Probabilistic Models For Heart Disease And Related Conditions

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Abstract

The topic of this thesis is mortality and the prevalence in the UK of ischaemic heart disease (IHD) and stroke. In particular, we consider changes in each of these between 1981 and 2000 and quantify the extent to which these changes are due to known risk factors for heart disease: body mass index, diabetes, hypertension, hypercholesterolaemia.

Chatterjee *et al.* (2008a) presented a multiple state Markov model for the development of heart disease and stroke. We develop two parameterisations for this model, one consistent with the 1981 prevalences in the UK of all the risk factors, and IHD, stroke and mortality, and the other consistent with the 2000 prevalences. By taking the 2000-consistent model and then changing the parameters for a given risk factor back to those in the 1981-consistent model, we can quantify the effect on IHD, stroke and mortality if this risk factor had not changed. We also carry out this exercise changing combinations of risk factors.

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Glossary

Abbreviation	Meaning
BMI	Body Mass Index
DBP	Diastolic Blood Pressure
ELT	English Life Table
GLM	Generalized Linear Model
H'chol/HCHOL	Hypercholesterolaemia
HS	Hard Stroke
HSE	Health Survey for England
H'ten/HTEN	Hypertension
HW	Heriot-Watt
IHD	Ischaemic Heart Disease
LDL	Low Density Lipoprotein
MI	Myocardial Infarction
NHS	The National Health Service
OC	Original Cohort
ONS	Office for National Statistics
OS	Offspring and Spouse
SBP	Systolic Blood Pressure
TC	Total Cholesterol
TI	Transition Intensities

Table 1: List of abbreviations.

Chapter 1

Introduction

1.1 Introduction

The main aim of this thesis is to investigate the effect of changes in the risk factors for ischeamic heart disease (IHD) and stroke on the prevalence of IHD and stroke and on mortality rates. Mortality in the UK changed during the 20^{th} century (Willets *et al.*, 2004). Tables 1.1 and 1.2 show the number of deaths in England and Wales (ONS, 2011) in 1981 and 2000 for males and females, respectively. Table 1.3 shows the standardised number of deaths in 1981 to 2000 populations by sex and age group, for England and Wales. From the Table 1.3, we can see that if the 2000 populations experienced the same mortality rates, there will be higher number of deaths in 2000. These show that there are higher mortality rates in 1981 than 2000, as shown in Tables 1.1 and 1.2. For age group 55-64, the standardised numbers of deaths in 1981 are 47,685 for males and 26,188 for females so if the 1981 mortality rates continue to 2000, there will be 47,685 more deaths for males and 26,188 more deaths for females in 2000. We choose years 1981 and 2000 as the time period to be researched and the reason why we choose 1981 and 2000 will be explained in Section 1.5.

1.2 Trends in mortality rates

Willets *et al.* (2004) identified five factors leading to mortality improvements: the cohort effect, the ageing mortality improvement, increased uncertainty at younger

Age group	Male	Female
25-34	3181	1821
35-44	5535	3742
45-54	16889	10513
55-64	46858	27211
65-74	92189	62762
75-84	86774	103554

Table 1.1: Number of deaths in 1981 for males and females.

Age group	Male	Female
25-34	3849	1702
35-44	6135	3853
45-54	13355	9108
55-64	28003	17722
65-74	60801	42318
75-84	87449	89651

Table 1.2: Number of deaths in 2000 for males and females.

Age group	Male	Female
25-34	3407	1998
35-44	6959	4859
45-54	20855	13172
55-64	47685	26188
65-74	93120	56308
75-84	120859	116441

Table 1.3: Standardised number of deaths in 1981 to 2000 populations.

ages as there are many causes of death which are common to young adults, changes in smoking prevalence and widening social class differentials. For men in their 40s, the biggest contribution to the improvements came from heart disease, and for women from improvement in cancer mortality. Men and women in their 50s and 60s have the highest mortality improvement compared to other age groups. Over the period 1989 to 2001, mortality rates for men in their 50s improved the most among all age groups by 2.71% and improvement in heart disease mortality contributed two thirds of this change.

The mortality from cancer, heart disease and stroke has fallen very steadily (Willets *et al.*, 2004). For men, the greatest reduction came from heart disease mortality followed by cancer. Factors behind the improvements for heart disease include the reduction in smoking, improvement in diet, medical advances and drug treatments for cardiovascular disease. For women at these ages, mortality improvement is dominated by cancer rather than heart disease. This reflects the improvement in treatment for cancer, especially breast cancer.

The Office for National Statistics (ONS, 2011) stated that for men and women aged 65 to 79, the biggest cause of deaths in the UK in 2009 was IHD. For those aged 80 and above, IHD and stroke were the leading causes of death for men and women. These are the leading causes of deaths for men aged 35 to 64 while for women in this

age group, the leading cause is breast cancer. Between 1989 and 2001, the largest improvements in mortality rates happened to age group 60 to 69 for males with an improvement of 3.35% (Willets *et al.*, 2004). For the same age group, mortality from heart disease and stroke accounted for 2.08% from the total improvement. Mortality from heart disease decreased at a higher rate for men and women and there were large improvements for age group 40 to 64 between 1989 and 2000 (Appendix 1 in Willets *et al.*, 2004). There was also improvement in stroke mortality in the UK although the rate of fall is slower than for IHD. The risk factors associated with stroke are similar to those for IHD.

The trend over time for the mortality rates from IHD has decreased in North America and many Western Europe countries although for some countries at a slower rate. Cooper *et al.* (2000) concluded that IHD mortality is still declining in the US but at a slower rate than in the 1980s and stroke mortality has had a small decline since 1990. The age-adjusted IHD mortality rates in the US decreased by more than 3% per year between 1970 and 1990 and 2.7% between 1990 and 1997. In some developing countries, such as in Russia, the age-standardised death rate from IHD is 575 per 100,000 population in 1982 and increased to 835 per 100,000 population in 2002 (Allender *et al.*, 2007). In Europe, a reduction in age-standardised IHD mortality has been observed in most countries including Denmark, Netherlands, Norway and the UK. Romania, Poland and Bulgaria are examples of European countries with an increasing trend in age-standardised IHD mortality between 1965 and 1998 (Levi *et al.*, 2002). Among Asian countries that were mentioned by Levi *et al.* (2002), which are Hong Kong, Japan and Singapore, only Japan has a decreasing trend in age-standardised IHD mortality between 1965 and 1998.

1.3 The risk factors and significant events

IHD is the leading cause of death worldwide, followed by stroke (Murray & Lopez, 1997). The major risk factors associated with IHD and stroke, in addition to age, sex and smoking, are body mass index (BMI), diabetes, hypertension and hypercholesterolaemia. Full descriptions of these risk factors will be given in Section 2.3. Tables 1.4 and 1.5 show the observed prevalence rates in 1981 and 2000 for males and females, respectively, taken from Health Survey for England (2006). Prevalence rate

is defined as the total number of cases of a disease existing in a population divided by the total population. Shown in the tables are the prevalence of IHD and stroke for males and females in England and Wales in 1981 and 2000. The observed prevalence rates for some age groups have shown some improvements and for some age groups have shown an increase in the IHD observed prevalence rates from 1981 and 2000. The prevalence of IHD and stroke has not changed much for females where as the prevalance of IHD and stroke has generally increased for males, particularly for the 75-84 age group.

Despite the improvement in some of the risk factors, the levels of obesity and diabetes are experiencing an adverse trend. England (2009) reported that in 2007, almost a quarter of adults were classified as obese. There has been an overall increase in the prevalence of obesity since 1993. González *et al.* (2008) reported the rise in new cases of diabetes: "The rates of diabetes are increasing at a faster rate in the UK than they are in North America, where prevalence of the condition is one of the highest in the world".

Tables 1.4 and 1.5 show the prevalence of obesity (BMI > 30) for males and females from 1981 and 2000. We can see that the observed prevalence rates for obesity have been increasing over the time period for all age groups for both males and females.

The observed prevalence rates for diabetes have been increasing for most of the age groups from 1981 to 2000 and the observed prevalence rates are shown in Tables 1.4 and 1.5 for males and females, respectively. From the same tables, we see that the observed prevalence rates for hypertension (systolic blood pressure > 140 and diastolic blood pressure > 80) have decreased from 1981 to 2000 for most of the age groups for males and females. There are positive changes compared to diabetes and obesity that experienced an adverse trend. The observed prevalence rates for hypercholesterolaemia (total cholesterol > 200) are shown in Tables 1.4 and 1.5 for males and females, respectively, in 1981 and 2000. The observed prevalence rates for hypercholesterolaemia have shown some reduction from 1981 to 2000. These changes in risk factors will have an impact on the prevalence of IHD, stroke and on mortality rates. After being attacked with IHD and stroke, the crude risk of death was greatest in the first year of stroke and particularly in the first 30 days from onset (Hardie *et al.*, 2005). So it is a significant factor to be looked into. Sudden death is defined as

death from any cause within one month following myocardial infarction or stroke.

Age group	IHD		Stroke		Obesity		Diabetes		Hypertension		Hypercholesterolaemia	
	1981	2000	1981	2000	1981	2000	1981	2000	1981	2000	1981	2000
25-34	0.41	0.25	0.21	0.05	6.20	20.30	0.00	0.54	23.84	18.07	63.22	53.50
35-44	0.39	0.56	0.00	0.29	9.58	21.30	1.00	2.08	27.68	22.40	89.37	78.60
45-54	2.35	3.28	0.00	0.76	9.53	25.00	2.00	3.18	44.50	34.87	98.84	82.65
55-64	9.98	10.46	2.79	2.95	10.38	25.80	1.14	6.72	58.33	48.00	99.10	83.10
65-74	21.22	20.90	5.85	6.82	8.22	24.47	0.29	8.96	66.42	60.83	99.70	85.35
75-84	16.31	25.55	3.73	10.85	1.43	17.09	2.14	9.22	66.33	67.15	99.90	86.48

Table 1.4: Prevalence rates for males in 1981 and 2000.

Age group	IHD		Stroke		Obesity		Diabetes		Hypertension		Hypercholesterolaemia	
	1981	2000	1981	2000	1981	2000	1981	2000	1981	2000	1981	2000
25-34	0.10	0.12	0.1000	0.1606	7.74	15.73	0.00	0.78	7.52	6.70	61.14	55.09
35-44	0.30	0.31	0.4000	0.3372	9.04	19.15	1.43	1.14	14.70	10.87	70.10	69.66
45-54	1.30	1.82	0.9000	0.7378	13.43	24.21	1.00	2.00	32.07	24.32	83.91	81.41
55-64	3.50	4.69	2.3000	2.0262	16.09	29.27	0.50	3.74	51.05	42.83	96.93	91.63
65-74	10.00	10.26	4.2000	3.8681	18.66	30.09	1.71	7.32	65.72	58.80	97.26	92.77
75-84	19.30	17.60	10.7000	9.1081	16.31	23.31	0.80	7.52	71.37	69.01	98.80	96.01

Table 1.5: Prevalence rates for females in 1981 and 2000.

1.4 The IMPACT Model

The IMPACT Model (2007) attempts to explain the decline in IHD deaths between 1981 and 2000 in England and Wales. In particular, IMPACT examines how much of the decrease in the number of deaths in England and Wales between 1981 and 2000 could be attributed to medical and surgical treatments and how much to changes in cardiovascular risk factors. The mortality fall from the changes in risk factors is called the number of deaths prevented or postponed (DPPs). The model is validated by comparing the estimated and observed mortality decreases for men and women in each age group.The original IMPACT model is the Scotland IMPACT Model (Capewell *et al.*, 1999) which explains the decline in IHD deaths in Scotland between 1974 and 1994. Further development was achieved by adding new risk factors and new treatments in the English IMPACT Model.

To calculate the mortality fall attributable to a change in a risk factor, the formula used by the IMPACT Model (2007) to calculate the number of deaths prevented or postponed, DPPs, is:

$$DPPs = IHD\ deaths\ in\ 1981 \times risk\ factor\ decline \times \beta\ coefficient \tag{1.1}$$

where β coefficient is the value that quantifies the independent relationship between population change in specific risk factors such as smoking, blood pressure and cholesterol and the consequent change in population IHD mortality rate. The IMPACT Model employs the β coefficients that were obtained from large cohort studies and MONICA analyses (Kuulasmaa *et al.*, 2000). The β coefficients are obtained for specific IHD risk factors such as smoking, blood pressure and cholesterol. For other risk factors such as obesity, diabetes and physical activity, there were no suitable β coefficients that can describe the relationship so the IMPACT Model uses the relative risks. These relative risks were taken from the largest and most recent studies.

