10

Discussion and conclusion

10.1 Introduction

The focus of this book was to explore the utility of the multistate life table technique in public health research and to investigate the life history of cardiovascular disease, its risk factors and the compression of morbidity. A substantial portion of this book has been devoted to delineating of the methodological issues in public health research. The multistate life table method was investigated and consistently applied to the lengthy period of follow-up of the original 'Framingham Heart Study' cohort. The general approach was to couple demographic methods with an epidemiological framework to develop new public health and life course indicators, which would be transparent and policy relevant. To some extent, this approach also shed light on the empirical investigation of the life course epidemiology of cardiovascular disease. Life course analysis is a new tool with a huge potential for public health epidemiology. This study pioneered the use of life course analysis on the Framingham Heart Study. This study exemplified that risk is an inevitable part of the human life course (Ben-Shlomo and Kuh, 2002).

The cardiovascular risk factors at middle age and their long-run impact on the disease history and post-disease mortality were investigated explicitly. The burden of cardiovascular disease was analyzed by risk factor status. We tried to identify which risk factor compressed cardiovascular disease and at which age compression occurred. We also estimated the multifactoral effects in the cardiovascular life history. The major strength of this study lies in its focus on a well- documented epidemiologically defined community-based population and 48 years of prospective, consistent follow-up of the same cohort in the Framingham Heart Study, and the combination of well-developed techniques from the discipline of epidemiology and demography.

This concluding chapter summarizes the major contributions of this research and draws attention to the future potentials of the cardiovascular disease history. An elaborate discussion of each chapter study can be found in the discussion sections of the separate chapters. In Section 10.2, we have summarized the major

findings of this study. The important contributions of this research, both methodological and substantive, are illustrated in Section 10.3. The implications of this study for public health research are briefly described in Section 10.4. Some of the future prospects of this study are indicated in Section 10.5. Finally, we bring our study to a close look with a concluding remark in Section 10.6.

10.2 Summary of findings

We applied multistate life table technique consistently throughout this study. The major strength of the multistate life table is its ability to capture the implications of age-related declines and improvements in health (i.e. inflow and outflow). This approach provides a more accurate assessment of the expected life cycle of disease history in the population compared to the prevalence-based measure (Sullivan method). We found the multistate life table technique to be an elegant method to address the debate of compression or expansion of morbidity. We illustrated the multistate life table technique with its generalization and statistical precision in a simplified way. The methodological features of the MSLT that might serve as an added contribution to the field of public health research was pointed out in *Chapter 2* of this book.

From a methodological point of view, the analyses performed in *Chapter 3* were of interest because:

- the chapter provided a detailed description of how the exact occurrence-exposure rates could be derived from the micro level information from longitudinal follow-up data;
- they transferred the transition rates into a multistate life table to analyze the life history of cardiovascular disease;
- the results exhibited the utility of transforming epidemiological data into time-based health policy measures; and
- it analyzed the possible model structure or state space for cardiovascular disease processes.

By transferring age-specific occurrence-exposure rates into a life table population, it was found that at age 40, FHS participants could expect to survive an average of 38.5 years, of which 84 percent free of cardiovascular disease. From the age of 40 on, nearly two-thirds of the men (67 percent) and more than half (55 percent) of the women would go on to develop cardiovascular disease in their lifetime. A disparity in the life trajectory of cardiovascular disease between males and females was observed. It was found that males spend more years of life with cardiovascular disease and its subtypes at middle age, but that the burden of cardiovascular disease at older ages (80+) was higher for females. We showed that the greater longevity of women was the primary cause of both their greater lifetime

probability of stroke and the greater number of years of life lost to an equivalent disease as compared to men. While epidemiological data enables prediction of the number of coronary heart disease events and deaths, the multistate life table technique enables estimation of the overall potential burden of specific diseases in terms of years of life lost to and lived with disease. In chronic disease modeling, this approach and the use of a life course indicator are new, and we found these to provide very transparent and robust outcomes that are furthermore relevant to public health policy.

