

*Analytical sensitivity analysis of the multistate life table. A new tool in
public health research*

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Abstract

The sensitivity of life expectancy to changes in the mortality rate and the related concept of entropy were introduced in demography by Demetrius and Keyfitz in the 1970s. To analyze the sensitivity of healthy or diseased life expectancy, one can use a multistate life table and assess the effect of changes in underlying rates. The object of this paper is to demonstrate analytical sensitivity analyses of a multistate life table applied to an illness-death model to quantify the effect of a health change in terms of compression or expansion of disability.

Most studies express the effect of a health change in terms of hazard ratios or relative risks compared to a standard without change. Policy makers are more interested in the effects of health changes on future disability, and how disability can be controlled. The object of this paper is to demonstrate analytical sensitivity analyses of a multistate life table applied to an illness-death model to quantify health changes in terms of compression or expansion of disability. We will demonstrate the strength of analytical sensitivity analysis by an application of a multistate illness-death model to the U.S. Health and Retirement Study, showing its usefulness for prevention and intervention decisions.

Introduction

The last decades, health improvements have caused mortality rates to decrease impressively at higher ages causing life expectancy to increase rapidly. Postponement of death also extends life with undesirable health conditions like disability, illness or cognitive impairment. It is often debated whether life expectancy with morbidity is more extended by mortality changes than life expectancy in good health. Sensitivity analysis is a powerful analytic tool to quantify the effect of an arbitrary change in the underlying parameters of a model to a particular output variable of interest. In the compression or expansion of morbidity debate (Manton, Gu and Lowrimore 2008; 2000; Peeters et al. 2003a), sensitivity analysis can examine how a change in its underlying age-specific rates alters the time span with morbidity. In general, analytical sensitivity analysis translates changes in rates into gains or losses in state-specific life years. Changes in rates may be expressed in absolute or relative terms. Similarly, the impact of these changes on life table indicators may be measured in absolute or in relative terms.

A large literature exists on the impact of changing mortality rates on life expectancy (Keyfitz and Caswell 2005; Pollard 1988; Vaupel and Canudas-Romo 2003). For the sensitivity of mortality rates to total life expectancy, often the term 'entropy' is used (Demetrius 1974, 1978; Keyfitz and Caswell 2005; Vaupel and Canudas-Romo 2003). The results of sensitivity analyses are often expressed as sensitivities (the sensitivity of y to x is the derivative dy/dx) and elasticities (the elasticity of y to x is $(x/y)dy/dx$) (Caswell 2008). In the recent debates about healthy ageing, expansion or compression of morbidity and future long term care needs, sensitivity analysis gains importance. The impact of changes on incidence rates, recovery rates and health-status specific mortality rates on life expectancy with and without illness or disability is conveniently studied with an illness-death model. Sensitivity analysis can provide insights that are of great importance for prevention and intervention policies. Which interventions contribute most to healthy or disabled life expectancy and at what ages an intervention would be most effective? Does a health change expand or compress the lifespan with disability?

Illness-death models are multistate models. The models are generally written as matrix equations and sensitivity analysis requires matrix differentiation techniques. Neudecker

(1969) defines matrix differentiation as the procedure of finding partial derivatives of the elements of a matrix function with respect to elements of the argument matrix. Matrix differentiation techniques are well established (Dwyer, 1969; Magnus and Neudecker, 1999). Although the technique was introduced into multistate demography decades ago (Ekamper and Keilman, 1993; Willekens, 1977), it is seldom used. New widely available software facilitates applications of sensitivity analysis in multistate models. The applications in this paper will demonstrate the absolute and relative gains and losses in life expectancy due to relative changes (of 1%) in the rates. In the multistate context, we will refer to state-specific elasticity as the relation between a relative gain or loss in state-specific life expectancy as a result of a 1% change in an underlying rate. State-specific elasticities are comprehensive measures of sensitivity and show the efficiency of compression or expansion of disability. Furthermore, we distinguish between changes in incidence, recovery and death rates at one particular age resulting from changes in health conditions, and changes over a range of ages, including a lifetime change. An illustration of decelerated ageing demonstrates the impact of a proportional decrease in incidence and death rates for all ages.