The β coefficient is used to calculate the mortality reduction as shown in Formula 1.1. For every percentage point fall in the risk factor, the IHD mortality is reduced by $\beta\%$. An example of the use of the β coefficient is smoking. Various studies show the impact of changes in risk factors on changes in IHD mortality. The best estimate for

the β coefficient for smoking is taken from Sigfusson *et al.* (1991). This is a study of IHD in Iceland and shows that every 1% fall in smoking prevalence will decrease the IHD mortality by 0.51%. Sigfusson *et al.* (1991) state that the change in risk factor for smoking for over 20 years is -29.3% for smokers who smoke 1 to 24 cigarettes daily (or cigars or pipe) and an increase of 3.6% for smokers who smoke more than 25 cigarettes daily. This makes the total fall in smoking risk factor equal to 25.7% (3.6 $-$ 29.3). It is also stated that this reduction decreased the risk of death from IHD by 8% in women and 13% in men. For men, a fall of 25.7% in smoking prevalence will decrease IHD mortality by 13%. The IMPACT Model uses this study as a reference to quantify the relationship for smoking.

As IHD mortality has been declining, this model explains how much of the decrease in the number of deaths in England and Wales between 1981 and 2000 can be attributed to medical and surgical treatments and how much to changes in cardiovascular risk factors. The IMPACT Model focuses on the reduction of risk factors and increases in medical and surgical treatment uptake to calculate the number of deaths prevented or postponed (DPPs).

The IMPACT Model has some limitations. There is a lack of transparency over the calculation of the mortality falls over 1981 and 2000 and the β coefficients are estimated from large studies from out of the UK. The model also lacks flexibility in terms of time period as we cannot just choose any time period that we want. The IMPACT Model also considers only IHD–related mortality and does not estimate the prevalence of IHD and stroke. The results in Unal *et al.* (2005) are not shown separately for males and females.

1.5 Aim of the thesis

The problems to be investigated in this thesis are how much of the changes in the prevalence of IHD/stroke is due to changes in each of the risk factors between 1981 and 2000 and how much of the reduction in mortality is due to changes in each of the risk factors between 1981 and 2000. We have chosen 1981-2000 as the period over which we will investigate changes as this is the period covered by the IMPACT model as explained in Section 1.4. We will focus on ages 45 to 84 last birthday. There are relatively few deaths and cases of IHD and stroke below age 45 and the upper age

limit, 84, is the same as the upper limit used for the IMPACT model (Unal *et al.*, 2005). To carry out this study, we need a model. This model is described in Chapter 2.

Chapter 2

The Model

2.1 Introduction

In this chapter, we describe the model we use to address the problem outlined in Section 1.5. The model is a multiple state model of an individual's lifetime, incorporating IHD and stroke and different levels of the risk factors for these events.

One approach to the study of multiple state models is using the transition intensities (TI) (Waters, 1984). By using the transition intensities, the natural setting for the multiple state models can be kept. As we are using stochastic modelling, any estimates of TIs derived from data will be subjected to random sampling variation. There will be a mean and variance matrix. Using the mean and variance matrix, multiple sets of parameters can be generated and we can use these to assess the impact of uncertainty by sampling the parameter space a number of times. These estimates will have a multivariate normal distribution. The TI approach can help to ascertain the variance of the estimator which can be used in situations if we want to smooth the parameter estimates while other approaches may not cope with this problem easily.

Waters (1984) explained the TI approach using the example in Figure 2.1. Transfer is possible between states 1 and 2. State 3 is an absorbing state where transfer from this state is not possible at all. This is a time continuous Markov chain with a finite state space. The conditional probabilities are defined as follows: ${}_tp_x^{gh}$ is the probability that the individual is in state h at age $x+t$ given that the individual was in state g at age x. The individual's state in the future depends only on the state at the present time and not on the previous history of the individual. The transition intensities are

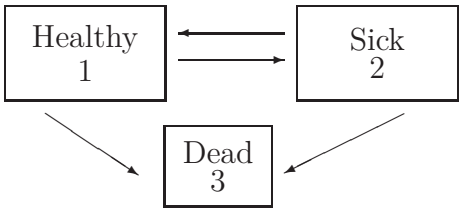

Figure 2.1: The basic structure for a 3 states model

then defined and from this, we can derive the probabilities for this model. Differential equations are derived and solved to calculate the transition probabilities.

Macdonald *et al.* (2005a) constructed a model for the development of IHD or stroke that either incorporates or includes pathways through the major risk factors of interest when underwriting for critical illness insurance. The model is useful in assessing the impact on insurance underwriting of genetic information relevant to IHD and/or stroke. It is a multiple state model with three absorbing states, which are IHD, stroke and dead. The remaining states are all transient. It has different combinations of the three risk factors, which are hypertension, hypercholesterolemia and diabetes. Sex, BMI and smoking are also taken as risk factors but are treated as static risk factors. The Macdonald *et al.* (2005a) model was parameterized using data from the Framingham Heart Study, Original Cohort data set, and the model does not allow for any backward transitions between categories of the risk factors. The method for estimating the transition intensities uses occurrence/exposure rates with an assumed Poisson distribution for the number of occurrences and a generalized linear model (GLM) with a log link to smooth the estimates. The intensities of moving between categories are calculated for diabetes, hypertension and hypercholesterolemia and are applied to those still alive who have not yet had an IHD event or a stroke.

Chatterjee *et al.* (2008a) further developed this model but did not focus on a specific insurance product. This model uses the same data as Macdonald *et al.* (2005a) but also includes the Framingham Offspring and Spouses data set to determine the structure of the model. Parameters for the transition intensities determined from the Framingham data were then adjusted by hand so that the model produces prevalence

rates consistent with the UK observed rates in 2003. Risk factors relevant to heart disease and stroke are incorporated in the model. It is different from the model developed by Macdonald *et al.* (2005a) since it includes BMI and allows backward transitions. Using this model, which we refer to as the Heriot-Watt Model (HW model), we can describe an individual's life history by having certain categories of risk factors and the effects of the risk factors moving from one level to another in the long term and we can compute the risk of having IHD and/or a stroke or death.

To produce results, the HW model requires an initial risk profile at the starting age to specify the distribution over the states in the model as mentioned in Chatterjee *et al.* (2008a). The initial profile is a disribution over the states of the model at the initial age. This model uses the observed prevalence rates from Sproston and Primatesta (2004) which are the HSE2003 observed prevalence rates for all risk factors except hypercholesterolaemia as the initial risk profile. For hypercholesterolaemia, the observed prevalence rates are taken from HSE1994 (Sproston and Primatesta, 2004).

The basic structure of the Chatterjee *et al.* (2008a) model is similar to Figure 2.1 where the healthy box is equivalent to "Event Free" and sick box is equivalent to "IHD and/or stroke". One difference is that it is not possible to transfer from "IHD and/or stroke" to "Event Free". There are 160 different states in the "Event Free" box and 1600 different states in the "IHD and/or stroke" box, one for each combination of the risk factors and the different IHD and/or stroke events.

2.2 Methodology

In detail, our aims in this thesis are:
(a) to consider the differences between the numbers of deaths in England and Wales in 1981, standardised to the population in 2000 (Table 1.3), and the actual numbers of deaths in 2000 (Table 1.2), and to determine the extent to which changes in the prevalence of IHD and stroke, their risk factors and changes in smoking patterns account for these differences, and,
(b) to determine the extent to which changes in the observed prevalence rates for the risk factors for IHD and stroke and changes in smoking patterns account for the difference between the observed prevalence rates for IHD and stroke from 1981 to 2000.

We choose 1981 to 2000 as our time interval because this is the time interval used by the IMPACT model to investigate point (a) above.

Our main tool for this investigation is the HW model (Chatterjee *et al.* (2008a)). This is a finite state space Markov model of a human lifetime where the states are all possible combinations of a set of (discretised) risk facors for IHD and stroke, together with combinations of conditions which constitute IHD or stroke and, finally, death. The risk factors for IHD and stroke we consider are:

(i) Obesity

(ii) Diabetes

(iii) Hypertension

(iv) Hypercholesterolaemia

The significant events which constitute IHD or stroke are:

(1) Myocardial infarction

(2) Angina pectoris

(3) Coronary insufficiency

(4) Hard stroke

(5) Transient ischaemic attack

The model is parameterised separately for males and females and the parameterisations depend on the (deterministic) smoking pattern throughout the individual's lifetime.

The model is a continuous time model, with time represented by the individual's age. Transitions between the states are governed by transition intensities, with the exception of sudden deaths from IHD or stroke, which are assumed to act immediately upon the occurrence of IHD or stroke and so are governed by probabilities. The transition intensities and probabilities of sudden death are functions of the individual's age, sex, smoking pattern and of their current state, in terms of risk facors and significant events; they are not functions of calendar time.

By placing the individual in a given starting state, i.e. combination of levels for the risk factors and significant events, at a given initial age, the model can be run forward to any later age, giving probabilities of being in any of the states. However, we will use the model to determine probabilities/prevalence rates for populations rather than individuals. We will do this by choosing a given starting age, sex, smoking pattern

and initial profile. The initial profile is a probability distribution over the states of the model and represents, for a given point in time, the proportion of the population in each of these states. Running the model forward we obtain for any later age/calendar time the prevalence of, for example, diabetes or IHD, and also the proportion of the population still alive.

We will use two different parameterisations of the HW model:

• a parameterisation which is consistent with observed prevalence rates in 1981 for the risk factors and significant events, and,

• a parameterisation which is consistent with observed prevalence rates in 2000 for the risk factors and significant events.

By changing the transition intensities for a given risk factor, or combination of risk factors, in the "2000 consistent" parameterisation to those from the "1981 consistent" parameterisation, we can quantify the effect on, say, the prevalence of IHD or the probability of death from 1981 to 2000 of the change in the risk factor(s).

Chatterjee *et al.* (2008a) produced a parameterisation of the HW model which is consistent with observed prevalence rates for the significant events and for different levels of each risk factor in England and Wales in 2003. They did this, to a large extent, by using data from the Framingham Heart Study (1948 - 1996) to produce an initial parameterisation and then manually adjusted this parameterisation so that the model produced prevalence rates consistent with England and Wales in 2003. Our approach will be to start with Chatterjee *et al.* 's (2008a) parameterisation and to adjust it manually to fit observed prevalence rates in England and Wales in 1981, and then separately in 2000. We will make use of some other data sources, particularly for estimating the probability of sudden death following the onset of IHD or stroke.

To produce either of these two separate parameterisations we need to calculate the prevalence rates produced by the HW model, and to do this we need to run it with an intial profile. Suppose, for example, we want an initial profile in 2000 for males aged 45 with a given smoking profile. The initial profile is the proportion of this part of the population in each of the states of our model. We can easily find data sources giving, for example, the proportion of the population in each of the categories of hypertension and, separately, the proportion in each of the categories of obesity. However, these are marginal distributions; what we need is the complete

multivariate distribution. i.e. the proportion of the population in each combination of the categories of hypertension and obesity, and the other risk factors. To achieve this we consider the marginal distributions for each risk factor and significant event for males aged 26 in 1981, with the given smoking profile. We then assume for simplicity that the distribution over each risk factor and significant event is independent of the other risk factors and significant events and run the model forward for 19 years. Running the model forward for 19 years gives prevalence rates in 2000 at age 45 which are not unduly influenced by the simplifying assumption at age 26. The parameters of the model can then be adjusted to achieve the required prevalence rates. The same procedure was used to produce the "1981 consistent" parameterisation using marginal distributions from 1961 and running the model forward for 20 years.

2.3 Description of the risk factors

The major risk factors, in addition to age, sex and smoking which are deterministic factors, are body mass index (BMI), diabetes, hypertension and hypercholesterolaemia. The risk factors are categorized into a small number of discrete levels as shown below:

- Diabetes: 2 levels shown in Table 2.1 where values are shown in two units, mg/dL and mmol/L,
- BMI: this is defined as Weight (kgs)/Height ($mtrs^2$). There are 5 levels as shown in Table 2.2,
- Hypertension: 4 levels determined by measurements of systolic (SBP) and diastolic blood pressure (DBP) as shown in Table 2.3. If the measurements of SBP and DBP indicate two different categories, the individual is assigned to the higher category of hypertension,
- Hypercholesterolaemia: 4 levels as shown in Table 2.4 where values are shown in terms of low density cholesterol (LDL) and total cholesterol (TC) in two units, mg/dL and mmom/L,
- Significant Events: the HW model has 11 conditions which are new myocardial infarction, angina pectoris, coronary insufficiency, transient ischaemic attack, new hard stroke, old myocardial infarction, old hard stroke, new hard stroke

from old myocardial infarction, new myocardial infarction from old hard stroke, old myocardial infarction and hard stroke, and dead.

