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RESEARCH MEMORANDUM

EXPECTED UTILITY OF LIFE TIME IN THE PRESENCE OF A CHRONIC NONCOMMUNICABLE DISEASE STATE

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Expected Utility of Life Time in the Presence of a Chronic Noncommunicable Disease State

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Abstract

Interventive action aimed at reducing the incidence of an irreversible chronic noncommunicable disease in a population has various effects. Hopefully, it increases total longevity in the population and it causes the disease to develop later in time in a smaller portion of the population. In this paper a statistical model is built by which these effects can be estimated. A three dimensional probability density function that underlies this model is changed by the interventive action. It is shown how a three dimensional utility function can be defined to appropriately judge this change.
Key words: chronic diseases, utility, longevity

1 Introduction

In this paper a model is presented for evaluating an intervention programme, aimed at reducing the incidence of a chronic (irreversible) noncommunicable disease in a population. Such an intervention programme influences two competing incidence rates, viz., the chronic disease incidence rate and the mortality rate from other causes. The effects of the programme are translated into changes in the population life time distribution, where life time may be decomposed into life time without the chronic disease and, if the disease develops, life time with the disease. Therefore, a stochastic illness-death model is described, in which changes of the stochastic structure (induced by intervention) can be evaluated by means of expected utility so that alternative intervention strategies can be ranked in terms of preference. The model is defined for an initially disease-free birth cohort of subjects, followed from a certain age (which needs not be the age of birth). This theoretical paper offers

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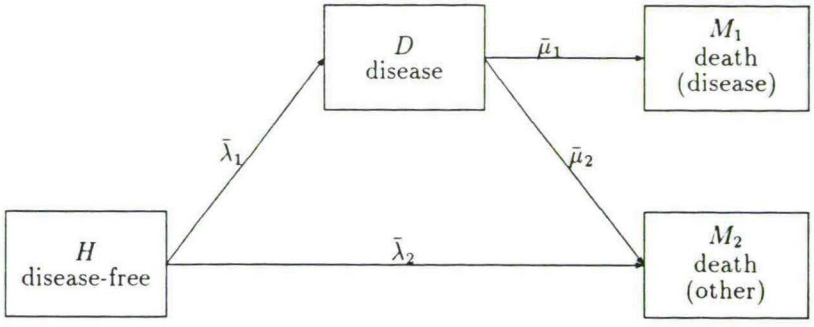

Figure 1: The illness-death model.

a more formal approach to the concept of "Quality Adjusted Life Year" (QALY) [9, 8] or "weighted life expectancy" [2].

In Section 2 the illness-death model, used to describe the various states, from a disease-free state towards the final state of death, is presented. Section 3 is concerned with life expectancy and a decomposition of life expectancy which is useful for evaluating an intervention programme. In Section 4 form and construction of a utility function are discussed. Also in Section 4 the actual computation of expected utility is presented. Section 5 treats the problem of how intervention is incorporated in the model. Section 6 concerns the practical evaluation.

2 The Illness-Death Model

At any time each subject of the cohort is in one of the mutually exclusive states of Figure 1. A subject is either dead or alive. In the latter case he is in one of the following two states:
state H: the disease-free ("healthy") state, which applies if the disease has as yet not developed;
state D: the state of chronic disease, which applies as soon as the disease starts to develop.
When the subject dies, he dies either from the disease or from other causes. In the latter case he was either in state H or in state D, previous to the time of his death. Hence, the following mortality states are considered:
state M_1: the state of mortality caused by the disease;
state M_2: the state of mortality caused by other diseases, which is reached from states H or D.

It remains to specify the intensities of the flows from one state to another. These intensities are also called hazard functions or hazard rates. These hazard functions are defined in such a way that they describe how the size of the original cohort in state H drops off in the course of time by absorption in the states M_1 (through the

state D) and M_2. It can easily be proved that these hazard functions are simply mean hazard functions relating to an arbitrary subject of the cohort being in a certain state at a certain time. Time, x, is supposed to coincide with the age of the cohort. The disease free state H can be left at time x as a result of two competing risk causes: either the start of the disease, with mean rate $\bar{\lambda}_1(x)$, or mortality from other diseases, with mean rate $\bar{\lambda}_2(x)$ in a disease-free cohort. Return to the disease free state H is impossible. The disease state D can also be left as a result of two competing risk causes: either mortality from the disease, with mean rate $\bar{\mu}_1(x|y)$, with $y \leq x$ the starting time of the disease, or mortality from other diseases, with mean rate $\bar{\mu}_2(x)$ in the cohort part having entered state D at time y and still being in state D at time $x \geq y$.