Background

Sensitivity analysis, also called perturbation or impact analysis, deals with the question how a small change in a parameter alters particular outcome variables that interest us. There are basically two ways to conduct sensitivity analysis. The first is the numerical or simulation method, also called arithmetic or empirical approach, which is simply computing the function of interest under the changed and the original transition rates (Ekamper and Keilman 1993; Keyfitz 1971; Laaksonen 1980). The numerical approach is commonly used to assess sensitivity of a model (Crimmins, Hayward and Saito 1994; Nusselder et al. 2000; Nusselder et al. 1996; van Baal et al. 2006). This method however, does not provide general insights in the mechanism of the model. We will use this numerical approach to verify the results of the second approach, the analytical method, which we will use here. The second way to conduct sensitivity analysis is to use mathematical expression that links changes in life expectancy to changes in underlying rates. The theoretical and mathematical aspects of analytical sensitivity analysis in multistate demography were developed before by Willekens (1977), Arthur (1984), Ekamper and Keilman (1993) and Hill (1997). Hill has derived formulas for the entropies of diseased and non-diseased life expectancy in relation to

changes in incidence and mortality rates. However, in this model the disease is irreversible and recovery is not possible. When including the possibility of reverse transitions like recovery, a system of equations needs to be solved by matrix algebra. Analyzing the sensitivity of a multistate illness-death model expressed in matrices requires matrix differentiation. In this paper we will show the multistate life table, derive the sensitivity functions and demonstrate an application to an illness-death model using the U.S. Health and Retirement Study.

Methods

Data and measures

We use data from the Health and Retirement Study (HRS) data file containing the HRS and the Asset and Health Dynamics Among the Oldest Old (AHEAD) which began in 1992 and 1993, respectively, and were merged in 1998. More information is available at <http://hrsonline.isr.umich.edu/>. The HRS and AHEAD surveys include a nationally representative sample of initially non-institutionalized persons born in 1931–1941 (HRS, aged 51–61 in 1992) and in 1923 or earlier (AHEAD, aged 70 and older in 1993). Sampled persons were re-interviewed biannually. We used data from 7 waves from 1992 to 2004. Response was on average 86% (HRS) and 90% (AHEAD). We selected white non-Hispanic men and women. Data on vital status and month and year of death are obtained through the mortality register (the National Death Index) and exit interviews.

Outcomes are all-cause mortality and disability. Disability is defined by the Katz basic activities of daily living (ADL): Walking, Bathing, Dressing, Toileting and Feeding (Katz et al. 1963). We classify as ADL disabled the person who answers “with difficulty” on at least one of the ADL.

Transition rates

The state space and possible transitions between the states are demonstrated in figure 1.

Figure 1 about here

Transition rates are estimated using occurrence-exposure rates per single age. Transitions from one health state to another are only observed at interview, hence, we assume that only

one transition occurs in the two-year interval. For ADL disability we assume transitions halfway between two waves. Exponential smoothing using Poisson regression is applied to reduce the variability of the rates (Mamun 2003). The assumption is that the hazards of death and disability increase exponentially with age, which fitted the transition rates to death and disability very well. To translate the rates in annual probabilities we assume the rates to be constant in the 1- year intervals, hence we assume a piecewise constant exponential model. We make the matrix $\mathbf{M}(x)$ an irreducible matrix by eliminating the last row and column that contain mortality rates. The diagonal includes transition rates to death:

1

$$\mathbf{M}(x) = \begin{bmatrix} \mu_{12}(x) + \mu_{13}(x) & -\mu_{21}(x) \\ -\mu_{12}(x) & \mu_{21}(x) + \mu_{23}(x) \end{bmatrix}$$

where μ_{ij} is the transition rate from state i to state j .

Status-based life expectancy

All multistate life table functions are derived from the transition rates matrix $\mathbf{M}(x)$. As we assume the transition intensities to remain constant in the one year age interval, the probability matrix $\mathbf{P}(x)$ can be calculated by the exponential model:

2

$$\mathbf{P}(x) = \exp(-\mathbf{M}(x))$$

The survivorship matrix $\mathbf{I}(x)$ consists of elements $l_{ij}(x)$ denoting the number of persons in state i at age x who are in state j at $x+1$:

3

$$\mathbf{I}(x+1) = \mathbf{P}(x)\mathbf{I}(x)$$

We define $\mathbf{I}(0)$, the radix, as a diagonal matrix with the arbitrary constant 100000.

