model and number of free parameters should reflect the availability and quality of data. In any case, however, time preference is an integral part of preference for health profiles and accordingly the estimation of discount factors is an integral part of health preference measurement. We hope that the present survey has contributed to a further elaboration of the implications of this point for the use of TTO and SG based procedures.

Finally, we mention two important limitations of our analysis. First, many experiments have indicated that respondents' judgements of probability are not linear in probability (see e.g. Kahneman and Tversky, 1979; Camerer, 1995; Gonzalez and Wu, 1999). In this paper we have restricted attention to deterministic situations or expected utility models. Wakker and Stiggelbout (1995) and more recent papers by Bleichrodt and Pinto (2000) and Bleichrodt, Pinto and Wakker (2001) have developed procedures that might be combined with methods outlined in Section 3, but an investigation of this is beyond the scope of the present paper (see also Miyamoto, 2000, and Bleichrodt, 2002).

Second, in many applications TTO and SG scores are obtained from a group of respondents and the scores are aggregated in some way to form the preferences of one 'representative' individual. We have not addressed methods for this, besides the trivial point that the TTO and SG scores we have assumed to be available could be interpreted as the mean or median of a sample of scores. One may also have TTO scores for more time spans than necessary and some systematic method for averaging or sorting out scores could be relevant. In order to deal with this, we will need to know the theoretical relationships

between scores and parameters as investigated in this paper, but for statistical analysis of 'noisy' empirical data, random utility extensions of the present framework would seem useful.

The micro-econometrics of the QALY appears to be largely unexplored, and we suggest that development of random utility QALY models and relevant statistical methods for model identification and parameter estimation in this specific context would be an interesting area for future research.

Appendix A. Plots of $h(t, a)$ against t

To provide some illustrative plots of $h(t, a)$ against t for different types of discounting, we use the same parameters as in the examples in Figure 1. Here, we also consider constant-proportional risk posture over exponentially discounted life years with $c = 0.95$ and $r = 0.8286$ such that the discount factor is equal to the other discount factors at $s = 10$.

The black curve is the case of exponential discounting ($c = 0.9$), gray curve is polynomial discounting ($z = -0.4576$), dashed curve is proportional discounting ($v = 0.1868$), dotted curve is hyperbolic discounting ($v = 4$, $w = 1.1349$) and dot-dashed curve is constant-proportional risk posture over exponentially discounted life years ($c = 0.95$, $r = 0.8286$).

We consider three cases: $u = 0.1$ (Figure 2), $u = 0.5$ (Figure 3) and $u = 0.9$ (Figure 4).

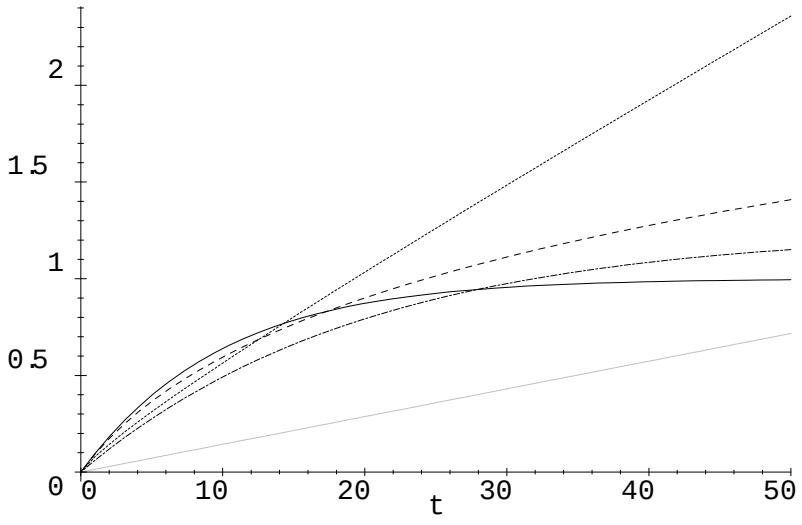

Figure 2. Plot of $h(t, a)$ against t, $u(a) = 0.1$.