This completes the description of the illness-death process. Similar models may be found in [6, 7, 1]. In the next section expected life time for this model and a relevant decomposition of expected life time is presented.

3 Life Expectancy and Its Decomposition

A first measure for evaluating the effects of intervention is life expectancy. Life expectancy of an arbitrary subject in the cohort is equal to the weighted sum of two expectations: the expectation of life time in the subcohort that will develop the chronic disease and the expectation of life time in the subcohort that will not develop the disease, with weights π_1 and $\pi_2 = 1 - \pi_1$, where π_1 is the portion that will develop the disease and π_2 is the portion that will die from other diseases without having developed the chronic disease.

Life expectancy LE for an arbitrary subject of the original cohort thus equals:

$$\mathrm{LE} = (1 - \pi_1)E_H(X|2) + \pi_1 \{E_H(X|1) + E_D(Z)\}, \tag{1}$$

where $E_H(X|1)$ denotes expected life time in state H, given development of the disease, $E_H(X|2)$ denotes expected life time in state H, given no development of the disease, and $E_D(Z)$ denotes expected life time in the disease state D. In Appendix A it is shown how these expectations can be expressed in the mean hazard rates as defined in the previous section. The decomposition of LE in the right hand side of (1) is useful for explaining the effects of a population-based health intervention programme aimed at reducing the incidence $\bar{\lambda}_1(x)$ of the disease in the cohort: a change in $\bar{\lambda}_1$, induced by the intervention programme, results in changes in the disease probability π_1 and in the expectations $E_H(X|1)$, $E_H(X|2)$ and $E_D(Z)$.

By combining two components in (1) life expectancy LE simplifies to

$$\mathrm{LE} = E_H(X) + \pi_1 E_D(Z) \tag{2}$$

with $E_H(X)$ defined as

$$E_H(X) = (1 - \pi_1)E_H(X|2) + \pi_1 E_H(X|1).$$

In the simpler decomposition as in (2) it is reasonably supposed that it is not relevant to distinguish life in state H with respect to the way in which this state will be left.

4 Evaluating the Stochastic Process

4.1 Expected Utility

Life expectancy LE is one evaluation parameter for the illness-death process. It does not define uniquely all situations of an illness-death process between which a decision maker may be indifferent. For instance, a second process with a higher value of $E_H(X|2)$, that is exactly cancelled out by a lower value of $E_D(Z)$, produces the same value of LE, while it is reasonable to assume that this second process is preferred by the decision maker to the first process. As the decision maker is facing changes, induced by intervention, of the stochastic illness-death process, the "rational" decision maker would not only look at expected life time, but also take the more general approach of calculating expected utilities of life times of two different processes. The decision maker is supposed to be an agency which has to decide on the introduction of a population based intervention programme for the cohort. The stochastic process with which this agency is confronted is the stochastic process of an arbitrary subject in the original cohort, which process is specified in the mean hazard rates as dealt with above.

A particular illness-death process can be described by the following joint density function of the triplet (X, W, J), with X disease free life time, W disease duration and J an indicator for the disease, having the value 1 if the disease develops and 2 if not:

$$h(x,w,j) = \begin{cases} \pi_1 f_1(x) g(w|x) & \text{for } x \geq 0,\ w \geq 0,\ j = 1 \\ (1-\pi_1) f_2(x) & \text{for } x \geq 0,\ w = 0,\ j = 2 \\ 0 & \text{otherwise,} \end{cases} \tag{3}$$

as follows from Appendix A. The random variable W coincides with the random variable Z of Appendix A, except that for $w = 0$ there is an additional probability mass of $1 - \pi_1$. The parameters $\bar{\lambda}_1$, $\bar{\lambda}_2$, $\bar{\mu}_1$ and $\bar{\mu}_2$ determine $h(x, w, j)$.

The decision maker is assumed to evaluate changes in $h(x, w, j)$, induced for example by certain intervention measures, by means of his expected utility of the triplet (X, W, J). The utility function U is defined as $U_H(x)$ for a disease free life time of x time units and as $U_D^*(x, w)$ for a life time in which the disease starts to develop at time x and lasts for w time units. So formally U is defined as:

$$U(x,w,j) = (j-1)U_H(x) + (2-j)U_D^*(x,w).$$

Expected utility equals:

$$E\big(U(X,W,J)\big) = (1-\pi_1)E\big(U_H(X)|J=2\big) + \pi_1 E\big(U_D^*(X,W)\big).$$