Category	Term	Blood glucose (mg/dL)	Blood glucose (mmol/L)
0	Non-diabetic	< 126	< 7
1	Diabetic	≥ 126	≥ 7

Table 2.1: Categories of diabetes.

Category	Term	BMI
0	Underweight	≤ 18.5
1	Lightweight	18.5–25
2	Overweight	25–30
3	Obese	30–40
4	Morbidly Obese	> 40

Table 2.2: Categories of body mass index.

Category	SBP (mmHg)	DBP (mmHg)
0	< 120	< 80
1	120–139	80–89
2	140–159	90–99
3	≥ 160	≥ 100

Table 2.3: Categories of hypertension.

Category	LDL (mg/dL)	LDL (mmol/L)	TC (mg/dL)	TC (mmol/L)
0	< 130	< 3.362	$< 200 < 5.17$	
1	130–160	3.362–4.138	200–230	5.17–5.95
2	160–190	4.138–4.913	230–260	5.95–6.72
3	≥ 190	≥ 4.913	≥ 260	≥ 6.72

Table 2.4: Categories of hypercholesterolaemia.

2.4 Calculation procedures

The HW model involves the Kolmogorov forward differential equations in order to calculate the occupancy probabilities between states after the parameters are known and the initial risk profile is included in the model. The numerical solution to these Kolmogorov forward differential approximations is found by using the Runge-Kutta method of order 4 and we will do the calculations in C++. The Kolmogorov forward differential equations for this process starting in state a are

$$\frac{\partial}{\partial t}{}_tp_x^{aj} = -\sum_{k=0,k\neq j}^{n}({}_tp_x^{ak}\mu_{x+t}^{kj} - {}_tp_x^{aj}\mu_{x+t}^{jk}) \quad j = 0, 1, \ldots n \tag{2.1}$$

$$= {}_tp_x^{a0}\mu_{x+t}^{0j} + {}_tp_x^{a1}\mu_{x+t}^{1j} + \ldots + {}_tp_x^{an}\mu_{x+t}^{nj} \tag{2.2}$$

where we have written :

$$\mu_{x+t}^{ii} \stackrel{\text{def}}{=} -\sum_{k=0,k\neq i}^{n}\mu_{x+t}^{ik} \tag{2.3}$$

We can re-write these equations as:

$$\frac{\partial}{\partial t}{}_tp_x^{aj} = f_j(t; {}_tp_x^{a0}, {}_tp_x^{a1}, \ldots {}_tp_x^{an}) \tag{2.4}$$

where:

$$f_j(t; {}_tp_x^{a0}, {}_tp_x^{a1}, \ldots {}_tp_x^{an}) = {}_tp_x^{a0}\mu_{x+t}^{0j} + {}_tp_x^{a1}\mu_{x+t}^{1j} + \ldots + {}_tp_x^{an}\mu_{x+t}^{nj} \tag{2.5}$$

Let h be a given step size. For $j = 0, 1, \ldots n$ we calculate successively:

$$k_{1,j} = hf_j(t; {}_tp_x^{a0}, {}_tp_x^{a1}, \ldots, {}_tp_x^{an}) \tag{2.6}$$

$$k_{2,j} = hf_j(t + h/2; {}_tp_x^{a0} + k_{1,0}/2, {}_tp_x^{a1} + k_{1,1}/2, \ldots, {}_tp_x^{an} + k_{1,n}/2) \tag{2.7}$$

$$k_{3,j} = hf_j(t + h/2; {}_tp_x^{a0} + k_{2,0}/2, {}_tp_x^{a1} + k_{2,1}/2, \ldots, {}_tp_x^{an} + k_{2,n}/2) \tag{2.8}$$

$$k_{4,j} = hf_j(t + h; {}_tp_x^{a0} + k_{3,0}, {}_tp_x^{a1} + k_{3,1}, \ldots, {}_tp_x^{an} + k_{3,n}) \tag{2.9}$$

Then:

$${}_{t+h}p_{x_0}^{aj} \approx {}_tp_{x_0}^{aj} + (k_{1,j} + 2k_{2,j} + 2k_{3,j} + k_{4,j})/6 \tag{2.10}$$

We will model the probability of sudden death following myocardial infarction or stroke using the R statistical package.

2.5 Data Requirements

We will need data to build the initial risk profiles in 1961 and 1981. If these rates are not available, we will interpolate or extrapolate using available data. We also need information on the population of England and Wales and smoking rates for males and females for all age group. We discuss the data that will be used and the prevalence rates in 1981 and 2000 will be shown together with prevalence rates from other sources in Chapter 3.

For the initial risk profiles and observed prevalence rates, data will be taken from:

(i) The National Heights and Weights Survey 1980 (HWS80) for the prevalence of BMI.

(ii) The Health and Lifestyle Survey 1984-1985 (HALS84) for the prevalences of BMI, diabetes and hypertension.

(iii) Data from the Health Survey for England (HSE, 2006) show for each sex and in, mostly, 10–year age groups, the proportion of the population of England and Wales in 1994, 1998, 2003 and 2006 with diabetes, in each of 5 categories of

BMI, in each of 4 categories of hypertension, in each of 2 categories of hypercholesterolaemia and in each of 4 categories of 'significant event' ('Event free', MI, HS or MI+HS).

For the population of England and Wales, data will be taken from the Office for National Statistics (ONS). Whereas data for the smoking rates will be taken from the ONS (Robinson & Lader, 2007) which give the percentages of the population of England and Wales in 1981 who were current smokers, CS, ex–smokers, XS, or had never smoked, NS.

To model the probability of sudden deaths following myocardial infarction or stroke, we will use these data:

(i) Data from the Framingham Heart Study for the original cohort (OC) which started in 1948 for Exam 1 to Exam 20 in 1986.

(ii) Data from the Framingham Heart Study for the offspring and spouses cohort (OS) which started in 1971 for Exam 1 with further examinations average 6 years apart. We have the data up to Exam 6 which was done around 1997.

Finally, we will need data from the ONS that show the mortality rates in 1981 and 2000 from ELT14 (ONS, 2007) and ELT16 (ONS, 2009) for each sex and age.

2.6 Thesis Outline

In Chapter 3 we discuss the various data sources that we will use in this thesis as mentioned in Section 2.5 and combine the observed prevalence rates for all available years to compare.

In Chapter 4 we discuss the adjustments to sudden deaths that will be applied to the HW model. This is then followed by adjustments to the other risk factors to match the HW model with 1981 and 2000 observed prevalence rates in Chapter 5.

In Chapter 6, we analyse the effect of changes in the risk factors between 1981 and 2000 and calculate the number of IHD events, stroke events and deaths due to changes in the associated risk factors. We investigate the effect of changes in a single factor and then the effect of changes in combinations of risk factors. In Chapter 7 we state our conclusions and discuss further work to be researched. Throughout this

thesis the term 'rate' refers to prevalence rate for a risk factor (or mortality rate if appropriate), unless otherwise stated.

Chapter 3

Data

3.1 Introduction

As mentioned in Section 2.5, we need data to calculate the observed prevalence rates for independent initial risk profiles in 1961 (denoted as $\mathcal{P}_x^{ind1961}(i)$) and 1981 (denoted as $\mathcal{P}_x^{ind1981}(i)$) to run the HW model. We also need observed prevalence rates in 1981 and 2000. If these rates are not available, we will interpolate or extrapolate using available data. We discuss the data that will be used and the observed prevalence rates in 1981 and 2000 will be shown together with observed prevalence rates from other sources.

3.2 Different Sources of Data

For our study, we need data such as the population of England and Wales, smoking rates and observed prevalence rates for the risk factors. All data used in this study are explained below. We use these data to calculate the observed prevalence rates in 1981 and 2000.

(i) Data from the Office for National Statistics (ONS) show the mid–year population of England and Wales in 1981 for integer ages last birthday for each sex (ONS, 1981). Table 3.1 shows the population at selected ages for males and females.

(ii) Data from the ONS (Robinson & Lader, 2007) give the percentages of the population of England and Wales in 1981 who were current smokers, CS, ex–smokers,

XS, or had never smoked, NS. Corresponding figures are given for the year 2000. These percentages are given separately for each sex and in, mostly, 10–year age groups. They are presented here as Tables 3.2, 3.3 and 3.4. Using linear interpolation between the mid–points for each age group, we can estimate the proportion of the population of England and Wales for each smoking status, SS, categorised by single years of age x and sex G.

(iii) Data from the Health Survey for England (Sproston & Primatesta, 2004) show for each sex and in, mostly, 10–year age groups, the proportion of the population of England and Wales in 1994, 1998, 2003 and 2006 with diabetes, in each of 5 categories of BMI, in each of 4 categories of hypertension, in each of 2 categories of hypercholesterolaemia and in each of 4 categories of 'significant event' ('Event free', MI, HS or MI+HS). The categories for hypertension and hypercholesterolaemia are shown in Tables 3.5 and 3.6 for hypertension and hypercholesterolaemia. For diabetes and BMI, the categories follow the same definition as in the HW model, shown in Tables 2.1 and 2.2. The prevalence of hypertension are given in Table 7.16 from Sproston & Primatesta (2004) as the normotensive treated, normotensive untreated, hypertensive treated and hypertensive untreated rates. To find the observed prevalence rates based on the categories of hypertension defined in the HW model, we use the normotensive treated and normotensive untreated rates as equivalent to hypertension levels 0 and 1 and we use the hypertensive untreated and treated rates as equivalent to levels 2 and 3. The hypertensive rates given in Table 7.16 are defined as those with SBP $\geq$ 140 mmHg and DBP $\geq$ 90 mmHg. To separate the observed prevalence rates for levels 2 and 3, we use the extra information in Table 7.17 (Sproston & Primatesta, 2004) where it includes the observed prevalence rates for hypertensive with SBP $\geq$ 160 mmHg and DBP $\geq$ 95 mmHg which is equal to the rates for hypertension level 3, based on the HW model categories. So in order to get the observed prevalence rates for level 2, we substract the information for hypertensive untreated and treated rates in Table 7.16 with the rates in Table 7.17. For hypercholesterolaemia, we subtract from the observed prevalence rates where HSE defines hypercholesterolaemia as greater than 5.0mmol/l to get hypercholesterolaemia level 0 based on the HW model definition. Extra

information on the observed prevalence rates based on definition of hypercholesterolaemia in HSE98 (greater than 6.5mmol/l) will be hypercholesterolaemia level 3 in the HW model. Using linear interpolation between the mid–points for each age group, we can estimate the proportion of the population of England and Wales in each category for each risk factor separately, categorised by single years of age x and sex G. We denote these proportions for year n $\Pi_{Diab,n}(i_D \mid x, G)$, $\Pi_{BMI,n}(i_B \mid x, G)$, $\Pi_{Htens,n}(i_H T \mid x, G)$, $\Pi_{Hchol,n}(i_H C \mid x, G)$ and $\Pi_{SigEv,n}(i_S E \mid x, G)$, respectively. More precisely, i_D, i_B, i_{HT}, i_{HC} and i_{SE} are levels for diabetes, BMI, hypertension, hypercholesterolaemia and significant events, respectively. Tables 3.7 and 3.8 show the extrapolated risk profiles in 1981 and 1961 using available data from Health Survey of England (Sproston & Primatesta, 2004).

(iv) Data from the UK Data Archive (UKDA) such as the National Heights and Weights Survey 1980, the Health and Lifestyle Survey 1984-1985 and the Dietary and Nutritional Survey of British Adults 1986-1987 data sets should provide information on individuals in 1980 and 1986 categorised by age, sex, smoking status, diabetes, BMI, hypertension, hypercholesterolaemia and significant event. Using these data, we can categorise the observed prevalence rates using the same definition of the category levels as the HW Model as mentioned in Tables 2.1, 2.2, 2.3 and 2.4.

(a) The National Heights and Weights Survey 1980 (HWS80) represents the heights and weights among the adult population of Great Britain aged 16 and over. It is a one-time study with 10,018 respondents. Variables such as age, sex, weight and height are available in the dataset and this will allow us to calculate the prevalence of BMI by age and sex in 1980.