The total number of personyears lived by individuals in age group x to $x+1$ is given by the matrix:

4

$$\mathbf{L}(x) = \mathbf{M}^{-1}(x)[\mathbf{I} - \exp(-\mathbf{M}(x))]$$

The most important and most frequently used life table function is that of life expectancy:

5

$$\mathbf{e}(x) = \left[\sum_{y=x}^z \mathbf{L}(y) \right] \mathbf{l}^{-1}(x) \quad \text{where } z \text{ is the first year of the highest open-ended age group.}$$

The status-based life expectancy $e_{ij}(x)$ expresses the expected number of years lived in health state j beyond age x by an individual who is in health state i at age x . Many scholars use population-based rather than status-based multistate life tables, indicating the life expectancy and health status of the entire life table population. To obtain population-based life tables, often the observed prevalence at starting age is used to distribute the radix population in each of the health states (Crimmins et al. 1994).

Sensitivity functions

In the analytic approach of sensitivity analysis, general formulas are derived to express the impact of a particular change in terms of the output variable and these formulas are called sensitivity functions.

Willekens has derived the sensitivity functions for all life table functions under the linear assumption (Willekens 1977). In this section we will differentiate the life table functions using the exponential model. The matrix differentiation techniques are elaborated in the appendix of Willekens, 1977 and in the book of Magnus and Neudecker (Magnus and Neudecker 1999).

A small change in the transition matrix $\mathbf{M}(x)$ is denoted by $d\mathbf{M}(x)$, indicating for which element of $\mathbf{M}(x)$ one wants to calculate the sensitivity to a small change δ . The change δ can be expressed in absolute or in relative terms. Matrix $d\mathbf{M}(x)$ consists of zeros except for the element of interest and the diagonal element of that column. (Ekamper and Keilman 1993) For example, an absolute change δ in rate $\mu_{12}(x)$ results in the following $d\mathbf{M}(x)$ matrix:

$$d\mathbf{M}(x) = \begin{bmatrix} -\delta & 0 \\ \delta & 0 \end{bmatrix}$$

6

The transition rate matrix, which is $\mathbf{M}(x)$ before the change, is $\mathbf{M}(x) + d\mathbf{M}(x)$ after the change. When δ is a relative change, $d\mathbf{M}(x)$ is

$$d\mathbf{M}(x) = \begin{bmatrix} -\delta & 0 \\ \delta & 0 \end{bmatrix} * \mu_{12}(x)$$

7

$d\mathbf{M}(x)$ can also express simultaneous changes in several rates.

First consider the sensitivity of transition probabilities to changes in transition rates. The sensitivity of the probability matrix $\mathbf{P}(x)$ only depends on $\mathbf{M}(x)$, as can be seen in equation 2. The derivation of the sensitivity function requires the differentiation of a matrix exponent. If \mathbf{M} is a matrix, then the differentiation of the exponent of \mathbf{M} using Taylor expansion yields (Magnus and Neudecker 1999):

8

$$d \exp(\mathbf{M}) = \sum_{k=0}^{\infty} \frac{1}{(k+1)!} \sum_{j=0}^k \mathbf{M}^j (d\mathbf{M}) \mathbf{M}^{k-j}$$

Applying this function to the definition in equation 2 yields:

$$d\mathbf{P}(x) = \sum_{k=0}^{\omega} \frac{1}{(k+1)!} \sum_{j=0}^k (-\mathbf{M}(x))^j (d\mathbf{M}(x)) (-\mathbf{M}(x))^{k-j}$$

Although the Taylor expansion is defined till infinity, convergence is reached after 3 terms.

Equation 3 shows that the survivorship function $\mathbf{l}(a)$ is only influenced by $\mathbf{P}(x)$ and hence $\mathbf{M}(x)$ when $a > x$. Following Willekens 1977, the sensitivity function of $\mathbf{l}(a)$ can be denoted as:

10

$$d\mathbf{l}(a) = \mathbf{l}(a)\mathbf{l}^{-1}(x)\mathbf{P}^{-1}(x)d\mathbf{P}(x)\mathbf{l}(x) \quad a > x$$

It becomes clear from equation 4 that also the function of personyears $\mathbf{L}(x)$ is not determined by transition rates at earlier ages. Hence, $\mathbf{M}(x)$ only affects $\mathbf{L}(a)$ when $a \geq x$.