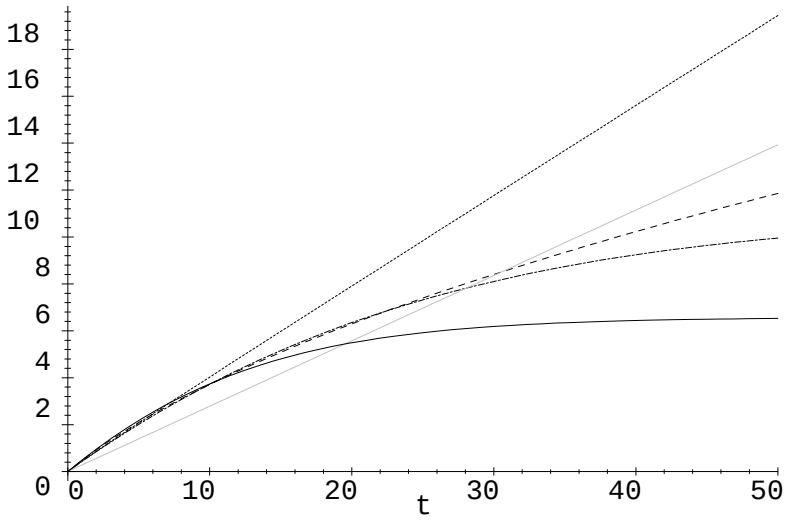

FIGURE 3. Plot of $h(t, a)$ against t, $u(a) = 0.5$.

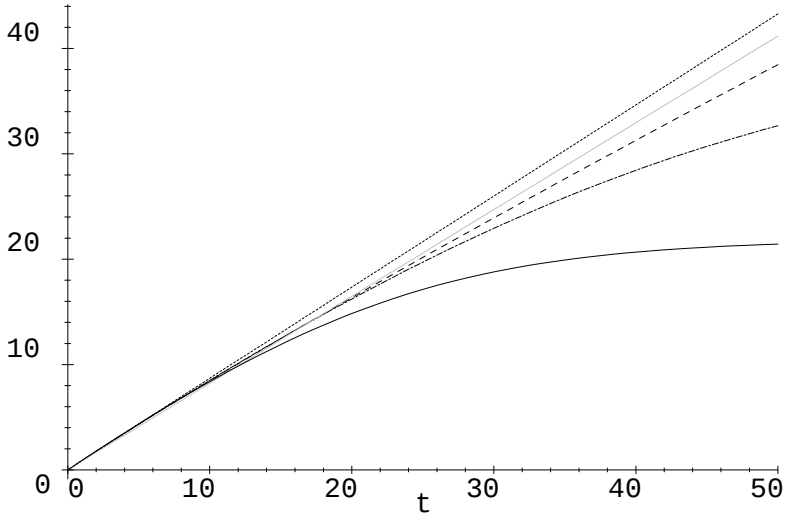

FIGURE 4. Plot of $h(t, a)$ against t, $u(a) = 0.9$.

APPENDIX B. PLOTS OF $h(t, a)$ AGAINST $g(a)$

This appendix contains plots of $h(t, a)$ against $g(a)$ $(= u(a))$. We use the same parameters as in Figure 1 and Appendix A. Again we have

exponential discounting (black curve), polynomial discounting (gray curve), proportional discounting (dashed curve), hyperbolic discounting (dotted curve) and constant-proportional risk-posture over exponentially discounted life years (dot-dashed curve). The thick black curve illustrates $h(t, a) = tu(a)$.

We consider $t = 1$ (Figure 5), $t = 10$ (Figure 6) and $t = 50$ (Figure 7).