(b) The Health and Lifestyle Survey 1984-1985 (HALS84) was designed to describe self-reported health, attitudes to health and beliefs about causes of disease in relation to measurement of health and lifestyle in adults of Great Britain. This study is a longitudinal study for adults aged 18 and over in Great Britain in 1984−1985 with 9,000 respondents. The second follow–up survey was conducted in 1991−1992 (HALS91). HALS84 contains variables that are needed to find the prevalence of BMI, hypertension and diabetes

in 1984−1985. Measurements such as weight, height and blood pressure were taken during the visit by a nurse and questions on diabetes were also asked. For diabetes, the observed prevalence rates are calculated based on self-reported health. The question asked is if the respondent has any long-standing illness, disability or infirmity. The codes are 1 for 'yes, this condition is declared' and 9 for 'condition not declared' for diabetes.

(c) The Dietary and Nutritional Survey of British Adults 1986-1987 (DNS86) involved 1,775 adults in Great Britain, aged 16 to 64. It was a one-time study and the purpose was to produce data on food and nutrient intake, nutritional status, anthropometric and blood pressure measurements. Their body measurements were also taken, so we have data on their weight and height. Although this study enables us to calculate the prevalence of obesity and hypertension, the data are not given by age and sex. The study also provides analysis on urine, haematology, serum and plasma. This provides results on the total cholesterol level for each respondent and allows us to calculate the prevalence of hypercholesterolaemia by age and sex in 1986-87.

These data will be used to model the probability of sudden deaths following myocardial infarction and hard stroke which will be explained in Chapter 4:

(i) Data from the Framingham Heart Study for the original cohort (OC) which started in 1948 for Exam 1 to Exam 20 in 1986.

(ii) Data from the Framingham Heart Study for the offspring and spouses cohort (OS) which started in 1971 for Exam 1 with further examinations average 6 years apart. We have the data up to Exam 6 which was done around 1997.

The population data outlined in (i) and (ii) allow us to calculate (approximately):

$N_{1981}(x \mid G, SS)$, the population of England and Wales in 1981 categorised by age, sex and smoking status.

However, the data in (iii) do not allow us to split $N_{1981}(x \mid G, SS)$ by the level of each of the risk factors because the proportions in (iii) are not given separately for each smoking status.

Age	Male	Female
20	402.8	391.2
30	341.1	335.3
40	268.9	265.0
50	281.9	282.5
60	301.1	330.1
70	199.1	258.8

Table 3.1: Population of England and Wales in 1981 for selected ages (in thousands).

Age	Male (%)		Female (%)	
	1981	2000	1981	2000
20-24	42	35	40	35
25-34	43.5	39	40.5	32
35-49	42.5	31	40.5	27
50-59	44.5	27	42	28
60+	34	16	23	15

Table 3.2: Prevalence of current smokers.

Age	Male (%)		Female (%)	
	1981	2000	1981	2000
20-24	9	7	9	11
25-34	19.5	12	14.5	13
35-49	30.5	20	14.5	19
50-59	37.5	36	19	24
60+	46	52	19	29

Table 3.3: Prevalence of ex–smokers.

Age	Male (%)		Female (%)	
	1981	2000	1981	2000
20-24	49	58	51	54
25-34	37	49	45	54
35-49	27	49	45	54
50-59	18	37	39	48
60+	20	32	58	56

Table 3.4: Percentage who have never smoked.

3.3 Risk Factors Prevalence Rates

We use the data mentioned in the previous section and here we discuss how the observed prevalence rates for each risk factor in 1981 and 2000 are calculated.

Category	Definition
Normontensive untreated	SBP $<$ 140 mmHg and DBP $<$ 90 mmHg, not currently taking drug specifically prescribed to treat their high blood pressure.
Normontensive treated	SBP $<$ 140 mmHg and DBP $<$ 90 mmHg, currently taking drug specifically prescribed to treat their high blood pressure.
Hypertensive treated	SBP $\geq$ 140 mmHg and DBP $\geq$ 90 mmHg, not currently taking drug specifically prescribed to treat their high blood pressure.
Hypertensive untreated	SBP $\geq$ 140 mmHg and DBP $\geq$ 90 mmHg, not currently taking drug specifically prescribed to treat their high blood pressure.

Table 3.5: Categories of hypertension.

Category	TC (mmol/l)
H'chol HSE03	≥ 5.0
H'chol HSE98	≥ 6.5

Table 3.6: Categories of hypercholesterolaemia.

Risk factor	Male					Female				
	20-24	25-34	35-44	45-54	55-64	20-24	25-34	35-44	45-54	55-64
Diabetes										
0	100	100	100	100	99	100	100	100	99.9	99.8
1	0	0	0	0	1	0	0	0	0.1	0.2
BMI										
0	1.1	3.4	0.0	0.0	1.3	2.9	2.6	2.6	2.3	1.3
1	74.6	70.9	64.0	47.0	40.9	76.8	86.1	76.5	62.1	39.3
2	24.3	25.7	36.0	51.5	53	20.3	11.3	20.8	35.3	46.8
3	0.0	0.0	0.0	0.9	0.2	0.0	0.0	0.2	0.3	12.6
4	0.0	0.0	0.0	0.2	0.0	0.0	0.0	0.0	0.0	0.0
H'ten										
0	20	24	20	9	5	2	3	4	1	3
1	25	25	20	8	6	78	65	58	22	7
2	48	38	40	45	44	15	24	28	45	45
3	7	13	20	38	45	5	8	10	32	45
H'chol										
0	15	8.8	1.4	3.6	2	26.3	30	26.1	8.5	2
1	35	10	7.9	5.7	4	32	25	23.9	10.5	10
2	35	39	35	30.5	25	33.6	40	47	25	12
3	15	42.2	55.7	60.2	69	8.1	5	3	56	76
Events										
¨ Event free¨	99.9	99.7	99.4	89.4	85.5	100	99.5	99.3	92.9	92.6
MI	0	0.2	0.5	5	6.3	0	0.2	0.3	6.8	6.9
HS	0.1	0.1	0.1	3.6	4.9	0	0.2	0.2	0.1	0.2
MI + HS	0	0	0	2	3.3	0	0.1	0.2	0.2	0.3

Table 3.7: Risk profiles by categories (percentages) in England and Wales in 1961.

Risk factor	Male					Female				
	20-24	25-34	35-44	45-54	55-64	20-24	25-34	35-44	45-54	55-64
Diabetes										
0	100	99.1	99.1	99.1	97.3	100	100	100	100	97.3
1	0	0.9	0.9	0.9	2.7	0	0	0	0	2.7
BMI										
0	3.3	2.2	0.2	0.7	0.4	4.5	2.4	1.9	1.5	1.3
1	69.1	60.7	49.5	40.1	40.7	71.1	70.7	63.0	53.0	36.4
2	25.1	35.1	44.2	53.1	55.5	21.0	19.8	25.5	37.5	41.8
3	2.5	2.0	6.1	1	3.4	3.2	6.6	9.2	14.5	19.3
4	0.0	0.0	0.0	0.0	0.0	0.2	0.5	0.4	0.0	1.2
H'ten										
0	34.2	32.2	30.2	20.8	12.8	7.6	9	10	2	5.6
1	32.2	31.2	30.3	20.6	6.9	79	78	72	48.6	18.4
2	31.9	29.9	27.9	35.2	39.7	13.4	12	14	33	37.8
3	1.7	6.7	11.6	23.4	40.6	0	1	4	16.4	38.2
H'chol										
0	58.9	34.8	10.6	11.3	5	47.8	38.9	29.9	16	3.1
1	18.3	19.8	21.4	19.2	19.5	22.7	21.2	19.8	15.2	11.7
2	19.6	23.7	27.8	23.5	24.5	23.8	31.9	40.1	27.8	14.3
3	3.2	21.7	40.2	46	51	5.7	8	10.2	41	70.9
Events										
¨ Event free¨	100	99.9	99.7	99.4	88.3	100	100	99.9	99.8	92.8
MI	0	0	0.2	0.5	7.8	0	0	0	0.1	6
HS	0	0.1	0.1	0.1	2.6	0	0	0.1	0.1	0.1
MI + HS	0	0	0	0	1.3	0	0	0	0	0.2

Table 3.8: Risk profiles by categories (percentages) in England and Wales in 1981.

3.3.1 Body Mass Index

For BMI observed prevalence rates, we will interpolate the 1981 observed prevalence rates using the HWS80 and HALS84 observed prevalence rates. The data are taken from the measurements for heights and weights during a nurse visit. These should provide reliable data to calculate the BMI observed prevalence rates in 1980 and 1984, respectively, for each age and sex. The observed prevalence rates for 2000 are taken from the Adult Trend Tables 2006 (NHS, 2006).

Figures 3.1, 3.2 and 3.3 show the observed prevalence rates for BMI level 0 for males taken from Framingham Study exams 1 to 6, UK data sources and UK data sources and Framingham exam 3 (1981), respectively. Figures 3.16, 3.17 and 3.18 show the same graphs for females. In the Framingham Study, there was no clear trend in the prevalence of BMI 0 over time for males and females. Figures 3.4 and 3.5 show the observed prevalence rates for BMI level 1 for males taken from Framingham Study exams 1 to 6 and UK data sources, respectively. Figure 3.6 shows the observed prevalence rates from UK data sources together with the Framingham exam 3 (1981). For females, these are shown in Figures 3.19, 3.20 and 3.21. Prevalence of BMI levels 0 and 1 in the UK are higher than in the Framingham Study for the same time period as we can see in Figure 3.3, where the observed prevalence rates in Exam 3 are lower than the interpolated 1981 observed prevalence rates. The observed prevalence rates for BMI level 1 for males and females decreased over time in Framingham and in the UK. The same trend can also be seen in BMI level 2 in Figures 3.7 and 3.8 for males and 3.22 and 3.23 for females for Framingham Study observed prevalence rates and UK data sources observed prevalence rates.

An increasing trend can be seen in BMI level 3 in the Framingham and UK observed prevalence rates in Figures 3.10 and 3.11 for males and Figures 3.25 and 3.26 for females. There is no clear trend for BMI level 4 for males in the Framingham observed prevalence rates, shown in Figure 3.13, but increasing trends are shown in Figure 3.14 for males and Figures 3.28 and 3.29 for females. Although the 1981 observed prevalence rates from the interpolation do not have the same level as the observed prevalence rates from Framingham Exam 3 for males, which are from the same year, the observed prevalence rates from HWS80 and HALS84 are reliable and follow the same trend as the HSE observed prevalence rates. Figures 3.21, 3.24, 3.27

and 3.30 for females show that the Framingham observed prevalence rates in Exam 3 are quite close to the observed prevalence rates in the 1980s except for level 0 in Figure 3.18.

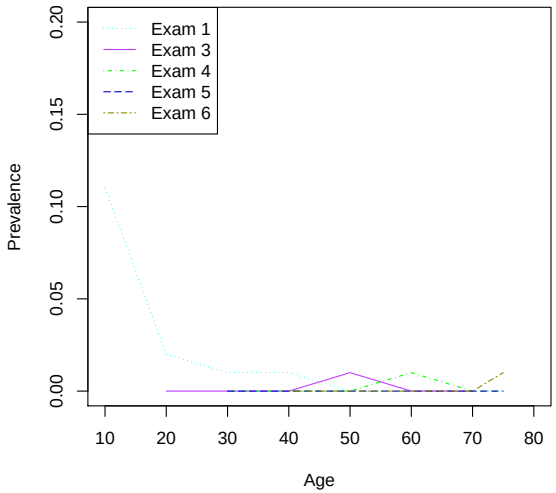

Figure 3.1: Prevalence of BMI level 0 for males in Framingham.

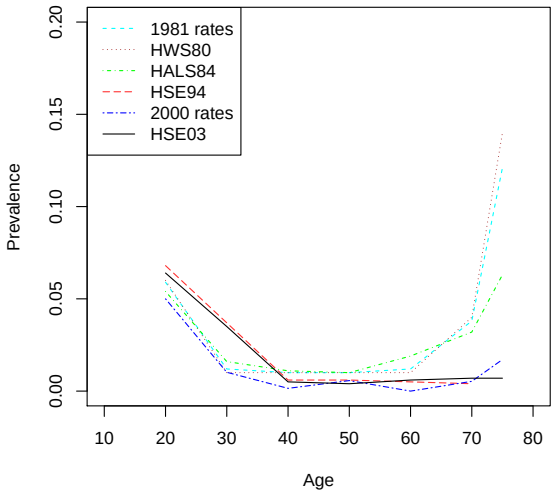

Figure 3.2: Prevalence of BMI level 0 for males in the UK.

