The effect of risk factors on disability
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Chapter 1
1. Introduction

During the 20th century, human life expectancy has increased by about 30 years in Western Europe, the United States (U.S.) and Japan. In recent decades, these gains in life expectancy have primarily been the result of reductions of mortality of the elderly as levels of mortality for children and younger adults were already very low. The question arises whether the improvement in health resulted in a postponement of morbidity as well. With increasing life expectancy and age-related morbidity, are years to live with morbidity expanded or compressed, or is it a mix? Lifestyle factors like smoking, BMI and education have proven to play an important role in the duration of morbidity, which deserves more attention.

Figure 1. Survival curves and life expectancy in good health (75 years) and ill health (7 years) of a synthetic cohort.
Setting the scene

Expansion or compression of morbidity

Ageing is the process of physical, psychological and social change in an organism over time. The process of ageing is slow, it is a continuous process, it is progressive and determined by, logically, age. At higher ages the risk of morbidity increases. When mortality rates decrease and many people will reach higher ages, the question is whether the additional life years are spent in good health or with morbidity. In other words, does increased life expectancy expand or compress the duration of morbidity? Figure 1 shows the survival curves and life expectancy in good and in ill health for a synthetic cohort.

Different theories exist about the future duration of morbidity in absolute and in relative terms. Advocates of the expansion of morbidity theory like Gruenberg and Olshansky assume that the increase in life expectancy is caused by a reduction in the fatality of chronic diseases rather than by a decline in the incidence of these diseases (Gruenberg 1977; Olshansky 1991). Advances in medical technology and public health would prevent the frail and disabled from dying and the increase in longevity should therefore go hand in hand with an increasing absolute number of years spent in poor health. Such absolute expansion of morbidity is demonstrated in the upper-left pane of Figure 2. In contrast, Fries (1980) proposed that there is a maximum average life span of 85 years. With improvements in health the onset of chronic diseases will be postponed, but given the maximum life span morbidity will then be compressed into a shorter period of time at the end of life. Hence, the absolute duration will be compressed (Figure 2: upper-right pane). Another alternative would be that life extension does add years with morbidity, but even more years in good health. This would increase the absolute duration in both states, but in relative terms of total life expectancy duration of morbidity would be compressed (Figure 2: lower-left pane). An final theory in the expansion or compression debate was given by Manton with his dynamic equilibrium theory (Manton 1982). This hypothesis highlights the significance of delay in the intermediate stage of the disease process, namely, in the progression from less severe to more severe (and more disabled) disease states. Screening and early diagnosis for example increase morbidity by early case detection but may postpone disability by treatment that lowers the risk of severe disease. If indeed people with chronic disease are living longer
because the rate of progression of their disease is slowing down we can expect increasing life expectancy to lead to an increase in overall prevalence of mild disabling diseases, but largely stable rates of severe disease (Figure 2: lower-right pane).

Figure 2. Theories of compression or expansion of morbidity.

The evidence for the recent trend in morbidity prevalence is mixed. The prevalence of diseases like type 2 diabetes, hypertension and some cancers have increased over time, partly explained by earlier diagnosis. Prevalence of heart diseases and arthritis has increased as well as reporting of multiple disorders. Studies on the trend in prevalence of disability show conflicting results (Cai and Lubitz 2007; Christensen et al. 2009; Jagger et al. 2008; Manton 2008).
Morbidity or ill health is a broad concept and it is hard to define. A widely used measure of health that is more objective is disability of activities of daily living or ADL disability. This is the measure we use in this study. When a person is unable to perform one of the activities of daily living independently, this person can be considered care dependent. We do not look into diseases. To complement the compression/expansion discussion, this study looks into the effect of risk factors on durations of disability and absolute compression or expansion of disability.

**Risk factors**

Apart from medical innovations, a large part of the gains in life expectancy are due to public health efforts advocating a more healthy lifestyle. An abundance of literature exists on the impact of lifestyle on health and mortality (Al Snih et al. 2007; Anttila et al. 2004; Calle, Teras and Thun 2005; Dobhhammer and Vaupel 2001; Franco et al. 2004; Hubert et al. 2002; Jagger et al. 2007; Mamun et al. 2004). The most well-known and influential factors described in the literature are smoking, alcohol use, overweight or obesity, marital status, race, education and socioeconomic status. In this study we will focus on the influence of smoking, overweight and obesity and education, aside from demographic characteristics sex and age.

The extreme mortality hazard as a result of smoking has often been studied and is well documented. Smoking is associated with a loss of average life expectancy by about 8 years for males and females aged 55 and over (Barendregt, Bonneux and van der Maas 1997; Nusselder et al. 2000). In the debate about compression or expansion of morbidity, the effect of smoking is perhaps paradoxical and in any case controversial: smoking, by being highly fatal, compresses life years with disease or disability by increasing mortality (Mamun 2003; Mamun et al. 2004; Nusselder et al. 2000).