We proposed a potential method to impute missing values of risk factors in a repeated measurement study (*Chapter 4*). The idea behind the proposed methodology is relevant to any study design subject to incomplete responses and having at least three repeated measurements. Using the proposed methods, we can easily reconstruct the risk career and measure the impact of this risk career on disease incidence and mortality. We applied this technique to impute missing values for smoking status in the FHS and to reconstruct the smoking career of the FHS population (*Chapter 5*). The analysis was intended to illustrate the usefulness of multistate life tables for describing how smoking evolves over the life course. Our smoking status definition included the updated information on smoking status throughout life rather than the status at a specific point in time, for instance, incidence of smoking. We described the smoking experience of an American cohort from the 1950s and translated the smoking career of this cohort into life years spent as non-smokers and life years spent smoking, within a synthetic cohort. At age 10, the total life expectancy of the FHS cohort was 66 years for males and 72 years for females. Males smoked for considerably more years than females. Males spent two-thirds of their expected lifetime (68%) smoking. For females, this was less than one third (28%). The difference declined at higher ages when males with a history of smoking had either quit or died. The smoking careers of males started 2 years earlier than that of females. Males started, on average, at age 15 (median) and females at age 17. Fifty-eight percent of the American males who started smoking manages to quit at some point. For females, the proportion of quitters was considerably lower, namely 37%. Compared to men, women smokers were more persistent. An individual who quit smoking was likely to do so between the ages of 50 and 70. The probability of a relapse was 26% for males and females. This knowledge of the historical smoking and quitting patterns is important for current studies interested in the cumulative smoking histories of current populations. Our approach demonstrated one of the ways the changes in risk factors throughout life could be explicitly taken into account. This method could also be used for other risk factors to indicate current risk factors in life courses.

When investigating cardiovascular disease in the life course of smokers and non-smokers (*Chapter 6*), we found that the risk of developing cardiovascular disease before age 70 was higher among smokers. We classified never smokers as

those with all available smoking records coded as a "non-smoker" and always smokers as those with all available smoking records coded as a "smoker". Associated with the longer life expectancy of male non-smokers were higher lifetime risks of coronary heart disease, myocardial infarction, stroke and congestive heart failure. Female non-smokers had higher lifetime risks of coronary heart disease and congestive heart failure. Non-smokers spent more years with cardiovascular disease as well as free of cardiovascular disease over the life course because they live longer. Not smoking will not compress cardiovascular morbidity, but it will postpone it to older ages. Smoking, by shortening life, decreases the years lived with cardiovascular disease throughout the life course. Paradoxically, in a non-smoking society, more people will live with cardiovascular disease but this will be concentrated at the end of life.

Two well-known rate models, the Cox and the Gompertz model, were compared with the empirical estimates of age-specific transition rates (*Chapter 7*). In the null model, the Cox and the observed rates were similar. When covariates were added to the Cox model, the estimated age-specific rate did not overlap with the observed rates. Instead, it fit less within the bounds because of its proportionality assumption. The Gompertz estimate behaved the same in the null model and in the model with covariates. Gompertz has fewer parameters, gives smooth transition rates and reduces the variability. On the multistate life tables of cardiovascular disease, with and without the presence of covariates or risk factors, the Gompertz model could be a better option compared to the observed rates and the Cox model.

We investigated the association of the risk factor status between the ages of 30 and 50, with the incidence of cardiovascular disease and its subtypes, and post-disease mortality over a long follow-up (*Chapter 8*). We considered the following major cardiovascular disease risk factors: smoking, body mass index, serum cholesterol level and blood pressure. Smoking status for each participant was allocated based on the current smoking status recorded at each available exam from age 30 to 50. We classified never smokers as those with all available smoking records coded as a "non-smoker" and always smokers as those with all available smoking records coded as a "smoker". Ever smokers were the rest of the participants, characterized by a mixture of smoking and non-smoking throughout the period from entry into the survey to age 50. Blood pressure (systolic or diastolic) at each exam was defined based on the mean value of recorded blood pressure from different examiners. We took an average of the recorded mean blood pressure between age 30 and 50 years. Likewise, the average levels of serum cholesterol and body mass index (BMI) recorded between age 30 and 50 were taken as predictors. Univariate analysis indicated that each risk factor had a substantial effect on the risk of CVD and mortality. For instance, obese males (BMI $\geq$ 30) had an 81% excess risk of CVD and a 47% excess mortality compared to males of normal weight. We investigated the long-term nature of relationships, not only of

primary relationships as shown in univariate analyses, but also of confounding relationships as shown in the changes of relative risk after adjusting for the levels of other risk factors. The effect of smoking is aggravated by the presence of other risk factors. For example, when we controlled for the level of other risk factors in male smokers, the upward change in excess risk was 29% for CVD. The presence of other risk factors reduced the effect of obesity, hypertension, or high cholesterol level on CVD (in the absence of any interaction effect). The direction in which the relative risk changes (e.g. upward for smoking and downward for obesity) is likely to be the result of the pattern of co-occurrence of risk factors in the population.