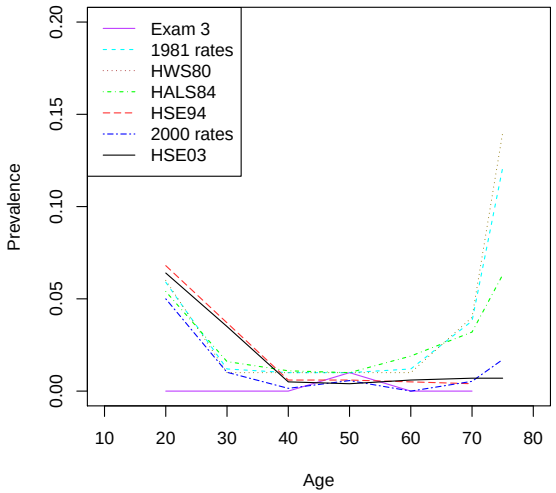

Figure 3.3: Prevalence of BMI level 0 for males in the UK and Framingham.

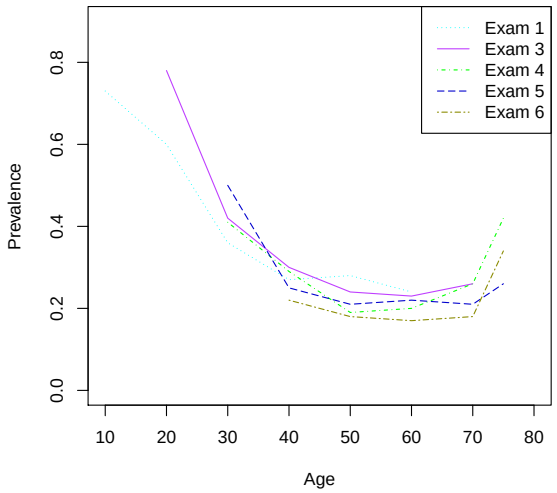

Figure 3.4: Prevalence of BMI level 1 for males in Framingham.

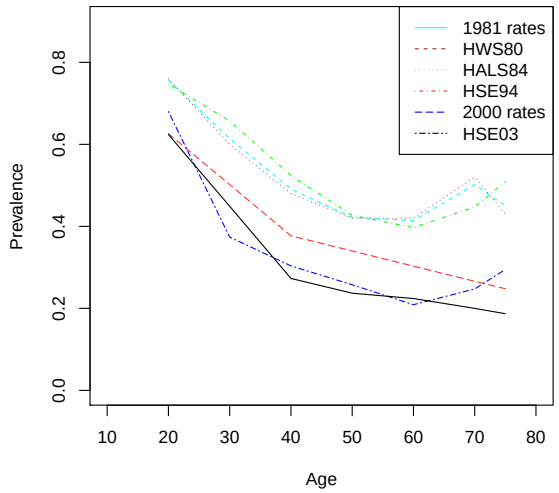

Figure 3.5: Prevalence of BMI level 1 for males in UK.

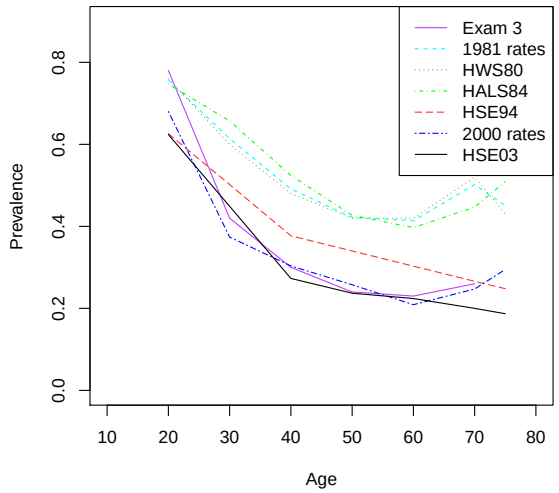

Figure 3.6: Prevalence of BMI level 1 for males in UK and Framingham.

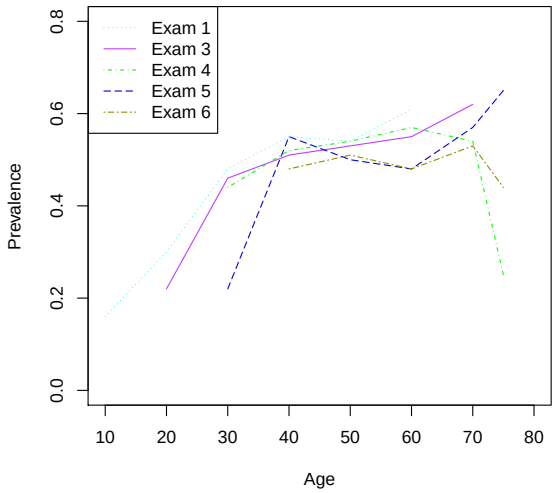

Figure 3.7: Prevalence of BMI level 2 for males in Framingham.

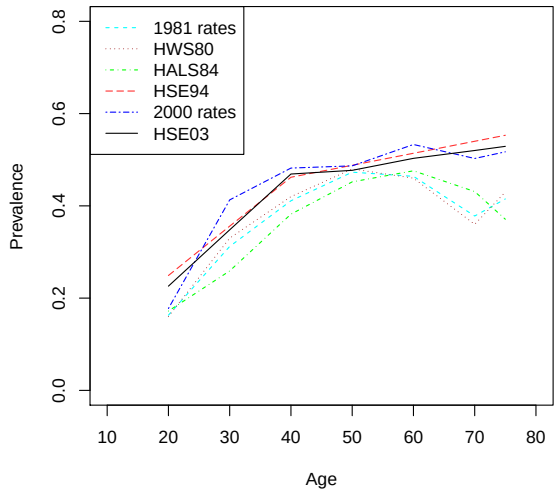

Figure 3.8: Prevalence of BMI level 2 for males in the UK.

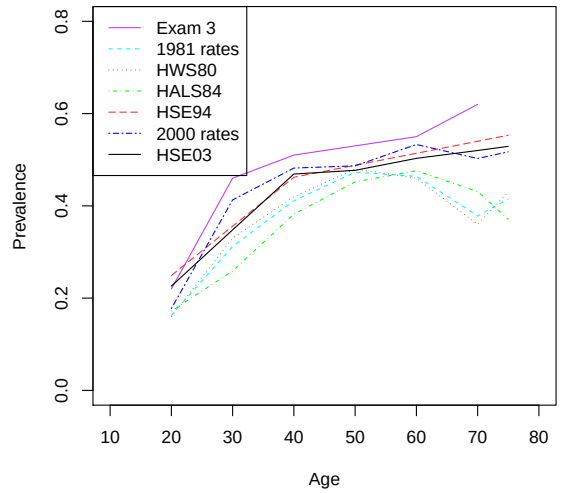

Figure 3.9: Prevalence of BMI level 2 for males in the UK and Framingham.

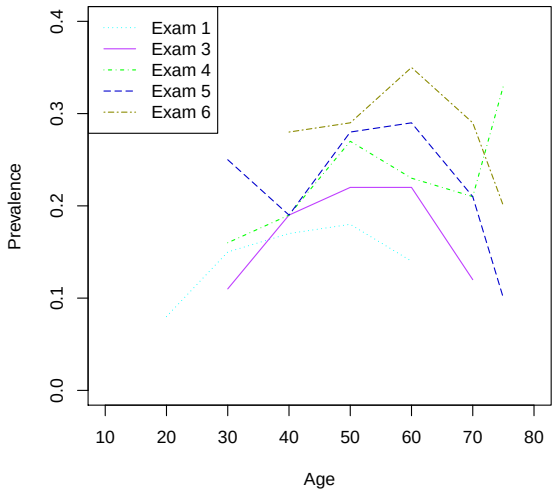

Figure 3.10: Prevalence of BMI level 3 for males in Framingham.

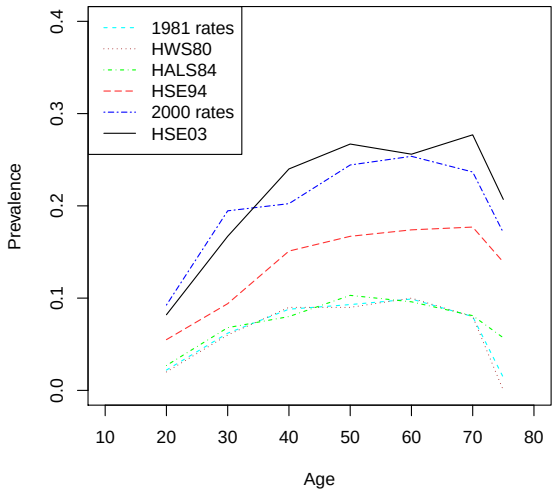

Figure 3.11: Prevalence of BMI level 3 for males in the UK.

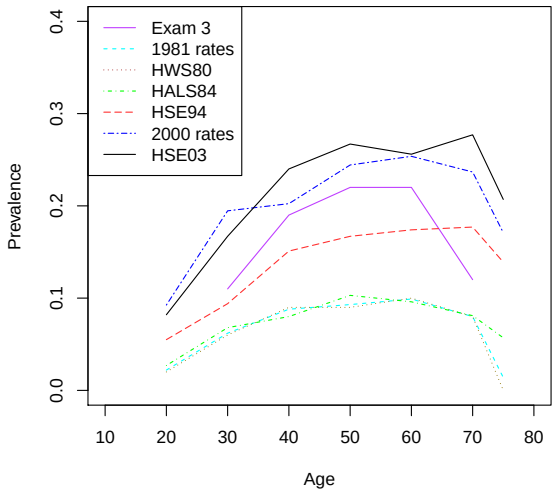

Figure 3.12: Prevalence of BMI level 3 for males in the UK and Framingham.

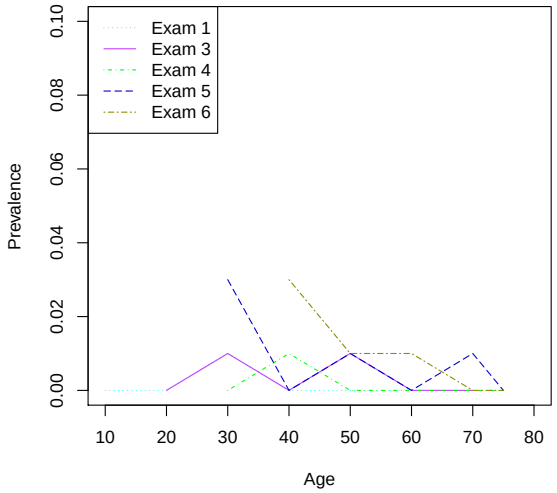

Figure 3.13: Prevalence of BMI level 4 for males in Framingham.

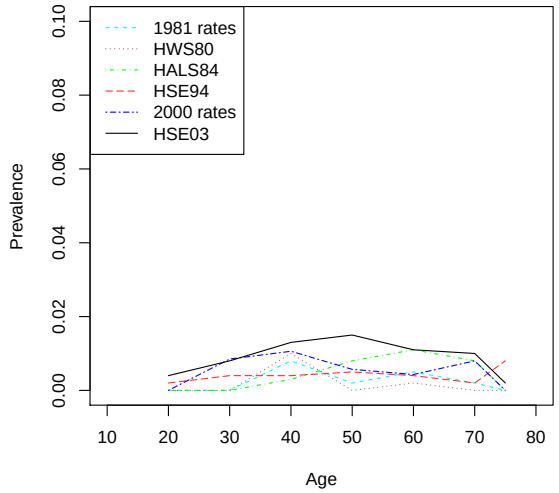

Figure 3.14: Prevalence of BMI level 4 for males in the UK.

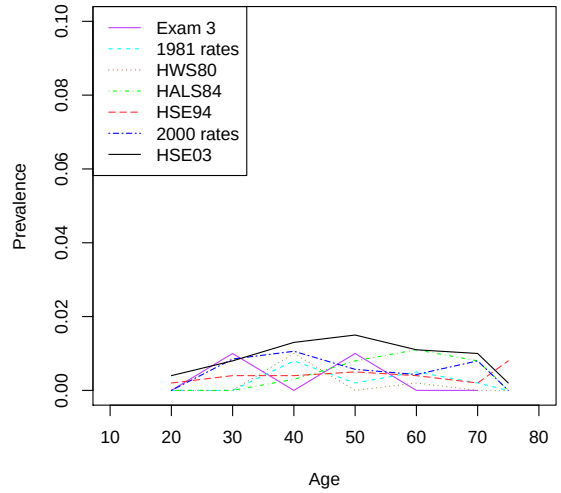

Figure 3.15: Prevalence of BMI level 4 for males in the UK and Framingham.