Applying the chain rule for differentiating equation 4 results in:

11

$$\begin{aligned} d\mathbf{L}(a) &= d\mathbf{M}^{-1}(x)[\mathbf{I} - \exp(-\mathbf{M}(x))] \\ &= d\mathbf{M}^{-1}(x)[\mathbf{I} - \exp(-\mathbf{M}(x))] + \mathbf{M}^{-1}(x)d[\mathbf{I} - \exp(-\mathbf{M}(x))] \end{aligned}$$

The derivative of the inverse can be written as (Magnus and Neudecker 1999):

12

$$d\mathbf{M}^{-1}(x) = -\mathbf{M}^{-1}(x)d\mathbf{M}(x)\mathbf{M}^{-1}(x)$$

Using equations 4 and 9, the sensitivity function for $\mathbf{L}(a)$ can be written as:

13

$$d\mathbf{L}(a) = -\mathbf{M}^{-1}(x)d\mathbf{M}^{-1}(x)\mathbf{L}(x) + \mathbf{M}^{-1}(x)[-d\mathbf{P}(x)] \quad a \geq x$$

We now consider the sensitivity of the life expectancy to a change in the transition rate. The life expectancy sensitivity function gives us the sensitivity of status-based life expectancy at age 55 to changes in one of the underlying transition rates $\mathbf{M}(x)$, where $x \geq 55$. Differentiating equation 5 gives:

14

$$d\mathbf{e}(x) = d \left[\sum_{y=x}^{\infty} \mathbf{L}(y) \right] \mathbf{l}^{-1}(x) + \left[\sum_{y=x}^{\infty} \mathbf{L}(y) \right] d\mathbf{l}^{-1}(x)$$

Since $\mathbf{l}(x)$ is independent of $\mathbf{M}(x)$, we can eliminate the second term resulting in:

15

$$d\mathbf{e}(x) = \left[\sum_{y=x}^{\infty} d\mathbf{L}(y) \right] \mathbf{l}^{-1}(x)$$

The sensitivity of the life expectancy at a given age a to a change in rates at another age x (with $a \geq x$) is

16

$$d\mathbf{e}(a) = \left[\sum_{y=x}^{\infty} d\mathbf{L}(y) \right] \mathbf{l}^{-1}(a)$$

From an epidemiological point of view it is realistic that a certain intervention brings about a lifelong change, altering the rates (proportionally or additively) from a given age onwards. To calculate the impact on life expectancy of a life long change from age x onwards, one can simply add the differentials over all ages:

17

$$de_{ij}(x^+) = \sum_x^{\infty} de_{ij}(a)$$

The resulting change in state-specific life expectancy can be expressed in absolute or in relative terms. It can be informative to express the gain or loss in terms of a proportion of

the original life expectancy. The relation between a proportional gain or loss in life expectancy and a proportional change in the rate causing this, is called *elasticity*. The elasticity is a measure of sensitivity. It reveals to what extent a 1% change ($\delta=0.01$) in a rate translates into a relative change in life expectancy. For status-based life expectancy, the state-specific elasticity can be expressed as:

18

$$E_{ij}(x) = \frac{de_{ij}(x)}{e_{ij}(x)} / \delta$$

where δ is a relative change in $\mu_{ij}(x)$ and $E_{ij}(x)$ indicates the percentage change in the number of years spent in state j beyond age x by a person in state i at age x , resulting from a δ percent change in the transition rate $\mu_{ij}(x)$. The concept of elasticity used here is very similar to the measure of entropy of the life table, as mentioned earlier, and defined by:

19

$$H = -\frac{de(x)}{e(x)} / \delta$$

where H is entropy. In this definition, entropy is bound between 0 and 1. In the multistate life table, with more than one living state, the relation between the change in the rate and the change in life expectancy can be both positive and negative. To avoid confusion with the entropy of equation 19, we will use the more widely used expression elasticity.

Results

Following the above procedure to estimate transition rates and constructing a multistate life table using the exponential model, we calculated status-based life expectancy in the two living states for population aged 55 and over in the United States. Estimated status-based life expectancy for White non-Hispanic U.S. males and females are given in table 1¹.

¹ Total life expectancy at age 55 for males, starting out healthy was 24.427 years with the linear and 24.429 years with the exponential model.