We examined whether optimal risk factor status throughout the age interval 30-50 compresses cardiovascular morbidity. Since one risk factor could compress cardiovascular morbidity and others might not, we performed both a univariate and multivariate analysis to examine the independent and partial impact on cardiovascular disease life history in terms of life table estimates (*Chapter 9*). In the case of the univariate analysis, across all risk factor categories, it was found that a male who did not smoke and a female who had optimal blood pressure at middle age had the highest life expectancies at age 50: 30.82 years for males and 34.72 years for females. For both males and females, the absence of major cardiovascular risk factors at middle age compressed cardiovascular morbidity. Non-smoking at middle age does not necessarily compress cardiovascular morbidity. Apparently, the balance between effects on incidence, case fatality and recovery of cardiovascular disease differs between smoking and the other risk factors.

We demonstrated the possibility of using multivariate Gompertz regression models for the long time continuous event histories to estimate the state transition rates and then to use the estimated transition rates in constructing a multistate life table in multiple covariate contexts. We compared optimal and high-risk profiles. In the multivariate case, an optimal risk profile was defined as an individual who was a never smoker, on average had optimal blood pressure (SBP<120 and DBP<80), optimal cholesterol level (SCL<200) and optimal BMI (BMI<25) between age 30 and 50. If an individual was a smoker, had high blood pressure (BP>140 or DBP>90), high cholesterol (SCL>240) and was obese (BMI>30), he or she was considered to have a high-risk profile. Multivariate analysis showed that an average of four in five males or females belonging to the optimal risk group, who were free of cardiovascular disease at age 50, would still be alive and free of cardiovascular disease twenty years later; only 1 or 2 in 5 of those considered to be at high risk, would remain in this state. The differences in additional number of survival years between males and females by optimal and high-risk profiles were found to be 12 and 14 years. A fifty-year-old male with an optimal risk profile could expect to survive 17 more years free of cardiovascular disease and a female of that age with same risk profile could expect to survive 16 more years, compared to individuals with high-risk profiles. For the synthetic cohort that was free of CVD at age 50, the

lifetime probability of developing cardiovascular disease was 82 percent for males (female 72 percent) in the high-risk group and 38 percent for males (35 percent females) in the low risk group.

The significant differences between optimal and high-risk profiles in life expectancy with and without cardiovascular disease indicates that risk factor status at middle age has a significant impact on later ages of life. High-risk profiles in adulthood shorten the duration of life, increase the lifetime probability of experiencing CVD, and extend the length of time spent living with cardiovascular disease. An optimal risk profile significantly increases the number of years lived without cardiovascular disease and decreases the years lived with disease, i.e. optimal risk profiles in middle age are associated with the compression of cardiovascular morbidity.

The findings provide empirical evidence of the importance of the prevention of major cardiovascular risk factors at adulthood and reconfirm the guidelines of the American Public Health Association (Pearson et al., 2002) and the recent life course epidemiology approach (WHO, 2002). In public health research, major priority should be given to targeting the high-risk group of middle-aged adults and motivating them to change their lifestyle.

10.3 Major contributions of this study

The present study has attempted to contribute to the methodology of public health research and to derive life course indicators for the cardiovascular disease history, focusing on the compression of morbidity hypothesis. We initiated a new public health approach to the compression of morbidity debate, coupling demographic techniques to the framework of epidemiology. Relating risk factor status with the disease incidence in the debate on the compression of morbidity is relatively new. Researchers hitherto mostly addressed this debate by linking either disability (Nusselder, 1998; Rogers et al., 1989; Crimmins et al., 1994) or degenerative disease (Barendregt and Bonneux, 1998) to the older population and their mortality. We focused on the adult risk factor and the compression of cardiovascular morbidity, and were first with the change of risk factor status at adult age and the compression of cardiovascular morbidity. Some of the methodological and substantive contributions that are made in this study are described below.