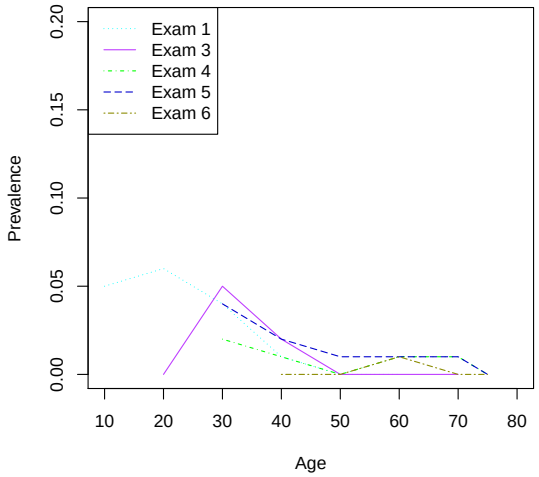

Figure 3.16: Prevalence of BMI level 0 for females in Framingham.

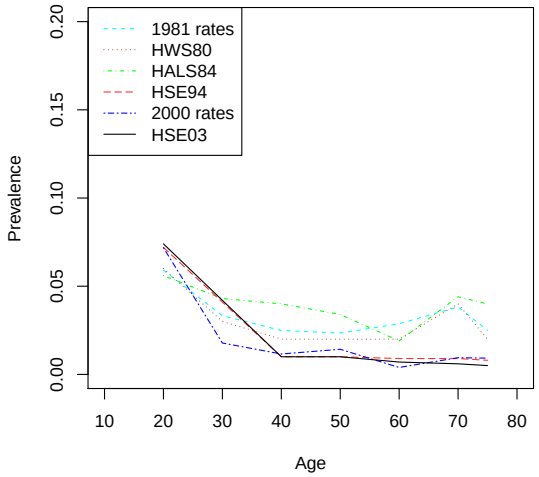

Figure 3.17: Prevalence of BMI level 0 for females in the UK.

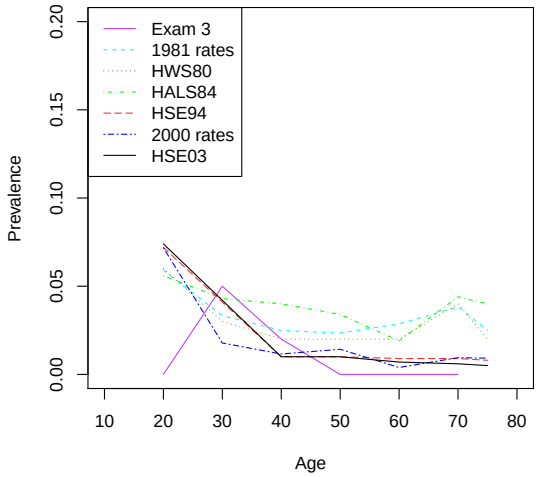

Figure 3.18: Prevalence of BMI level 0 for females in the UK and Framingham.

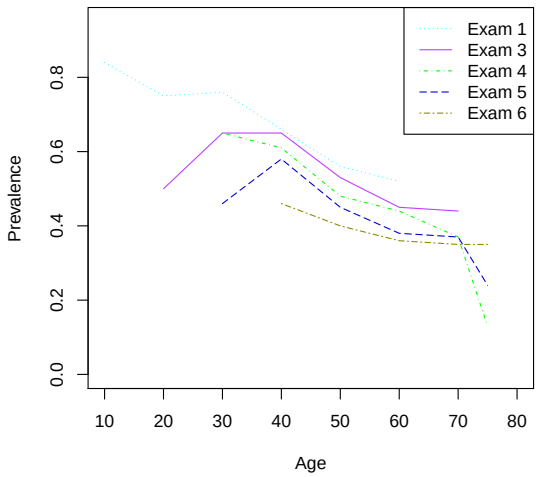

Figure 3.19: Prevalence of BMI level 1 for females in Framingham.

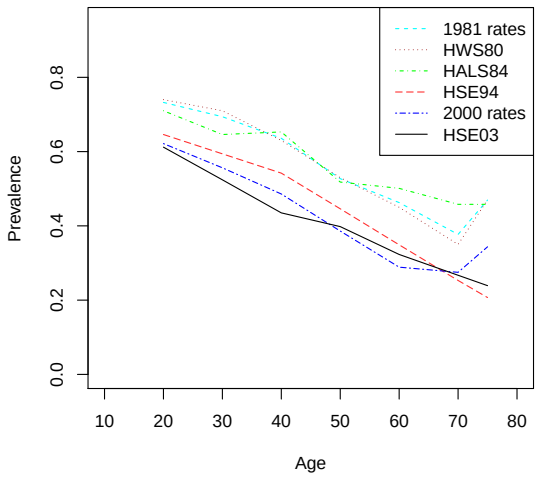

Figure 3.20: Prevalence of BMI level 1 for females in the UK.

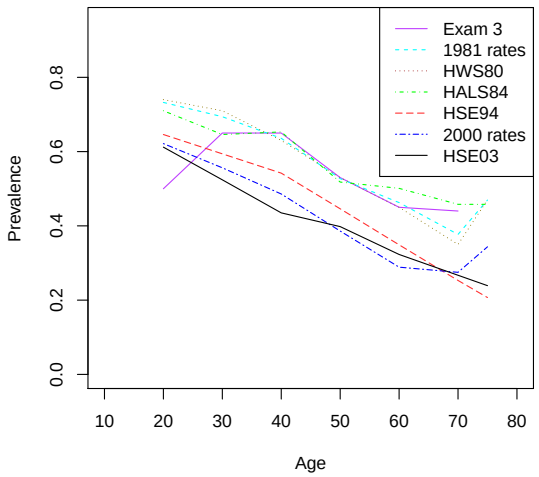

Figure 3.21: Prevalence of BMI level 1 for females in the UK and Framingham.

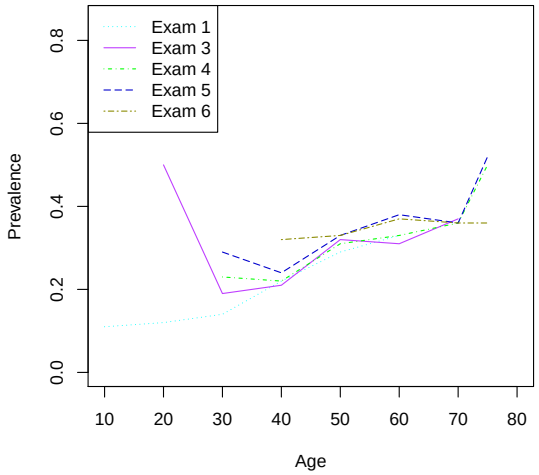

Figure 3.22: Prevalence of BMI level 2 for females in Framingham.

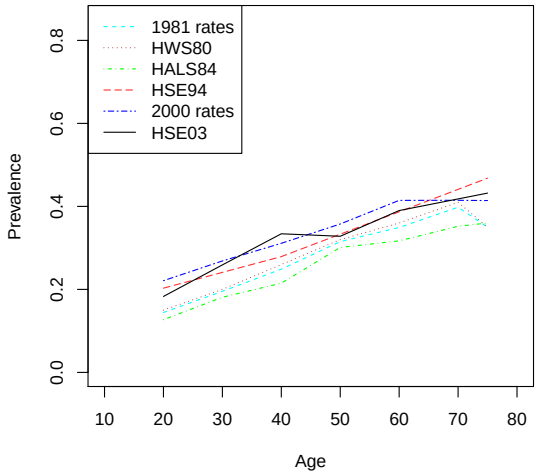

Figure 3.23: Prevalence of BMI level 2 for females in the UK.

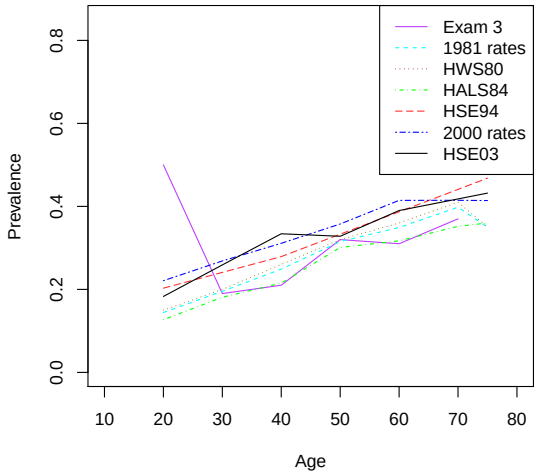

Figure 3.24: Prevalence of BMI level 2 for females in the UK and Framingham.

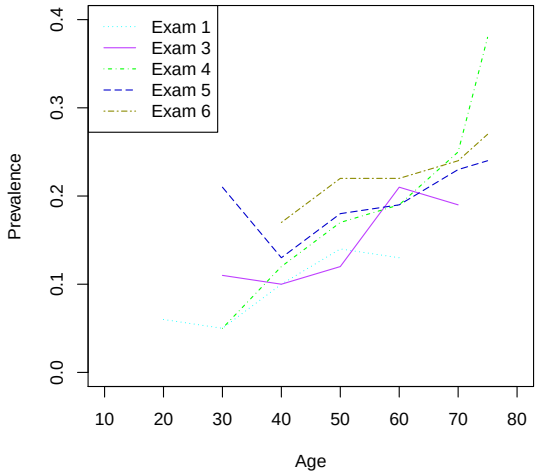

Figure 3.25: Prevalence of BMI level 3 for females in Framingham.

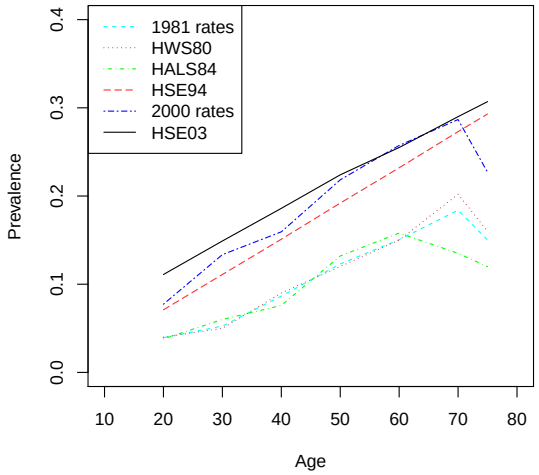

Figure 3.26: Prevalence of BMI level 3 for females in the UK.

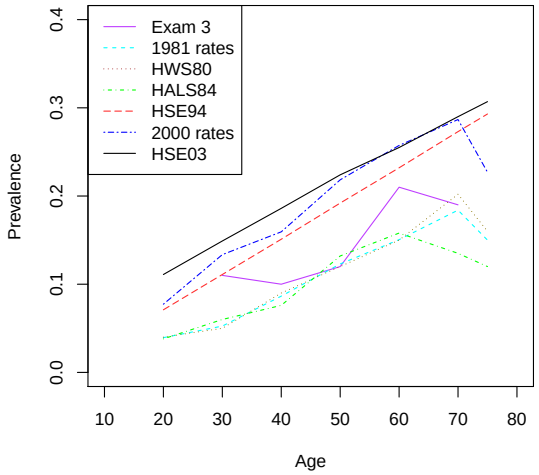

Figure 3.27: Prevalence of BMI level 3 for females in the UK and Framingham.

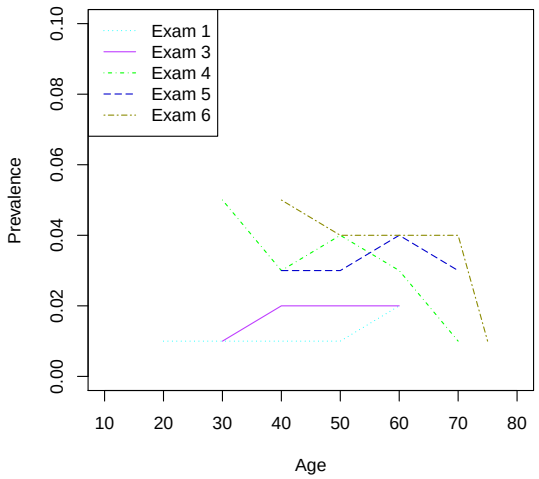

Figure 3.28: Prevalence of BMI level 4 for females in Framingham.