For the sequel $U_D^*(x,w)$ is assumed to be as follows:

$$U_D^*(x,w) = U_H(x) + U_D(x,w),$$

i.e. the utility of a life time w with the disease, which started at time x, may be separately added to the utility of the disease free time of life. The utility function then becomes:

$$U(x,w,j) = U_H(x) + (2-j)U_D(x,w),$$

with expectation:

$$\begin{aligned} E(U(X,W,J)) &= (1-\pi_1)E(U_H(X)|J=2) + \\ &\quad + \pi_1\left\{E(U_H(X)|J=1) + E(U_D(X,W))\right\}, \end{aligned} \tag{4}$$

which is analogous to (1). Analogously to (2) the decomposition in (4) may be simplified to:

$$E(U(X,W,J)) = E(U_H(X)) + \pi_1 E(U_D(X,W)), \tag{5}$$

with $E(UH(X))$ equal to expected utility in state H, irrespective of the cause by which state H is left. Using (3) in (5) gives:

$$\begin{aligned} E(U) &= \int_0^\infty U_H(x)\{\pi_1 f_1(x) + (1-\pi_1)f_2(x)\}\,dx + \\ &\quad + \pi_1 \int_0^\infty\int_0^\infty U_D(x,z) f_1(x) g(z|x)\,dx\,dz, \end{aligned}$$

which for computational purposes may be written as:

$$\begin{aligned} E(U) &= -\int_0^\infty U_H(x)\,dS_H + \\ &\quad - \int_0^\infty \bar{\lambda}_1(x) S_H(x)\left\{\int_0^\infty U_D(x,z)\,dS_D(z|x)\right\}dx. \end{aligned} \tag{6}$$

Integrating (6) by parts results in:

$$\begin{aligned} E(U) &= \int_0^\infty u_H(x) S_H(x)\,dx + \\ &\quad + \int_0^\infty \bar{\lambda}_1(x) S_H(x)\left\{\int_0^\infty u_D(x,z) S_D(z|x)\,dz\right\}dx, \end{aligned} \tag{7}$$

where $u_H(x) = dU_H(x)/dx$ and $u_D(x,z) = \partial U_D(x,z)/\partial z$ are marginal utilities and where it has been assumed that $U_H(x)S_H(x) \to 0$ as $x \to \infty$ and $U_D(x,z)S_D(z|x) \to 0$ as $z \to \infty$. An alternative formulation is obtained after interchanging the order

of integration and changing of variables in the second term on the righthand side of (7):

$$E(U) = \int_0^\infty u_H(x) S_H(x)\, dx + \\ + \int_0^\infty \int_0^x \bar{\lambda}_1(y) S_H(y) u_D(y, x-y) S_D(x-y|y)\, dy\, dx, \qquad (8)$$

where $y \leq x$ is the time of developing the disease. The usefulness of (7) and (8) will become clear after more has been said about the specification of the utility function.

4.2 Specifying the Utility Function

In order to specify the utility function further, it is supposed that the decision maker is able to comparatively judge the health condition in both states H and D at different time points and disease durations, respectively. Therefore, the decision-making agency considers the average health condition of all subjects in a particular state at a particular age or sojourn time in that state. There should be political consensus about the way in which the comparative judgement is made by a decision-making agency. For example, in an economic context some kind of capacity index of the cohort at a certain time point may be defined as the mean productivity across the subjects in the cohort at that time. Throughout this paper the term health index will be used.

Two assumedly independent types of health indices are distinguished: a general health index in state H, i.e. when not suffering from the chronic disease considered, and a (disease) specific health index in state D, when suffering from the chronic disease. The decision maker is supposedly able to compare the general health index at one age with that at another age, and to compare the (disease) specific health index for any given age and disease duration with the general health index. The decision maker is also supposed to include time preference in his judgements, independently of the health index. A comparison of the health indices at two different ages, also means a comparison of two different points in time, as age coincides with time in a birth cohort. According to the economic principle of time preference, the decision maker is supposed to prefer an increase in the health index arising now (at the present age) to that same increase arising later in time (at a higher age). It is also supposed that this time preference can be quantitated by the decision maker when comparing one age (= one time point) with another age (= another time point), independently of the way in which the health index at these ages is quantitated.