Methodological

The methodological contributions of this research can be summarized in at least ***six*** points:

1. We made an explicit distinction between prevalence and incidence based measures of population health status, and shed light on the utility of the multistate life table to address the compression or expansion of morbidity. We generalized the multistate life table technique and consistently applied it to estimate the compression of cardiovascular morbidity by risk factor status. The statistical competence of the multistate life table outcomes was tested using a non-parametric bootstrapping technique. We consistently analyzed the 48 years of follow-up data from the Framingham Heart Study. To our knowledge, no one has hitherto analyzed the follow-up data over such a lengthy period in a multistate life table framework.
2. A methodology to measure the combined effect of several risk factors in the life history of cardiovascular disease was proposed, which is the added contribution in both the life table and cardiovascular risk factor analysis. Using the methodology developed by Anderson et al., (1991) and Wilson et al., (1998) the probability of developing cardiovascular or coronary heart disease in the shorter term can be measured, using our approach estimates can be made of the lifetime probability of developing cardiovascular disease, the number of years lived with and without disease.
3. We proposed potential techniques to impute missing values for both the categorical and continuous risk factors in the repeated measurement study.
4. We assessed the well-known and widely used transition rate models, Cox and Gompertz, against the empirical occurrence-exposure rates and life table outcomes. On the multistate life table of cardiovascular disease, with and without the presence of covariates or risk factors, the Gompertz model could be a better option than the observed rates and the Cox model.
5. One way in which the risk career can be analyzed was demonstrated using the very common risk factor of smoking. Our novel approach demonstrated the importance of explicitly taking into account the changes in risk factors throughout life. Other risk factors can be analyzed in the same fashion, enabling researchers to gain more insight into the impact of other risk factors throughout life.
6. We used age as a time variable, both in the multistate life table and when estimating the relative risks. Disease incidence, risk factor exposure and their relationship, depend strongly on age. To estimate the relative risk of disease or mortality, most researchers use age at baseline, an independent variable that they call age adjusted relative risk. In survival analysis, most of the researchers use follow-up time as the time variable, instead of using age at transition.

Substantive

The substantive contributions made in this study are summarized in the following points:

1. Using a multistate life table, we derived new indicators for the cardiovascular disease life history. At age 40, an FHS participant could expect to live an average of 38.5 years, of which 84 percent free of cardiovascular disease. At age 50, a male could expect to spend 25 percent of his remaining life expectancy with the disease; females, 18 percent. Although males survive longer with CVD during middle age, the burden of CVD at later ages is higher for females.
2. Although the lifetime risk of developing coronary heart disease was previously estimated by Lloyd-Jones and Levy (1999), in the present study we have estimated the lifetime risk of developing *cardiovascular disease* and its sub-types: *coronary heart disease*, *acute myocardial infarction*, *angina pectoris*, *congestive heart failure* and *stroke*. On the basis of the data obtained from the FHS, , the lifetime probability for a 40-year-old male and female American without CVD of developing CVD, CHD, MI, CHF and stroke was calculated to be 67% vs. 55%, 50% vs. 33%, 33% vs. 17%, 18% vs. 16% and 20% vs. 18%.
3. By analyzing the smoking career, we derived different episodes of smoking, patterns of quitting, of restarting, of number of years lived as smokers and non-smokers and the lifetime probability of quitting smoking which are the new indicators in public health research. We re-created the smoking careers of American males and females followed from the 1950s. Over the life course, females quit smoking 21 percent less compared to males. The restarting rate in males was twice that of females. Over the lifetime, more than 50 percent of the American smokers did not quit smoking; individuals who did quit were likely to do so between the ages of 50 and 70. We found that a knowledge of the historical smoking and quitting patterns could be important for current studies interested in the cumulative smoking histories of current populations.
4. The risk of developing any cardiovascular disease before age 70 is higher among smokers. Associated with their longer life expectancy, male non-smokers have higher lifetime risks of coronary heart disease, myocardial infarction, stroke and congestive heart failure, while female non-smokers have higher lifetime risks of coronary heart disease and congestive heart failure. Non-smokers spend more years with cardiovascular disease over the life course. Non-smokers also live more years free of cardiovascular disease. Not smoking will not eliminate cardiovascular disease, but it will postpone it to older ages. Smoking, by shortening life, decreases the years lived with cardiovascular disease throughout the life course. Paradoxically, in a non-smoking society, more people will live with cardiovascular disease but this will be concentrated at the end of life.
5. We investigated the association of the risk factor status between ages 30 and 50, with the incidence of cardiovascular disease and its subtypes, and post-disease