Table 1 about here

Women live much longer with and without ADL disability than men. Women who are healthy at 55 may expect to live 29.2 years, 29 percent with ADL disability. Women who are ADL disabled at age 55 can expect to live fewer years (22.3 years) and a much larger share (90 percent) with ADL disability.

The sensitivity of the life expectancy to changes in transition rates are determined by equation 16. What is the effect of a 1 percent reduction in healthy to ADL disability rate at age 55 on the life expectancy at that age? The resulting change in life expectancy can be expressed in absolute or relative gains or losses. $d\mathbf{M}(x)$ would be:

20

$$d\mathbf{M}(55) = \begin{bmatrix} -\delta * \mu_{12}(55) & 0 \\ \delta * \mu_{12}(55) & 0 \end{bmatrix} \quad \text{where } \delta=0.01$$

One of the research questions that can be answered by sensitivity analyses is at what age an intervention is most effective in terms of prolonging healthy or total life expectancy. Let's examine the influence of a 1% decrease in transition rates at each particular age. Figure 2 shows the effect of these changes. The black lines in figure 2 show the sensitivities for individuals starting out healthy at age 55 (H) and the grey lines show the sensitivities for individuals who are severely disabled at 55 (S). The upper right panel for example shows the effect a decline in healthy to disability rate. The gains in life expectancy decline after age 70 as a consequence of the declining probability of being healthy at these advanced ages and hence to be exposed to the risk of transition to ADL disability. The benefits for an individual starting out disabled at age 55 (S) are small as the person needs to recover first to be able to profit from the decreased incidence rate.

Figure 2 about here

Decreasing healthy to death rate and healthy to disability rate is most efficient at young ages: the sooner the intervention, the better. However, for the recovery and survival of disabled persons there is a clear optimal age for an intervention to be most efficient. The age at which most effect can be reached depends on the probability to be exposed to the risks, the initial

rates at that age and the life years to be saved. The prospects of individuals who started out with ADL disability at age 55 (grey lines in figure 2) are naturally most sensitive to changes in recovery and survival.

We verified the results by means of the numerical approach and the linear differentiation. Differences between the linear and exponential model are negligible. As long as the change δ remains small, the analytical differentiation approaches (linear and exponential) are practically identical to the numerical method.

A simultaneous change: decelerating ageing

The analytical sensitivity analysis can also assess the impact on the life expectancy of simultaneous changes in two or more rates. Imagine a slowing down of the biological process of ageing: suppose that both mortality and transition to disability would come down by 1%.

The state-specific life expectancy sensitivity functions show at what age this would have the largest effect for men and women. As about 87% of males and 85% of females are healthy at age 55, the elasticities for individuals starting out healthy are most interesting and shown here.

Figure 3 about here

Figure 3 demonstrates that in terms of absolute gains in healthy life expectancy (HE) decelerating ageing should start as early as possible. To optimize gains in total life expectancy (LE), the most effective age to slow down the pace of ageing is around age 70 to 75, which will however also increase disabled life expectancy (DE). After age 75, for both males and females decelerated ageing benefits disabled life expectancy more than healthy life expectancy: the prevented incidences of disability do not outweigh the number of disabled that were saved from dying.

Table 2 about here

An important question is whether decelerated ageing expands or compresses the lifespan with ADL disability. Table 2 shows the gains in state-specific life expectancy for men and women starting out healthy and the proportion of disabled life before and after a 1 %

reduction in disability and death rates. In absolute terms decelerated ageing causes an expansion of disability for both males and females: life expectancy with disability increases by 0.007 and 0.006 years respectively. In relative terms however, disability is compressed for both men and women, as shown in table 2.

The impact of a lifelong change

Many interventions, treatments or lifestyle changes bring about a permanent and lifelong change to health conditions. Elasticity can equally express the resulting relative change in life expectancy as a result of a lifelong 1 percent change in the original rate by adding up the elasticities per age (see equation 17). An illustration of state-specific elasticities of lifelong proportional changes by rate are given in figure 4 for individuals starting out healthy.

Figure 4 about here

Most elasticities are negative as a reduction in a rate increases life expectancy, except for recovery. The figure clearly demonstrates that the most effective way to improve healthy life expectancy for those starting out healthy, is to reduce the healthy to disability rate.