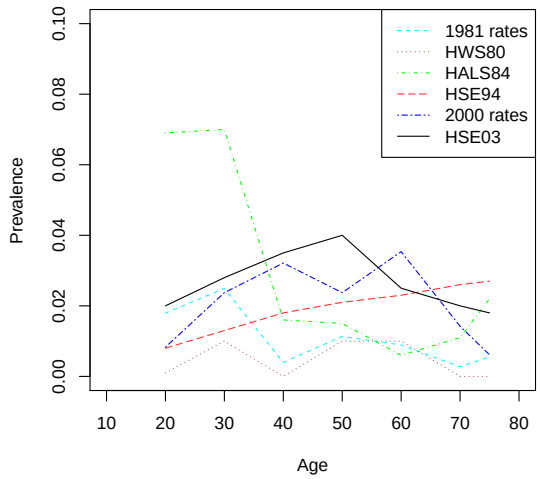

Figure 3.29: Prevalence of BMI level 4 for females in the UK.

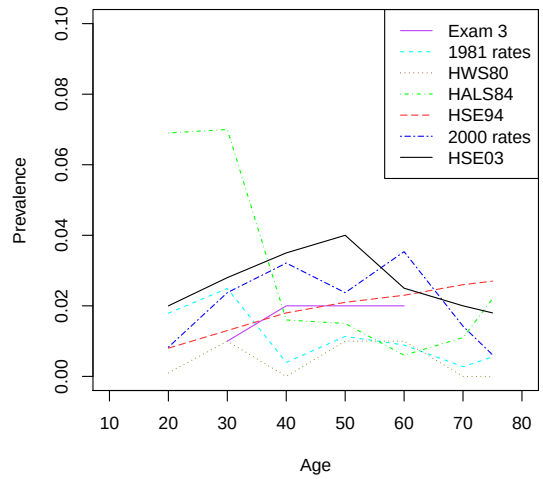

Figure 3.30: Prevalence of BMI level 4 for females in the UK and Framingham.

3.3.2 Diabetes

For diabetes, we have data from the Health and Lifestyle Survey 1984-1985 (HALS84) where diabetes is a self-reported condition. This is also the same as in the Health Survey for England (HSE). We use these observed prevalence rates as HLS84 has the same condition as HSE and it also follows the same trends as HSE and Framingham. As we only have one dataset for diabetes that represents the 1980s, we extrapolate the 1981 observed prevalence rates using HALS84 and HSE1991.

Figures 3.31, 3.32 and 3.33 show the diabetes rates from Framingham Study, UK data sources and UK data sources and Framingham Study Exam 3, respectively. No clear time trend can be seen from Figure 3.31 but we can see an increasing trend over time in the UK data sources observed prevalence rates. Figures 3.34, 3.35 and 3.36 are the observed prevalence rates for females and follow the same trend as males. Figures 3.31 and 3.36 show that the observed prevalence rates from Framingham Study Exam 3 that took place in 1981 are higher than the 1981 observed prevalence rates that we have extrapolated from HALS84 and HSE91. However, for diabetes, we use data from HALS84 and HSE91 as the data are reliable. For the observed prevalence rates in 2000, we interpolate the HSE observed prevalence rates which are available in 1998 and 2003 in NHS (2006).

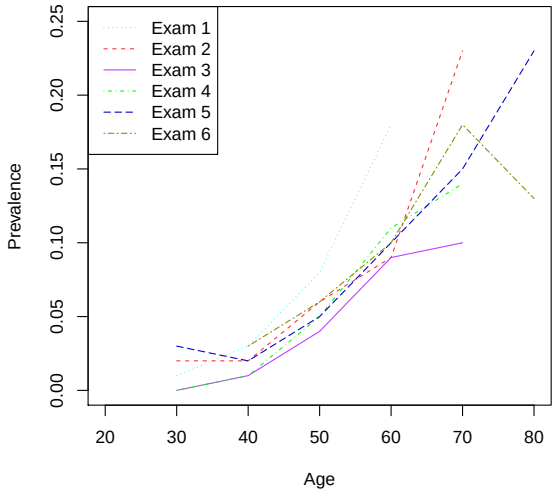

Figure 3.31: Prevalence of diabetes for males in Framingham.

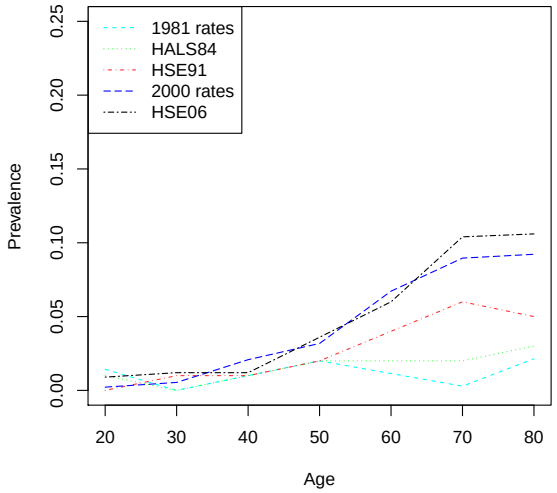

Figure 3.32: Prevalence of diabetes for males in the UK.

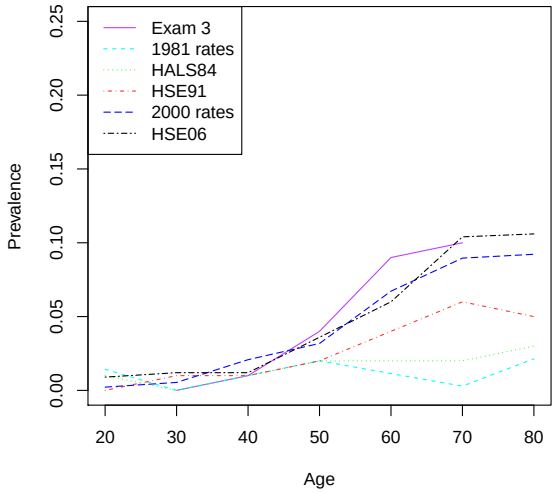

Figure 3.33: Prevalence of diabetes for males in the UK and Framingham.

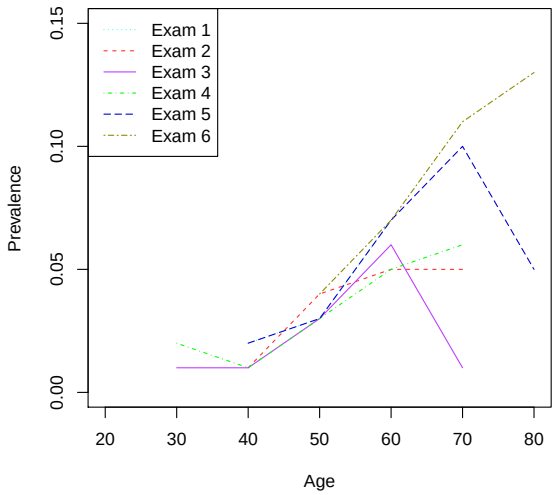

Figure 3.34: Prevalence of diabetes for females in Framingham.

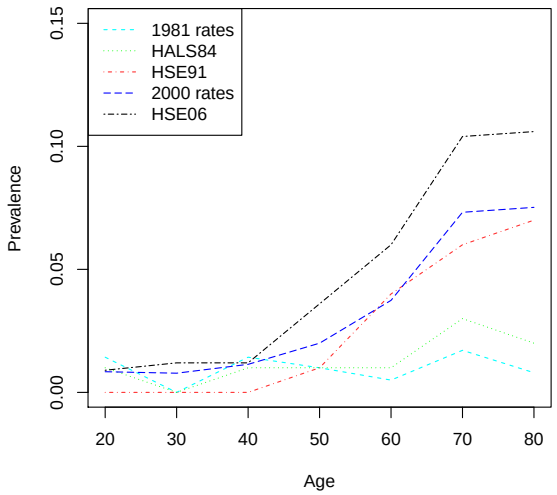

Figure 3.35: Prevalence of diabetes for females in the UK.

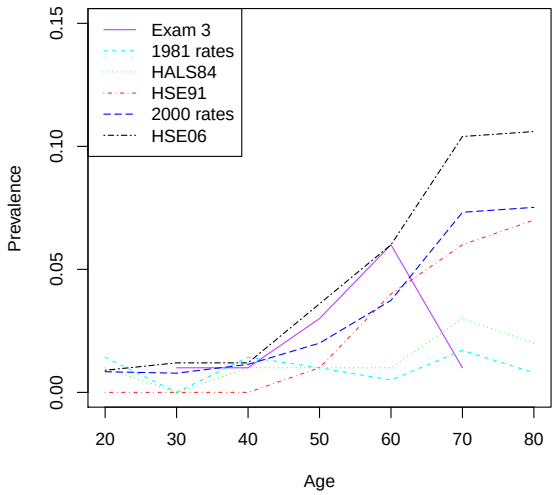

Figure 3.36: Prevalence of diabetes for females in the UK and Framingham.

3.3.3 Hypertension

For hypertension, we will use data from HALS84 and HALS91 to extrapolate the 1981 observed prevalence rates. Although the trend over time is not consistent with HSE as shown in Figures 3.41 and 3.44, these surveys are reliable to represent the trend and observed prevalence rates in the 1980s. Some rates are also consistent with the Framingham observed prevalence rates for Exam 3 which was carried out in 1981. For 2000 observed prevalence rates, we interpolate the observed prevalence rates from HSE94 and HSE03 taken from Sproston & Primatesta (2004) for males and females.

Figures 3.37, 3.38 and 3.39 show the observed prevalence rates for hypertension level 0 from Framingham Study Exams 1 to 6, UK data sources and UK data sources and Framingham Exam 3, respectively. Increasing trend over time can be seen in Figures 3.37 and 3.38. The Exam 3 observed prevalence rates from the Framingham Study (1981) is higher than the 1981 observed prevalence rates in the UK, as shown in Figure 3.39. Hypertension level 1 observed prevalence rates for males are shown in Figures 3.40, 3.41 and 3.42 from Framingham Study Exams 1 to 6, UK data sources and UK data sources and Framingham Exam 3, respectively. As mentioned before, the UKBA observed prevalence rates have different trends than the HSE observed prevalence rates and the 1981 Exam 3 observed prevalence rates from the Framingham Study are close to UK observed prevalence rates in 2000 which can be seen in Figures 3.41 and 3.42, respectively.

Figure 3.43 shows the observed prevalence rates for level 2 from the Framingham Study and we can see there is a decreasing trend over time. The trend is similar to the trend in HSE observed prevalence rates as shown in Figure 3.44 and we can see in Figure 3.45 that the Exam 3 observed prevalence rates from the Framingham Study are close to the observed prevalence rates in 1980s. Figures 3.46, 3.47 and 3.48 show the observed prevalence rates for hypertension level 3 from Framingham Study Exam 1 to 6, UK data sources and UK data sources and Framingham Exam 3, respectively. A decreasing trend over time can be seen in Figures 3.46 and 3.47 but the observed prevalence rates in Exam 3 from the Framingham Study are lower than the UK observed prevalence rates, as shown in Figure 3.48.

The increasing trend over time for level 0 is also similar for females as shown in Figure 3.49 and in the HSE observed prevalence rates in Figure 3.50. Exam 3 observed

rates from the Framingham Study have similar trends as the UKBA observed rates, shown in Figure 3.51. Figures 3.52, 3.53 and 3.54 show the observed prevalence rates for hypertension level 1 for females from Framingham Study Exam 1 to 6, UK data sources and UK data sources and Framingham Exam 3, respectively. There is a decreasing trend shown in Figure 3.52 and the trend over age for UKBA observed prevalence rates is similar to Exam 3 observed prevalence rates from the Framingham Study, shown in Figure 3.54.

Figures 3.55, 3.56 and 3.57 show the observed prevalence rates for hypertension level 2 and Figures 3.58, 3.59 and 3.60 show the observed prevalence rates for hypertension level 3 from Framingham Study Exams 1 to 6, UK data sources and UK data sources and Framingham Exam 3, respectively. The trends between the UKDA observed prevalence rates are similar to HSE observed prevalence rates and Exam 3 observed prevalence rates from the Framingham Study for levels 2 and 3, but the levels are different. As we can see from Figures 3.56 and 3.59, the 1980s observed prevalence rates are in between with observed prevalence rates from HSE94 and HSE2000.

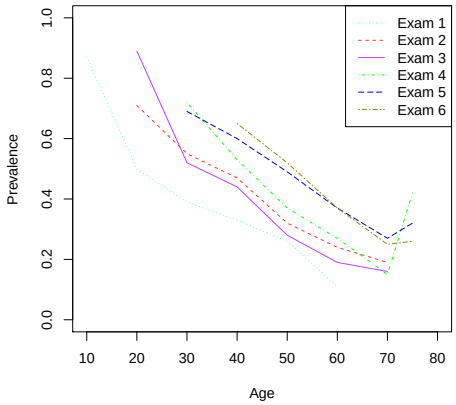

Figure 3.37: Prevalence of hypertension level 0 for males in Framingham.