Let $q_H(y)$ denote the general health index at age y. The function $q_H(y)$ assumedly is a non-negative number, that is equal to 1 at age y^* where the general health index is maximal. This function can be determined from the decision maker's judged indifference between one unit of life time at age y (without the disease) and $q_H(y)/q_H(y^*) = q_H(y)$ units of life time at age y^*, for all pairs (y, y^*), irrespective of time preference. Similarly, a time preference function $q_T(y)$ of time y can be

defined with a maximum of 1, which acts multiplicatively on $q_H(y)$. Irrespective of the general health index, present time is preferred to future time by the decision maker, which can be quantitated by means of discounting. The utility of a life time x without the disease is by reasonable assumption equal to the weighted sum (integral) of the successive health conditions (with the time preferences as weights), starting from time 0 (which generally is not the time of birth):

$$U_H(x) = \int_0^\infty q_H(y)q_T(y)\,dy.$$

With this construction of $U_H(x)$, it follows for marginal utility $u_H(x)$:

$$u_H(x) = q_H(x)q_T(x). \tag{9}$$

Further, let $q_D(y)$ denote the disease specific health index for an average subject already having the disease for a time period y. Without loss of generality, it is assumed that $q_D(y)$ has a maximum of 1. The time x of the start of the disease is introduced as follows. The general health index weighted by time preference at time $x+y$ is represented by the value $q_H(x+y)q_T(x+y)$, on which value the disease specific health index $q_D(y)$ is assumed to act multiplicatively in order to produce the weighted overall health index at time $x+y$ with value $q_H(x+y)q_T(x+y)q_D(y)$. The utility of a life time z with the disease that started at time x, is by assumption equal to the weighted sum (integral) of the successive health conditions, starting from time x:

$$U_D(x,z) = \int_0^z q_H(x+y)q_T(x+y)q_D(y)\,dy.$$

With this construction of $U_D(x,z)$ it follows for marginal utility $u_D(x,z)$:

$$u_D(x,z) = q_H(x+z)q_T(x+z)q_D(z). \tag{10}$$

Returning to $E(U)$ in (7), it is seen that, given the above construction of $U_H(x)$ and $U_D(x,z)$, $u_H(x)$ and $u_D(x,z)$ in (7) may be replaced by (9) and (10), respectively.

The special case $q_H(x) = q_T(x) = q_D(z) = 1$, meaning that the decision maker judges the marginal utilities as constant, so that $U_H(x) = x$ and $U_D(x,z) = z$, specifies the case of the previous section, i.e. life expectancy LE; see (5) and (2). Life expectancy LE may simply be deduced from (7) or (8) with $u_H = u_D = 1$. For example, LE follows from (8) as

$$\mathrm{LE} = \int_0^\infty \{S_H(x) + S_D(x)\}\,dx,$$

where $S_D(x)$ is the probability that a subject is in state D at time x. This probability can be considered to be the net result at time x of the flows in and out of state D before time x:

$$S_D(x) = \int_0^x \bar{\lambda}_1(y)S_H(y)S_D(x-y|y)\,dy,$$

of which the integral over x is the second term in the righthand side of (8).

4.3 Example

An example of a general health index $q_H(x)$ is:

$$q_H(x) = \exp(-r_H x),$$

specifying that the general health index of the cohort is at its maximum at age 0 and decreases at rate $r_H > 0$, due to increasing non-vitality when the cohort grows older. A time preference index $q_T(x)$ may be similarly defined:

$$q_T(x) = \exp(-r_T x),$$

specifying that the highest preference 1 holds for the present time, decreasing at a discount rate $r_T > 0$ for future time points. The utility $U_H(x)$ of a disease free life time from 0 to x then becomes:

$$U_H(x) = \int_0^x \exp\bigl(-(r_H + r_T)y\bigr)\, dy = \frac{1 - \exp\bigl(-(r_H + r_T)x\bigr)}{r_H + r_T},$$

with $U_H(x) \to 1/(r_H + r_T)$ as $x \to \infty$.

Two examples of a disease specific health index are:

$$q_D(z) = \exp(-r_D z) \tag{11}$$

$$q_D(z) = 1 - \{1 - q_D(0)\}\exp(-r_D z). \tag{12}$$

(11) specifies a disease that becomes more serious with the disease duration: it causes the disease specific health index to decay exponentially with the disease duration. It implies that, from the start of the disease at age x, the weighted overall health index at time $y \geq x$ is $q_T(y)q_H(y)\exp\bigl(-r_D(y - x)\bigr)$. (12) specifies a disease by which weighted overall health index immediately jumps downwards by a factor $q_D(0)$ at the disease onset, whereafter this decrement exponentially decays towards zero, meaning that the disease becomes less serious with its duration. It implies that, at the start of the disease at age x, the weighted overall health index decreases by an amount $q_T(x)q_H(x)\{1 - q_D(0)\}$, while at time $y > x$ this decrement has become $q_T(y)q_H(y)\{1 - q_D(0)\}\exp\bigl(-r_D(y - x)\bigr)$.