Improvements in recovery rates have very little effect: a 1% increase in recovery rate causes a 0.02% increase in healthy life expectancy. Lifelong proportional interventions are more effective for males than for females, except for the impact of healthy to disability rate on healthy life expectancy.

Summary and discussion

This study demonstrates analytical sensitivity analysis of a multistate life table and its usefulness for research on compression and expansion of disability. It builds on existing research on sensitivity analysis, multistate life table functions, entropy of the survival curve and matrix differentiation. The linkage between a change in one of the rates and the resulting change in life expectancy is not straightforward, but depends on the initial level of the rate, the exposed risk and life years to be saved. The sensitivity functions of the status-based life expectancy tell us for which rate and at what age an intervention would be most effective to gain (healthy) life years. The state- and rate specific elasticities directly translate relative risks into relative losses or gains in a life expectancy with and without disability. It is an intuitive

measure to quantify the effect of a health change, for example a lifestyle change or an intervention, in terms of compression or expansion of morbidity.

Decelerated ageing, a reduction in disability and death rates, leads to longer lives in better health before age 75. After 75, decelerated ageing adds years but most are years with disability: prevented disability does not outweigh the averted mortality of the disabled. Overall, decelerated ageing expands the number of years with and without disability, but expressed as share of total lifespan life with disability is compressed for both men and women. The most effective intervention to increase healthy life expectancy is to reduce ADL disability incidence: improvements in recovery rates have very little impact. Generally, health interventions are more effective for males than for females, a consequence of higher rates.

Like all differentiation methods, the sensitivity functions derived by matrix differentiation only hold as long as the changes under study are small. When the values in the change matrix $d\mathbf{M}(x)$ grow larger, the resulting gains or losses in life expectancy from the analytical sensitivity method will diverge from the real effects on life expectancy. One can easily test the accuracy of the analytical method by means of the numerical method.

Although multistate models in health research are considered superior to several other epidemiological models like the multiple-decrement life table or Sullivan's method (Barendregt, Bonneux and Van der Maas 1994), multistate models are not as wide-spread as one might expect or would wish for. One of the reasons could be the need for longitudinal data of at least two waves to estimate transition rates. Another possible explanation for researchers' reluctance might be the unfamiliarity with matrix algebra. Sensitivity analysis of multistate models using matrix differentiation has received very little attention in the literature, probably because of that same reason. This paper tries to demonstrate the usefulness of analytical sensitivity analysis in multistate illness-death models and shows applications that could serve researchers and policymakers in studies and debate about compression and expansion of disability.

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Table 1: Status-based life expectancy at age 55 for U.S. males and females.

	Males		Females	
	Healthy at age 55	Disabled at age 55	Healthy at age 55	Disabled at age 55
Healthy ex	19.44	2.11	21.84	2.19
Disabled ex	4.98	15.84	7.35	20.10
Total ex	24.43	17.96	29.19	22.29

Table 2: Compression or expansion of disability in years and in proportion of total lifespan after a 1% reduction in disability and mortality rates from age 55 onwards for males and females, starting out healthy.

	Males						Females					
	Before		After		Gains/losses		Before		After		Gains/losses	
	years	share	years	share	years	points)	years	share	years	share	years	points)
Healthy ex (HE)	19.44	79.6%	19.55	79.7%	0.11	0.06%	21.84	74.8%	21.96	74.9%	0.12	0.09%
Disabled ex (DE)	4.98	20.4%	4.99	20.3%	0.01	-0.06%	7.35	25.2%	7.36	25.1%	0.01	-0.09%
Total ex (LE)	24.43	100.0%	24.54	100.0%	0.11		29.19	100.0%	29.31	100.0%	0.12	

Figure 1: Statespace of the multistate illness-death model

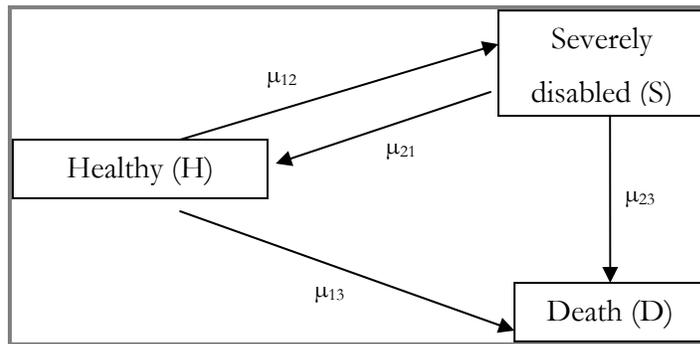


Figure 2: Absolute effect of a 1% decrease in one of the rates at different ages on status-based life expectancy for males starting out healthy at age 55 (H - black lines) and males starting out severely disabled (S - grey lines).