mortality over a long-follow-up. The major risk factors at middle age are strong predictors of incidence of cardiovascular disease and mortality at older ages. The effect of smoking is upward when the confounding effect of other risk factors is present. The effect of obesity, hypertension or high cholesterol is downward when the confounding effect of other risk factors is removed. In the FHS population, smokers are probably less exposed to other risk factors than non-smokers, which is why the relative risk goes up; obese people more than non-obese people, which is why the relative risk goes down. Smoking prevents obesity, and obesity leads to high serum cholesterol and high blood pressure.

6. Contributions from the multistate life table analyzed by univariate risk factor status at middle age can be summarized as follows:
    - Tobacco use at middle age decreased life expectancy at age 50, by 4.4 years for males or females. Male or female non-smokers survive 4.2 or 3.0 years longer without CVD at age 50, and 0.3 or 1.4 years more with CVD. Male or female smokers spend more years with CVD before age 75 or 65. Non-smoking at middle age does not necessarily compress cardiovascular morbidity.
    - High blood pressure at middle age decreased life expectancy at age 50, by 5.7 years for males and 4.9 years for females. Males or females with optimal BP survive 6.8 or 7.8 years longer without CVD at age 50 and 1.1 or 3.0 years less with CVD. Males with high blood pressure spend more years with CVD before age 78. Females with high blood pressure spend more years with CVD throughout life. Optimal BP at middle age compresses cardiovascular morbidity.
    - High cholesterol at middle age decreased life expectancy at age 50, by 2.2 years for males or females. Males or females with optimal SCL survive 4.82 or 3.0 years longer without CVD at age 50 and 3.7 or 0.6 years less with CVD. Males with high serum cholesterol levels spend more years with CVD throughout life and females with high serum cholesterol spend more years with CVD before age 82. Optimal SCL at middle age compresses cardiovascular morbidity.
    - Obesity at middle age decreased life expectancy at age 50, by 4 years for males or females. Males or females with normal weight survive 5.4 or 5.6 years longer free of CVD at age 50 and 1.6 or 1.8 years less with CVD. Both obese males and females spend more years with CVD before age 82. Normal weight at middle age compresses cardiovascular morbidity.

7. Contributions made by the multivariate risk factor analysis are:
    - Fifty-year-old males with an optimal risk profile at middle age can expect to survive 6 additional years compared to the total male respondents in the FHS. This indicates that American male life expectancy could be extended by 6 years (i.e. male life expectancy would be 83 years) if males were all to belong to the optimal risk group between the ages of 30 and 50. Similarly, fifty-year-old females with an optimal risk profile at middle age, can expect to survive 5 additional years compared to the total female respondents in the FHS. This indicates that American females can expect to survive 5 years more (i.e. female life expectancy would become be 87 years) if they were all to belong to the optimal risk group between the ages of 30 and 50.
    - A 50-year-old man with an optimal risk profile can expect to live 17 years longer without cardiovascular disease than a member of the high-risk group. A woman of that age with an optimal risk profile can expect to survive 16 additional years free of cardiovascular disease.
    - Individuals who are free of CVD at age 50 have a lifetime probability of developing cardiovascular disease of 82 percent if they are a high-risk male, and 69 percent if they are female and belong to the high-risk group, and 38 or 35 percent if they belong to the optimal risk group.
    - High-risk profiles at adulthood shorten the duration of life, increase the lifetime probability of experiencing CVD, but extend the period of life spent with cardiovascular disease. An optimal risk profile importantly increases the number of years lived free of cardiovascular disease i.e. an optimal risk profile compresses the cardiovascular morbidity. Males with high-risk profiles spend more years with CVD before age 83 and females with high-risk profiles spend more years with CVD before age 81.