5 Intervention

An intervention strategy is by definition only effective for the cohort in state H. Such a strategy influences the stochastic structure (3) of the whole process through the mean rates $\bar{\lambda}_1(x)$ and $\bar{\lambda}_2(x)$ in the cohort. The individual rates λ_1 and λ_2 depend on a vector of covariables which have a certain multivariate distribution in the cohort in state H. In the course of time this cohort is subjected to two simultaneously acting stochastic processes: disease-free survivor selection (described by the rates λ_1 and λ_2) and ageing. The ageing process is defined as a stochastic model that describes

how the values of the covariables evolve in time in individuals as long as they survive disease-free in state H. The parameters of this ageing process are supposed to be influenced by an intervention programme. An analytically tractable model with two simultaneous equations has been built by Woodbury et al. [10], which is consistent with the assumed multivariate Gaussian distribution of the covariables in the cohort in state H. In this model the rates λ_1 and λ_2 are positive-definite quadratic forms in the covariables; the ageing process is a stochastic linear differential equation in the covariables (including random walk). This model makes the mean vector and the (co)variance matrix of the vector of covariables analytically expressible in the two sets of parameters, viz. those of the disease-free survivor selection process and those of the ageing process. The latter set of parameters is supposed to be influenced by intervention, of which the effects on the time paths of the mean vector and (co)variance matrix of the covariables can be directly translated into effects on the mean rates $\bar{\lambda}_1(x)$ and $\bar{\lambda}_2(x)$.

The original model developed by Woodbury et al. [10] is a continuous time model, which is not directly empirically applicable, as epidemiological observations are usually made at discrete time points only.

6 Applicability

For practical applications it is assumed that the continuous stochastic process can be discretely approximated by assuming the mean rates to be constant in time intervals of predetermined width. It is supposed that the mean incidence of the disease $\bar{\lambda}_1(x)$ and the mortality rates $\bar{\lambda}_2(x)$ and $\bar{\mu}_2(x)$ of other diseases are so slow in time as to justify these rates being constant in unit (= one year) intervals $[x, x+1)$, $x = 0, 1, 2, \ldots$. On the other hand, the disease mortality rate $\bar{\mu}_1(x|y)$ may vary so fastly with time x after the disease onset at time $y \leq x$, that constancy in time may only be assumed in much smaller time intervals of width $1/T$, with T an integer greater than one. For example, $T = 12$ for months. So each unit time interval $[x, x+1)$ is subdivided in T subintervals $\left[x + \tau/T, x + (\tau+1)/T\right)$ for $\tau = 0, 1, 2, \ldots, T-1$. In Appendix B the discrete version of formula (8) for expected utility is presented, using these two time scales, as well as the discrete versions of the survivor functions (13) and (14) of Appendix A that are part of the expected utility formula.

Because the covariables are in practice only measured at discrete (equidistant) time points, Woodbury et al. [11] developed and applied a discrete time version of their model, in which it is assumed that the total dynamics of two simultaneously acting stochastic processes in continuous time are mimicked by two separate processes acting consecutively in relatively small (say, one year) discrete time intervals. In this discrete approach, of which the technical details can be found in Appendix C, the covariables $\boldsymbol{c}_x$ are supposed to be only measured at the start of these time intervals x and to be constant during such an interval. Given the values of the

covariables at the start of the one-year interval, the disease-free survivor selection is applied during that interval through the rates λ_1 and λ_2; see equations (17) and (18) of Appendix C. Just before leaving the interval, the ageing process is applied in order to update the mean vector $\boldsymbol{\gamma}_x$ and (co)variance matrix $\boldsymbol{V}_x$ of the covariables towards the next time interval $x+1$ for the portion $s_H(x)$ of the cohort that remains to enter the next time interval alive and disease-free; see equations (19) to (22) of Appendix C. This updating of the covariables at the end of each time interval is done by means of a first order autoregressive structure (19) as the discrete alternative to a continuous linear differential equation. Intervention is supposed to influence the parameters of this first order autoregressive structure and hence it influences, through the mean vector $\boldsymbol{\gamma}_x$ and (co)variance matrix $\boldsymbol{V}_x$ of the covariables in (20) of Appendix C, the survivor function (16) of Appendix B, which leads to changes in expected utility (15) of Appendix B. Within the model described in Appendix C intervention strategies are defined as linear transformations of the covariables $\boldsymbol{c}_x$. An application for a simpler model (without an intermediate chronic disease state D) is given in [5].