The evidence on the impact of overweight and obesity on health is mixed, depending among others on the definition of good health, the age of the study population and the time period of the study. However, most researchers agree that the prevalence of overweight and obesity is increasing rapidly and that the obesity epidemic is a serious threat for population health. In 2001-2004, 30% of men and 34% of women in the U.S. 20-74 year of age were obese (BMI 30 and over) (Centers for Disease Control and Prevention 2006). Many countries follow the
U.S. lead (York et al. 2004). Several studies suggest that obesity could overtake smoking as actual cause of death (Mokdad et al. 2004; Peeters et al. 2003a). However, more recent studies suggest otherwise, demonstrating that at middle and old age, overweight lowers mortality, especially for men (Flegal et al. 2005; McGee 2005). Cardiovascular risk management like cholesterol lowering drugs palliated the cardiovascular disease risk and lowered obesity related mortality, but not the non-fatal disability causes. If disability is increased but not mortality, numbers of obese survivors expand morbidity, increasing life years lived with disability, care dependence and health-care costs (Andreyeva, Sturm and Ringel 2004; Reynolds, Saito and Crimmins 2005).

Education has a more indirect effect on health and mortality than smoking and BMI. Education, just as socioeconomic status, can be seen as a proxy for a health and risk-averse lifestyle. The role of education in cognitive decline is particularly interesting. The hazard to become cognitively impaired increases rapidly with age and as higher educated reach higher ages, one can expect higher chances to ever experience cognitive impairment. At the same time, a large cognitive reserve prevents against cognitive impairment (Fratiglioni and Wang 2007). The influence of education and other risk factors on life years with cognitive decline is described in Chapter 4.

Although many researchers have studied the impact of the risk factors smoking, BMI and education on health and disability, we express the effects in terms of durations, hence life years. We will also refer to life years with or without (physical or mental) disability as state-specific life expectancy. This life expectancy depends on the net balance between incidence, recovery and death. The power of our approach lies in expressing the results in terms of durations, summarizing the simultaneous influence of the risk factors on all transition rates.

**This study**

The objective of this study is to unravel the effect of risk factors on compression and expansion of the absolute duration of disability at middle and old age. The multistate model offers the analytical framework at both the population and individual level.

The main research questions are:
1) How do risk factors influence the life expectancy with and without physical or cognitive disability?

2) What is the distribution of individual disability that underlie the expansion or compression of disability caused by risk factors?

3) How sensitive is life expectancy with and without disability to a change in mortality, incidence and recovery rates?

Data and definitions

All analyses and applications in this study were conducted using the U.S. Health and Retirement Study (HRS). This panel study is publicly available, follows a large cohort of individuals and has conducted 8 waves so far, providing a wealth of information for longitudinal data analysis. The European equivalent of HRS, the Study of Health and Retirement in Europe (SHARE), can answer similar research questions regarding the European population with similar methods as in this study, when more waves are available.

We used the RAND version of the U.S. Health and Retirement Study data file containing the HRS and the Asset and Health Dynamics Among the Oldest (AHEAD) to answer the research questions. The combined dataset is also called HRS, to which we will refer to. The HRS include a nationally representative sample of initially noninstitutionalized persons aged 50 and over. Sampled persons were reinterviewed biannually. Our sample covers survey rounds from 1992 to 2004. We selected the white non-Hispanic individuals for the analyses. We found that the non-white population behaved very differently and the complex and sensitive study of race is beyond the scope of this study. Only the analyses on cognitive impairment (Chapter 4) include race as covariate.

Studying population health is much more complicated than studying mortality. Mortality is a discrete and unambiguous measure while health is ambiguous and continuous. Furthermore, many health surveys suffer low participation or follow-up, especially among the less healthy. The measure we use for physical disability is the Katz Activities of Daily Living. This indicator is based on an evaluation of the functional dependence or independence of patients in bathing, dressing, going to the toilet, transferring, continence and feeding (Katz et al. 1963). We reckoned that failing the ability to perform one of these activities of daily living,
makes an individual dependent on care: a particular interesting piece of information for policymakers. Besides, the measure of ADL disability is often used in the literature, making results easier to compare. For measurement of cognitive impairment we make use of a modified version of the TICS (The Telephone Interview Cognitive Screen) instrument, a telephone interview adapted from the MMSE (Mini Mental State Examination) (Brandt, Spencer and Folstein 1988; Folstein, Robins and Helzer 1983). In case of inability to answer, a proxy would represent the respondent.

**Methods**

All methods used in this study are based on the multistate model. Multistate models allow individuals of a population to move in and out of living states. These movements are estimated by transition rates, that are the fundamental concepts of the multistate framework (Mamun 2003). The multistate approach using transition rates is preferred over the Sullivan method that uses prevalence rates. Transition rates more accurately reflect population changes and developments than prevalence, that includes the entire history of a population (Mathers and Robine 1997).