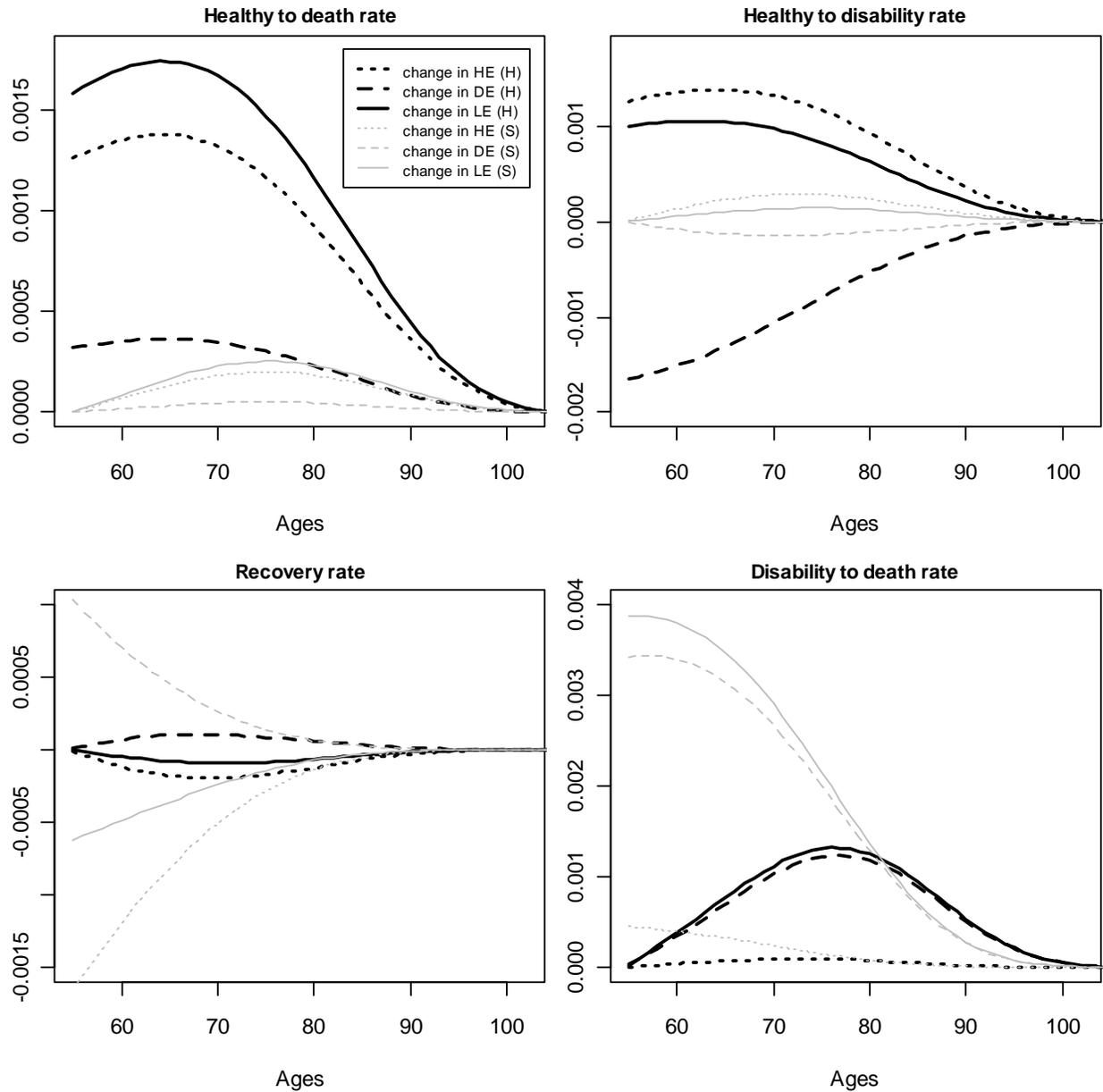


Figure 3: Absolute changes in state-specific life expectancy as a result of decelerated ageing (1%) for men and women who started out healthy at age 55.