7 Discussion

In this paper a stochastic illness-death process is defined for a chronic disease; it is shown how changes in this process are evaluated by means of expected utility. It is only after the definition of the stochastic process that it makes sense to define a utility function, because the random outcome variables of the stochastic process are the arguments of the utility function. Hence, defining the stochastic process is of primary importance. The way in which this process is defined in this paper is, as any model, of course, a simplifying abstraction. Yet, if one realizes that the stochastic process holds for an arbitrary subject of the birth cohort, meaning, for example, that the "healthy" state is a state of average health of an arbitrary subject in the cohort not suffering from the chronic disease considered, the approach is valid and may be useful for planning health intervention policies in a society.

After having defined the stochastic process, its random outcome variables are identified and a utility function can be defined. Within the model settings of Sections 5 and 6 only linear transformations of the explanatory variables can be considered typical intervention strategies. As practical effectuation of intervention strategies one could think of health education or of government's support of screening and treatment facilities. Of course, it is always the individual's choice to participate in an intervention programme. The term "participation" is broadly defined here: besides true participation in a screening programme, it may also be understood as picking up a health education message. All kinds of detailed complications on the micro level (consumers behaviour) may play their part here, eventually leading to changes in the coefficients of the evolution and diffusion process (called ageing process) of the covariables as specified in (19) of Appendix C. These are the (antici-

pated) changes of which the effect can be evaluated in terms of expected utility; also sensitivity analyses of various scenarios can be done by a decision-making agency using the theory described in this paper. This may lead to quantitatively supported conclusions about the type of population based intervention programmes that are most beneficial to society.

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A Appendix

Let $S_H(x)$ denote the so called survivor function for an arbitrary subject of the original cohort in the disease free state H, i.e. $S_H(x)$ is the mean probability of surviving in state H at time x in the original cohort. $S_H(x)$ is expressed in the mean rates $\bar{\lambda}_1(x)$ and $\bar{\lambda}_2(x)$ as follows:

$$S_H(x) = \exp\left(-\int_0^x \{\bar{\lambda}_1(t) + \bar{\lambda}_2(t)\}\, dt\right). \tag{13}$$

The density function of time x, given "failure" from cause j, $(j = 1, 2)$, is:

$$f_j(x) = \frac{\bar{\lambda}_j(x) S_H(x)}{\pi_j}, \qquad (j = 1, 2),$$

see e.g. [3, 4]. Evidently, π_j equals:

$$\pi_j = \int_0^\infty \bar{\lambda}_j(x) S_H(x)\, dx, \qquad (j = 1, 2).$$

Expected life time $E_H(X|2)$ in state H, given no development of the disease, is equal to:

$$E_H(X|2) = \int_0^\infty x f_2(x)\, dx.$$

Expected life time $E_H(X|1)$ in state H, given development of the disease, equals:

$$E_H(X|1) = \int_0^\infty x f_1(x)\, dx.$$

Expected life time $E_D(Z)$ in state D equals:

$$E_D(Z) = \int_0^\infty \int_0^\infty z f_1(x) g(z|x)\, dx\, dz,$$

where $g(z|x)$ is the density function of z, life time with the disease, given that x is the starting time of the disease. The density function $g(z|x)$ is derived from the survivor function $S_D(z|x)$:

$$S_D(z|x) = \exp\left(-\int_0^z \{\bar{\mu}_1(x + y|x) + \bar{\mu}_2(x + y)\}\right) dy. \tag{14}$$

From this one derives $g(z|x)$ as $-dSD/dz$:

$$g(z|x) = \{\bar{\mu}_1(x + z|x) + \bar{\mu}_2(x + z)\} S_D(z|x).$$

B Appendix

Assuming that the mortality process $\bar{\mu}_1$ is properly approximated in smaller time intervals $[x+\tau/T, x+(\tau+1)/T)$, with integers $x \geq 0$, $T \geq 1$ and $0 \leq \tau \leq T-1$, the discrete approximation to expected utility in (8) becomes

$$
\begin{aligned}
E(U) = & \qquad (15)\\
& \frac{1}{2}u_H(0) + \sum_{x\geq 1} u_H(x)S_H(x) + \frac{\bar{\lambda}_1(0)}{2T}u_D(0,0) + \\
& - \frac{\bar{\lambda}_1(0)}{2T}\sum_{t=1}^{T-1}\left\{S\left(\frac{t}{T},0\right) + S\left(\frac{t}{T},\frac{t}{T}\right)\right\} + \\
& - \frac{1}{2T}\sum_{x\geq 1}\sum_{t=0}^{T-1}\left\{\bar{\lambda}_1(0)S\left(x+\frac{t}{T},0\right) + \bar{\lambda}_1(x)S\left(x+\frac{t}{T},x+\frac{t}{T}\right)\right\} + \\
& + \frac{1}{T}\sum_{x\geq 1}\sum_{t=0}^{T-1}\sum_{\xi=0}^{x-1}\bar{\lambda}_1(\xi)\sum_{\tau=0}^{T-1}S\left(x+\frac{t}{T},\xi+\frac{\tau}{T}\right) + \\
& + \frac{1}{T}\sum_{x\geq 1}\sum_{t=0}^{T-1}\bar{\lambda}_1(x)\sum_{\tau=0}^{t}S\left(x+\frac{t}{T},x+\frac{\tau}{T}\right),
\end{aligned}
$$