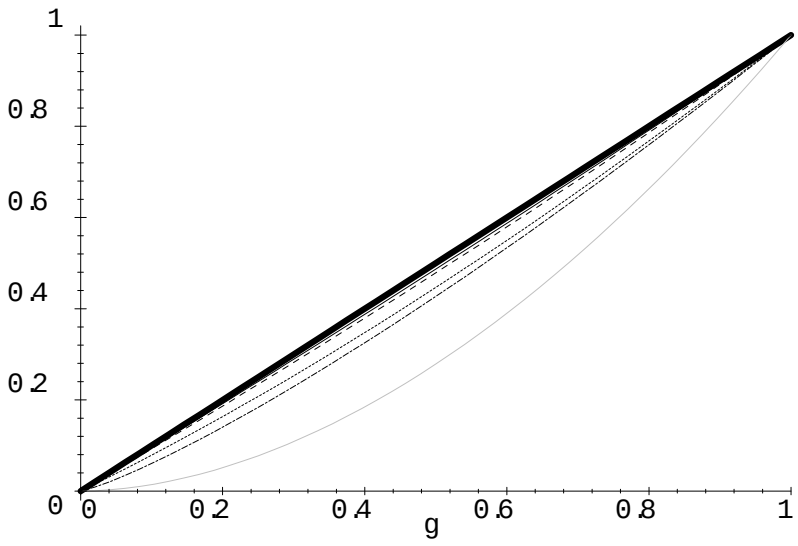

FIGURE 5. Plot of $h(1, a)$ against $g(a)$.

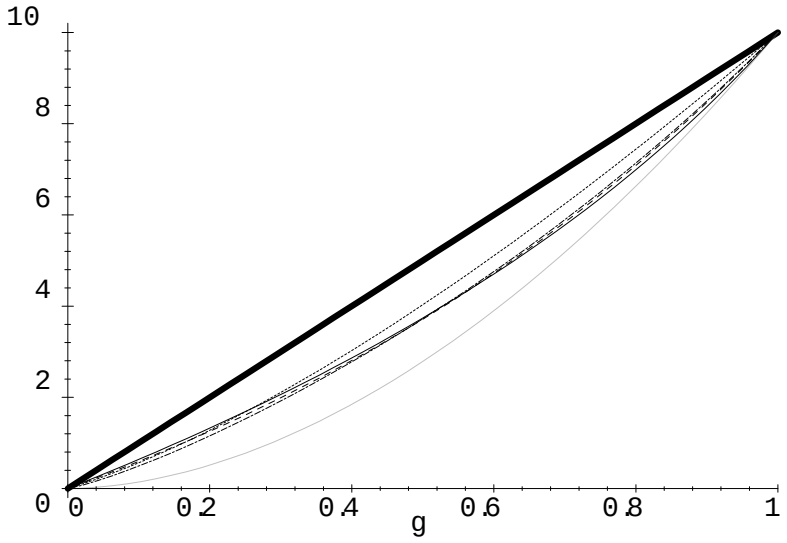

FIGURE 6. Plot of $h(10, a)$ against $g(a)$.

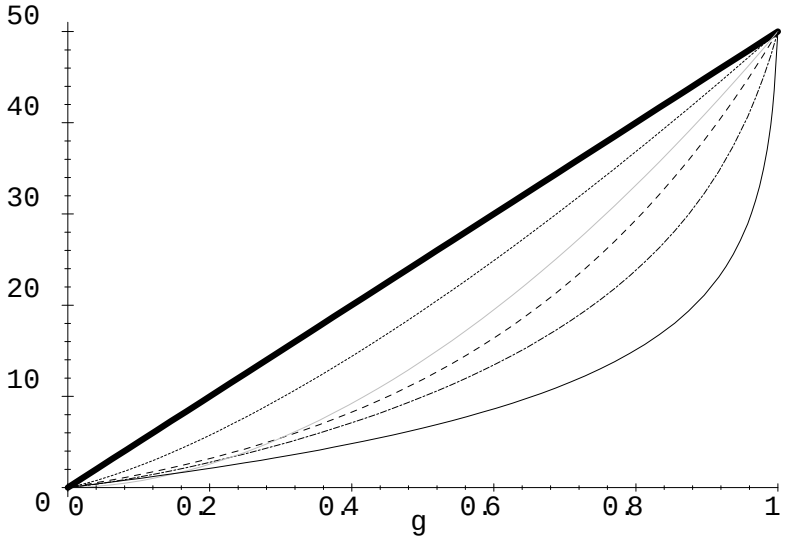

FIGURE 7. Plot of $h(50, a)$ against $g(a)$.

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