Limitations

This research had some limitations as well. The limitations are listed below:

1. To construct an MSLT for the cardiovascular disease or chronic disease, we need micro-level longitudinal information. The Framingham Heart Study is unique in its length of follow-up. However, the problem with the FHS is precisely its length; a very long follow-up study means that the first stages of data are very old, leading to questions about the validity for current populations. The innovative ways to combine other data sources will be a new area of research if policymakers wish to make decisions based on something other than cardiovascular disease.
2. We used longitudinal follow-up data on a historical cohort. The risk factors status and disease incidence changes over the time. However, we took this into account in different ways: smoking status throughout life (*Chapter* 6) and risk factor status between the ages 30-50 (*Chapters* 8 and 9). A key area of future

research will be to define risk factor status prior to outcome, taking into account changes in risk factor status over time. Defining risk factor status is almost impossible if there is more than one outcome, such as CVD and death, where smoking status is only defined at middle age and may represent status prior to CVD, but not death.

3. In modeling cardiovascular disease, we did not consider back transitions. Return transitions were possible in the model structures illustrated in *Chapter* 3, except for models 3(a) and 3(b). If such data is available, however, the method we have described could be used for any situation (as demonstrated in *Chapter* 5).
4. Disease severity, co-morbidity and the quality of life after having cardiovascular disease was not considered. However, we considered the fatal cases. Our conclusions regarding the compression of morbidity are restricted to cardiovascular morbidity and do not tell us whether these risk factors would also lead to a general compression of morbidity.
5. To measure the impact of risk factors, we mainly considered the major adult risk factors. Many of the established risk factors are acquired in childhood; exposures in foetal life, infancy, childhood, and adolescence, can strongly affect risk of chronic diseases later in life, such as cardiovascular diseases (WHO, 2002; Ben-Shlomo and Kuh, 2002). This was not considered in this study. However, we believe that our described novel approach can be applied for any population in the same fashion.

10.4 Implications for public health

In this research, we have initiated a new public health approach to the compression of morbidity debate, in which demographic techniques are coupled to the framework of epidemiology. We recommend using such methods to assess the health impact of risk factors and interventions. The life table approach can integrate the effect of risk factors (at a specific point or at different stages of life) on disease occurrences, age at developing disease, years lived with disease, years free of disease, lifetime risks of developing disease and mortality. This approach can provide a synthetic life course measure of population health status. Using short-term or long-term follow-up data this method can be used to reconstruct an individual biography (micro perspectives) or the age spectrum (population health perspectives). This method also provides the range of outcome measures necessary to better understand the individual and population health consequences of potential prevention or intervention of risk exposures. The life table indicators, such as those presented in this study, can help inform choices between strategies for improving the health of aging populations. These indicators are also important from the perspective of an individual making choices about a change in lifestyle.

The findings presented in this thesis indicate that people with a high risk profile at middle age spend much time with CVD and survive fewer years than those in the optimal risk group. Risk factors in middle age strongly affect lifetime CVD, which is why we suggest that more emphasis should be given to prevention prior to middle age. However, the effect of eradicating a risk factor cannot be simplistically thought to lead to less chronic disease in society or throughout life. The effect obviously differs for different risk factors. For instance, this study shows that the impact of smoking on cardiovascular morbidity is different from other major risk factors, such as serum cholesterol, blood pressure and body mass index. Therefore, in addition to the balance between increased risks of chronic disease, disability and mortality, a greater understanding of the role of risk factors throughout life is needed to decrease the burden of chronic disease, disability and mortality.

We recommend that the new indicators such as life expectancy with disease, life expectancy free of disease or lifetime probability of disease given the risk factor status at a specific age or at different stages of life, be taken into account when drafting public health campaigns. These types of indicators form the health benefits in the context of the life course and are more easily understood than traditional risk measures such as odds ratios or relative risks. Our approach offers a new tool with great potential for public health epidemiology. We need similar approaches to be applied to changes in risk factor status, to predict the most beneficial public health strategies.

10.5 Some future prospects

This study demonstrated that the multistate life table could be used as a tool to analyze the life history of cardiovascular disease and its risk factors. Using the same method, it would be possible to derive life course indicators in any other life course research. Adding health interventions, health care cost, health care quality, disease severity and co-morbidity to the illustrated multistate life tables, public health researchers, clinical decision makers and health policymakers can easily transfer the epidemiological or disease information into time–based health policy measures. Different risk factors have different treatments and health benefits. The number of health benefits from a certain treatment that could possibly be achieved could be an extension of our present study.