One of the methods applied in this study is the Cox Proportional Hazard model, a widely used technique for transition data analysis. The Cox model does not parameterize the baseline, but estimates proportional effects. We use age as time scale and express the effect of risk factors as proportional hazard ratios. However, to answer our questions on absolute durations with or without disability, multistate life table analysis was used. The research question about the distribution of disability trajectories is answered using microsimulation techniques. In our study, we do not focus on the origin and developments of the methods. We merely apply the techniques to answer our research questions appropriately. Only Chapter 6 is method-oriented: it develops and improves existing sensitivity analyses of multistate life tables.

To estimate the actual transition rates we use occurrence-exposure rates, smoothed by Poisson regression to reduce variability. The assumption is that transitions to disability and death increase exponentially with age, which fitted the empirical data very well. I assume that events occur halfway between two interviews and only one event occurs in the interval. 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. Given the discrete nature of the status information at interview, it would be more appropriate to estimate probabilities rather than transition rates. There are two methods to do this. The first is to estimate probabilities based on the average length of the intervals (Cai et al. 2010). A second possibility is to estimate transition probabilities with different lengths of intervals by finding the embedded Markov chain (Laditka and Wolf 2006; Laditka 1998). However, both alternative methods have some practical limitations and the differences with the use of occurrence-exposure rates, are very small (Wolf and Gill 2009). More on the estimation of the transition rates will follow in the discussion. The Poisson regression which estimates the transition rates returns standard errors of the parameters. However, we use bootstrapping to obtain confidence intervals in the multistate life table analyses and we start from the point estimates of the transition rates as starting point for the microsimulation.

All models and methods used in this study are based on the estimated age- and sex-specific transition rates. These rates can be summarized into a population-based measure of state-specific life expectancy, by using multistate life table analysis. The multistate life table generates a synthetic cohort that experiences the estimated transition rates. In this study we use population-based multistate life tables with two living states, healthy and physically or cognitively disabled. Status-based multistate life table functions are used only in Chapter 6. The most important result of the multistate life table is state-specific life expectancy, a comprehensive measure of absolute compression or expansion of disability. The effect of risk factors can be intuitively expressed by means of gains or losses in state-specific life expectancy. One should keep in mind that the data reflects the disability and death experience during a short time period (1992-2004). The life table approach applies these rates to an entire (synthetic) cohort. We used bootstrapping to obtain confidence intervals.

A different approach to analyze durations of disability and the impact of risk factors is to investigate the distribution of individual disability trajectories. Individual trajectories provide additional information which is not provided by the cohort average. Individual disability trajectories can be produced by microsimulation. It creates individual biographies that are synthetic and fully determined by (1) the empirical transition rates and (2) the random Monte Carlo simulation technique, that identifies which individuals experience a transition during a given interval (Imhoff and Post 1998). The aggregated results are consistent with the
multistate life table results when based on the same rates. In this study we use continuous-time microsimulation to demonstrate the effect of risk factors on disability trajectories that underlie the compression or expansion of disability.

A final method used in the multistate framework of this study is sensitivity analysis. Sensitivity analysis deals with the question how a small change in a parameter alters particular outcome variables that interest us. Analytical sensitivity analysis of the multistate life table requires differentiation of the life table functions and hence matrix differentiation. The sensitivity function of state-specific life expectancy tells us for which rate and at what age an intervention would be most effective to gain (healthy) life years. The effectiveness can be expressed in absolute years or in relative life expectancy gain. Elasticities express the relative impact of a relative change. In our multistate illness-death model, elasticities express how sensitive healthy or disabled life expectancy is to changes in incidence, recovery and mortality. It is an intuitive measure to quantify the effect of a health change, for example because of a risk factor, in terms of compression or expansion of disability.

Outline of the book

Chapter 2 of this book studies the impact of the risk factors BMI, smoking and education on mortality, expressed in proportional hazard ratios and life years lost or gained. Chapter 3 adds a disability state and analyzes the effect of risk factors on life expectancy with and without disability. Chapter 4 studies the duration of cognitive impairment and the impact of risk factors. As race turned out to be an important factor, we included this characteristic in the analysis. Chapter 5 assesses which individual disability trajectories underlie expansion or compression of disability caused by risk factors, using microsimulation. Chapter 6 derives the analytical sensitivity functions of the multistate life table, using matrix differentiation. In an application we study decelerated ageing, meaning a reduction of incidence and mortality rates. The sensitivity analysis quantifies the impact of decelerated ageing on compression or expansion of disability. The last chapter summarizes the main results. It discusses the contributions of this study, limitations of our methodological approach and the societal relevance. Finally, we will have a look into the future and propose recommendations for further research.
References