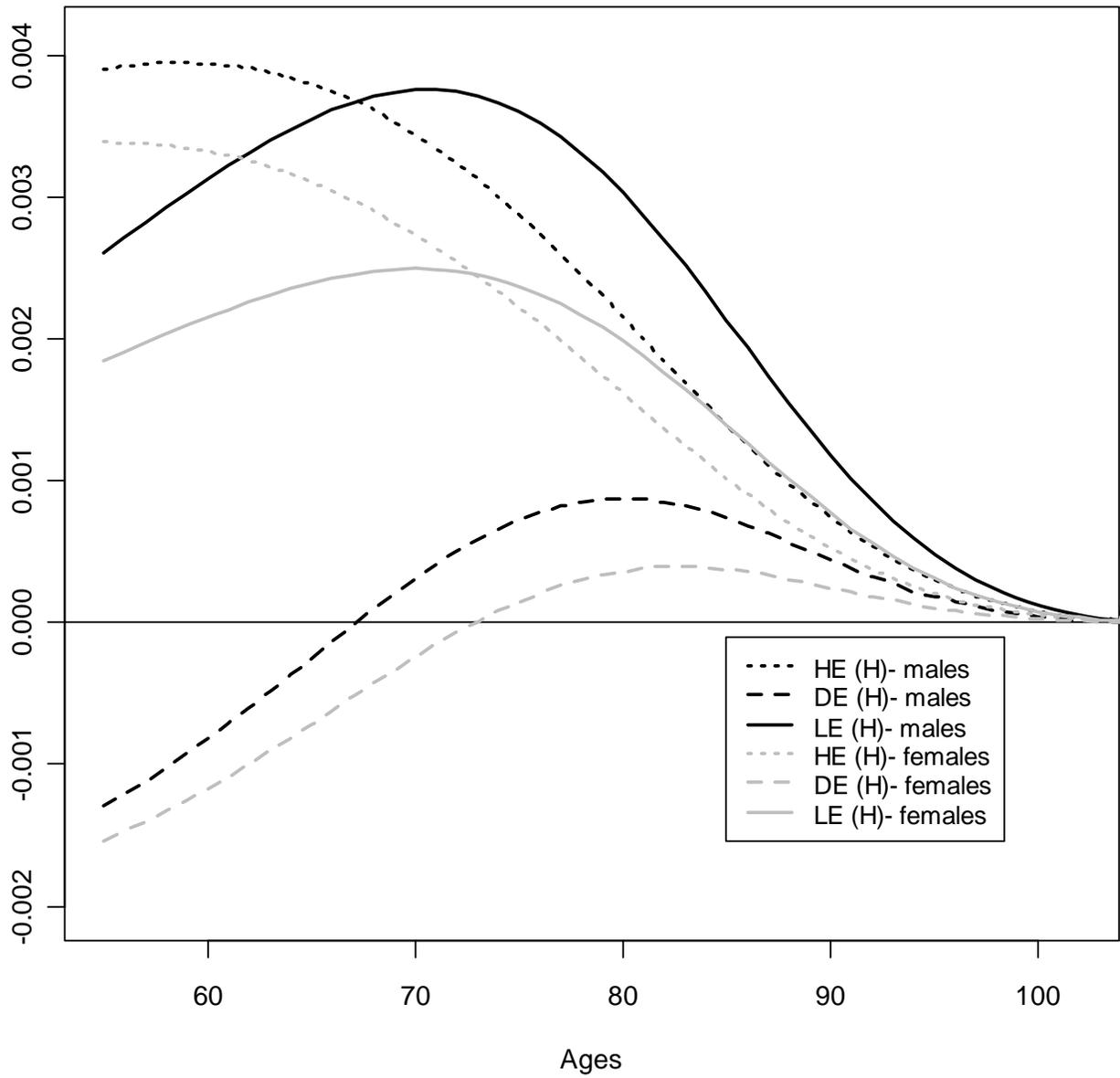


Figure 4: Healthy (HE) and Disabled life expectancy (DE) elasticities for each rate for individuals starting out healthy at age 55. (H-D = Healthy to Death, H-S = Healthy to Severely disabled, S-H = Severely disabled to Healthy (recovery), S-D = Severely disabled to Death).