This study shows that the presence of any major (single or multiple) risk factor at middle age has enormous impact on the life history of cardiovascular morbidity in terms of lifetime probability of disease, number of years spent free of disease and number of years spent with disease. We observed that more than one third (38% for males and 35% for females) of the people who had optimal risk profiles as adults developed cardiovascular disease at older ages. This development could be

caused by other adult risk factors (e.g. diabetes), genetic factor, environmental factors, and aging itself. However, this study has demonstrated the methods and shown how to estimate the impact of risk factor status in disease incidence and mortality in terms of the life table outcomes. Therefore, when the information on other risk factors becomes available, it can be investigated in the same way. For instance, by combining the three Framingham generations (Framingham original cohort, Offspring cohort and third generation) and using our methodology, more insight and mechanisms could be gained into the life course of cardiovascular disease.

We did not investigate the mechanisms of why smoking was different from the other risk factors. This is something to be investigated in the future, using our methodology in order to identify characteristics of risk factors which predict whether they will be associated with compression or expansion of morbidity. We investigated only cardiovascular disease, but the risk factors of cardiovascular disease are also accountable for many other chronic diseases and disability (Norrish et al., 1995). However, using the same approach and with the appropriate data, we can analyze the life history of other chronic diseases and address the debate of compression of morbidity hypothesis.

The life course effects of smoking, obesity, hypertension and cholesterol have been evaluated in a stationary cohort life table; further research exploring the same methodology will be able to extend life course methodology to assess changes in the life course: quitting smoking, losing weight, changing diet, treating hypertension.

A recent study conducted in the United States found that, although serum cholesterol levels declined significantly during the period 1970s and 1980s across the population, no further decline in serum cholesterol has occurred over the past decade (Arnett et al., 2002). There have been upsetting trends in the health status of teenagers (Surgeon General, 2001), among whom there are troubling increases in the prevalence of cigarette smoking (Murray and Lopez, 1996), obesity (Mokdad et al., 2001; Fontaine et al., 2003; WHO, 1998) and decreases in participation in physical activity programs (Surgeon General, 1996). Recent investigation shows that southern Asia (representing one quarter of the world population) is likely to be more strongly affected by the increase in cardiovascular disease in the future (Nishtar, 2002). Therefore, globally, cardiovascular disease will play an ever-growing role as a major cause of morbidity and mortality (WHO, 2002; Hennekens, 1998; Murray and Lopez, 1996). Thus the alarming trends and backslide in the health status of growing teenagers, the risk factor profiles of young adults and the emerging pandemic of cardiovascular disease all underscore the critical need to intensify and to give high priority to more efficient prevention and treatment in public health.

10.6 Concluding remarks

Except for smoking, other major cardiovascular risk factors demonstrated that cardiovascular disease could be postponed by adopting a healthy life style. This was the second proposition of Fries' (1980) compression of morbidity hypothesis. Not smoking will not compress cardiovascular morbidity, but it will postpone it to older ages. Belonging to the optimal categories of blood pressure, optimal categories of serum cholesterol levels or normal weight at adult life compresses cardiovascular morbidity. Similarly, belonging to the combined optimal risk (optimal blood pressure, optimal cholesterol, normal weight and never smokers) profiles at middle age also compresses cardiovascular morbidity to a larger extent compared to the single risk factor.

In chronic disease modeling, our approach and the use of a life course indicator is new, and these provide very transparent outcomes that are public health policy relevant. This study also shows the health benefits of belonging to optimal risk profiles as an adult and the relationship of risk factor status to the compression of morbidity hypothesis. Since life course research is a new focus in scientific community, our described methodology can be use as a tool to measure the life course indicators, not only in public health but also in any other discipline.

With consistent application of the multistate life tables in public health research, the population health status, health care costs, quality of life and other dimensions of health could be measured. We need appropriate crucial prevention or intervention on major cardiovascular risk factors at middle age. This prevention or intervention will have the potential to bring about a significant reduction in long-term risk and to increase the number of years spent without cardiovascular disease in population health.

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