with

$$
\begin{aligned}
& S\left(x+\frac{t}{T},\xi+\frac{\tau}{T}\right) = \\
& S_H\left(\xi+\frac{\tau}{T}\right)u_D\left(\xi+\frac{\tau}{T},x-\xi+\frac{t-\tau}{T}\right)S_D\left(x-\xi+\frac{t-\tau}{T}\,\middle|\,\xi+\frac{\tau}{T}\right).
\end{aligned}
$$

For the clarification of (15) it is mentioned that time is represented by two variables: the (larger) unit intervals are counted by x or ξ and the (smaller) subintervals are counted by t or τ. For the outer integrals in (8) x and t are used and for the inner integral ξ and τ. Function values at the lower and upper limit of a time interval are only counted half in approximating the area under the curve in this time interval; the relevant corrections are made in (15).

The discrete version of the survivor function S_H in (13) of Appendix A is defined as follows:

$$
S_H\left(\xi+\frac{\tau}{T}\right) = \exp\left(-\sum_{y=0}^{\xi-1}\left\{\bar{\lambda}_1(y)+\bar{\lambda}_2(y)\right\} - \frac{\tau}{T}\left\{\bar{\lambda}_1(\xi)+\bar{\lambda}_2(\xi)\right\}\right). \qquad (16)
$$

For $\xi = 0$, the summation from $y = 0$ to $y = \xi$ is suppressed. For $\xi \leq x-2$, the discrete version of the survivor function S_D in (14) of Appendix A is defined as

follows:

$$
\begin{aligned}
S_D\left(x-\xi+\frac{t-\tau}{T}\Big|\xi+\frac{\tau}{T}\right) = \\
\exp\left(-\frac{T-\tau}{T}\bar{\mu}_2(\xi)-\sum_{y=\xi+1}^{x-1}\bar{\mu}_2(y)-\frac{t}{T}\bar{\mu}_2(x)\right)\times \\
\times\exp\left(-\frac{1}{T}\sum_{v=\tau}^{t-1}\bar{\mu}_1\left(x-\xi+\frac{t-\tau}{T}\Big|\xi+\frac{v}{T}\right)\right)\times \\
\times\exp\left(-\frac{1}{T}\sum_{y=\xi+1}^{x-1}\sum_{v=0}^{T-1}\bar{\mu}_1\left(x-\xi+\frac{t-\tau}{T}\Big|y+\frac{v}{T}\right)\right)\times \\
\times\exp\left(-\frac{1}{T}\sum_{v=0}^{T-1}\bar{\mu}_1\left(x-\xi+\frac{t-\tau}{T}\Big|x+\frac{v}{T}\right)\right).
\end{aligned}
$$

For $\xi = x-1$, the summations from $y=\xi+1$ to $y=x-1$ are suppressed. For $x=\xi$ and $t>\tau$, S_D reduces to

$$
S_D\left(\frac{t-\tau}{T}\Big|\xi+\frac{\tau}{T}\right)=\exp\left(-\frac{t-\tau}{T}\bar{\mu}_2(\xi)-\frac{1}{T}\sum_{v=\tau}^{t-1}\bar{\mu}_1\left(\frac{t-\tau}{T}\Big|\xi+\frac{v}{T}\right)\right).
$$

If, moreover, t equals τ, then S_D equals 1.

C Appendix

At the start of the one-year time interval $[x, x+1)$ a vector of covariables $\boldsymbol{c}_x$ is normally (Gaussian) distributed in the disease-free cohort in state H with mean vector $\boldsymbol{\gamma}_x$ and (co)variance matrix $\boldsymbol{V}_x$. During year x the covariables $\boldsymbol{c}_x$ are assumed to be constant, so that the subjects of the cohort are subjected to constant rates $\lambda_1(\boldsymbol{c}_x)$ and $\lambda_2(\boldsymbol{c}_x)$, which are specified as positive quadratic functions of the covariables $\boldsymbol{c}_x$:

$$
\lambda_j(\boldsymbol{c}_x)=\beta_{0jx}+\boldsymbol{\beta}_{jx}^T\boldsymbol{c}_x+\frac{1}{2}\boldsymbol{c}_x^T\boldsymbol{B}_{jx}\boldsymbol{c}_x,\qquad (j=1,2), \tag{17}
$$

with β_{0jx} a constant scalar, $\boldsymbol{\beta}_{jx}$ a vector of coefficients for the linear effects of $\boldsymbol{c}_x$ on λ_j and $\boldsymbol{B}_{jx}$ a symmetric matrix of coefficients for the quadratic (and cross-product) effects of $\boldsymbol{c}_x$ on λ_j. Just before the end of year x, after the disease-free survival selection during year x, the mean and (co)variance matrix of the covariables have become:

$$
\begin{aligned}
\boldsymbol{\gamma}_x^* &= \boldsymbol{D}_x(\boldsymbol{\gamma}_x-\boldsymbol{V}_x\boldsymbol{\beta}_x) \\
\boldsymbol{V}_x^* &= \boldsymbol{D}_x\boldsymbol{V}_x
\end{aligned} \tag{18}
$$

with the matrix $\boldsymbol{D}_x$ given by

$$\boldsymbol{D}_x = (\boldsymbol{I} + \boldsymbol{V}_x \boldsymbol{B}_x)^{-1},$$

with $\boldsymbol{I}$ the identity matrix, and $\boldsymbol{\beta}_x = \sum_j \boldsymbol{\beta}_{jx}$ and $\boldsymbol{B}_x = \sum_j \boldsymbol{B}_{jx}$. In the portion $s_H(x)$ of the cohort entering year x that remains alive and disease-free to enter year $x+1$, the covariables $\boldsymbol{c}_x$ are updated towards $\boldsymbol{c}_{x+1}$ just before entering year $x+1$ as follows:

$$\boldsymbol{c}_{x+1} = \boldsymbol{\alpha}_{ox} + \boldsymbol{A}_x \boldsymbol{c}_x + \boldsymbol{\varepsilon}_x, \tag{19}$$

with $\boldsymbol{\alpha}_{ox}$ a vector of shift parameters, $\boldsymbol{A}_x$ a matrix of regression parameters and $\boldsymbol{\varepsilon}_x$ a vector of residuals, normally distributed with mean vector zero and (co)variance matrix $\boldsymbol{\Sigma}_x$, called the diffusion matrix. The portion $s_H(x)$ can be calculated as

$$\begin{aligned} &s_H(x) = \\ &|\boldsymbol{D}_x|^{1/2} \exp\left(-\beta_{0x} - \boldsymbol{\beta}_x^T \boldsymbol{D}_x \boldsymbol{\gamma}_x + \frac{1}{2}\boldsymbol{\beta}_x^T \boldsymbol{D}_x \boldsymbol{V}_x \boldsymbol{\beta}_x - \frac{1}{2}\boldsymbol{\gamma}_x^T \boldsymbol{B}_x \boldsymbol{D}_x \boldsymbol{\gamma}_x\right), \end{aligned} \tag{20}$$

implying for (16) of Appendix B:

$$S_H\left(\xi + \frac{\tau}{T}\right) = s_H(\xi)^{\tau/T} \prod_{y=0}^{\xi-1} s_H(y).$$

After updating $\boldsymbol{\gamma}_x^*$ and $\boldsymbol{V}_x^*$ of (18) according to (19) as follows

$$\begin{aligned} \boldsymbol{\gamma}_{x+1} &= \boldsymbol{\alpha}_{ox} + \boldsymbol{A}_x \boldsymbol{\gamma}_x^* \\ \boldsymbol{V}_{x+1} &= \boldsymbol{\Sigma}_x + \boldsymbol{A}_x \boldsymbol{V}_x^* \boldsymbol{A}_x^T, \end{aligned} \tag{21}$$

the circle is round for the next year $x+1$. An approximation for the proportion $s_H(x)$ is obtained by using

$$s_H(x) = \exp\left(-\bar{\lambda}_1(x) - \bar{\lambda}_2(x)\right)$$

and by substituting herein $\bar{\lambda}_1(x)$ and $\bar{\lambda}_2(x)$ by

$$\bar{\lambda}_j(x) = \beta_{0jx} + \boldsymbol{\beta}_{jx}^T \boldsymbol{\gamma}_x + \frac{1}{2}\boldsymbol{\gamma}_x^T \boldsymbol{B}_{jx} \boldsymbol{\gamma}_x + \frac{1}{2}\mathrm{tr}\,(\boldsymbol{B}_{jx} \boldsymbol{V}_x), \qquad (j = 1, 2).$$

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