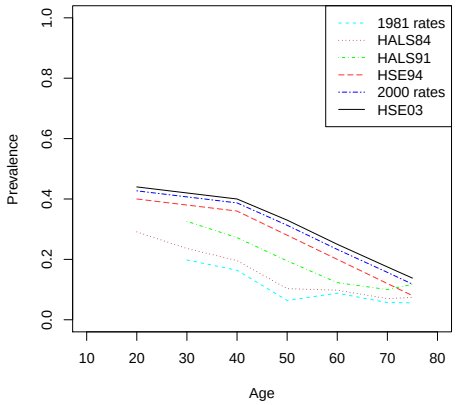

Figure 3.38: Prevalence of hypertension level 0 for males in the UK.

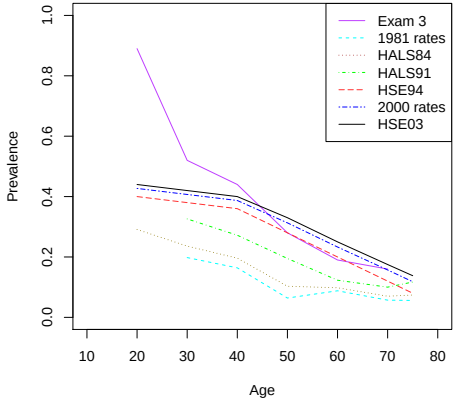

Figure 3.39: Prevalence of hypertension level 0 for males in the UK and Framingham.

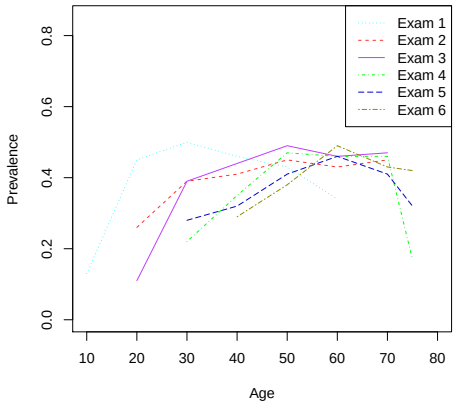

Figure 3.40: Prevalence of hypertension level 1 for males in Framingham.

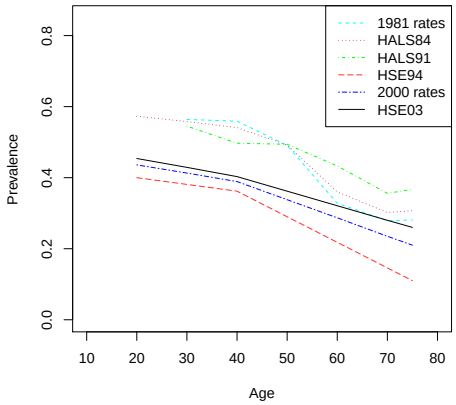

Figure 3.41: Prevalence of hypertension level 1 for males in the UK.

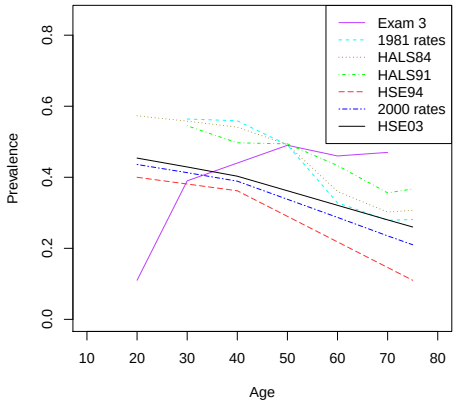

Figure 3.42: Prevalence of hypertension level 1 for males in the UK and Framingham.

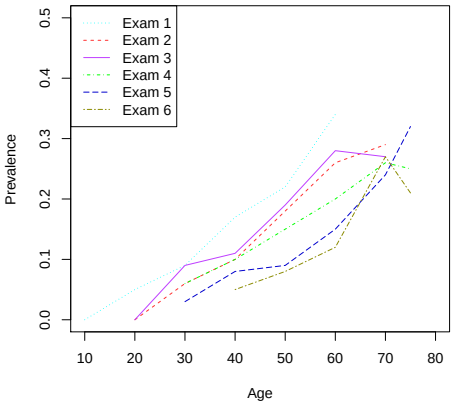

Figure 3.43: Prevalence of hypertension level 2 for males in Framingham.

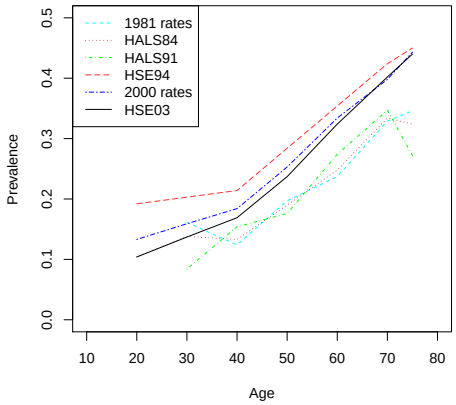

Figure 3.44: Prevalence of hypertension level 2 for males in the UK.

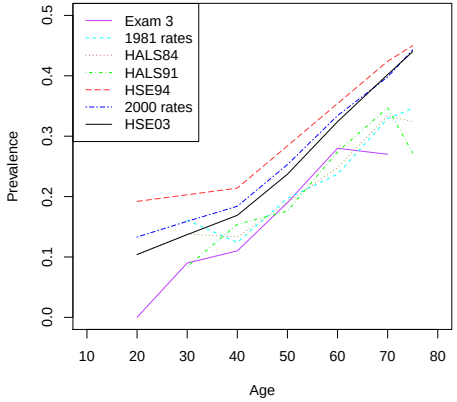

Figure 3.45: Prevalence of hypertension level 2 for males in the UK and Framingham.

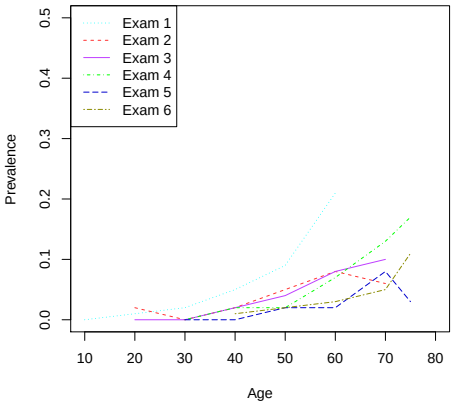

Figure 3.46: Prevalence of hypertension level 3 for males in Framingham.

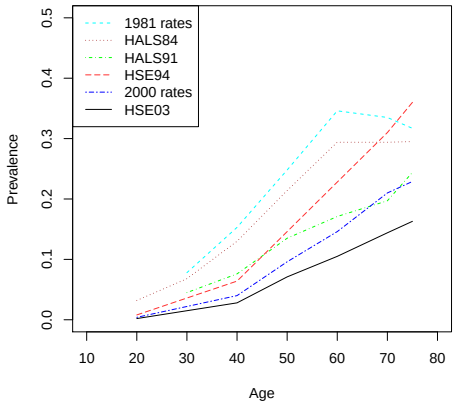

Figure 3.47: Prevalence of hypertension level 3 for males in the UK.

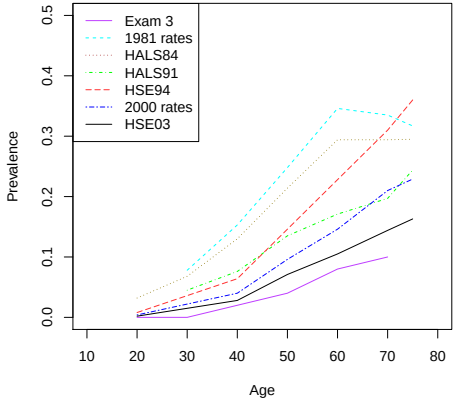

Figure 3.48: Prevalence of hypertension level 3 for males in the UK and Framingham.

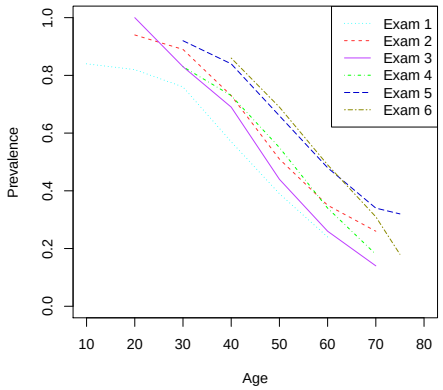

Figure 3.49: Prevalence of hypertension level 0 for females in Framingham.

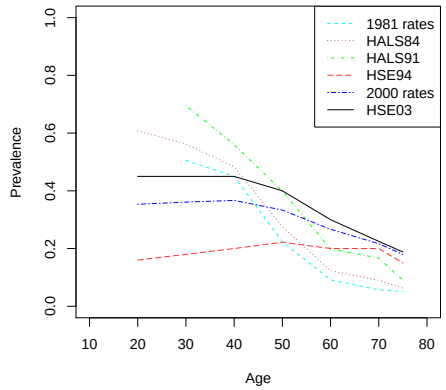

Figure 3.50: Prevalence of hypertension level 0 for females in the UK.

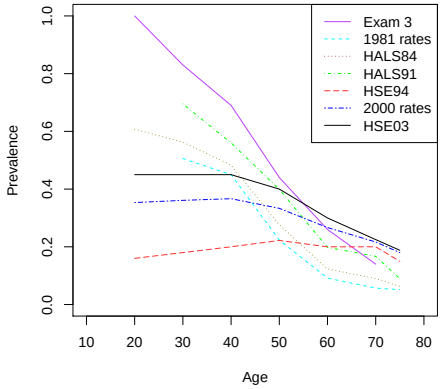

Figure 3.51: Prevalence of hypertension level 0 for females in the UK and Framingham.

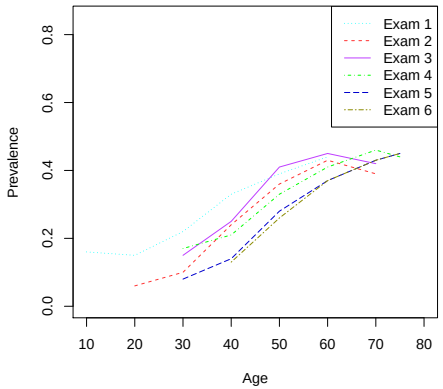

Figure 3.52: Prevalence of hypertension level 1 for females in Framingham.

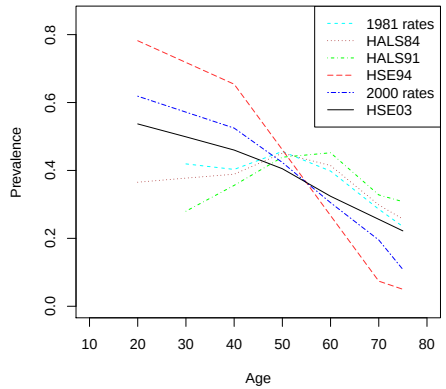

Figure 3.53: Prevalence of hypertension level 1 for females in the UK.

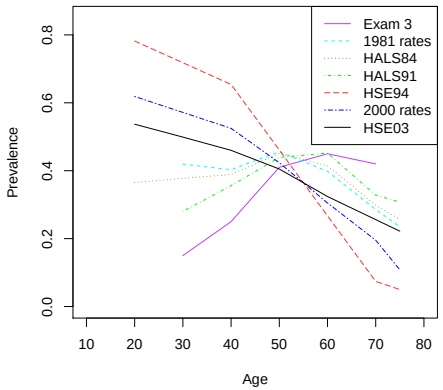

Figure 3.54: Prevalence of hypertension level 1 for females in the UK and Framingham.

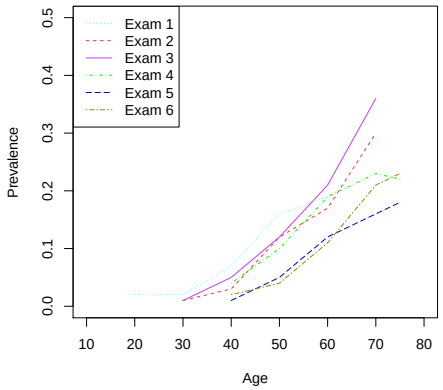

Figure 3.55: Prevalence of hypertension 2 1 for females in Framingham.

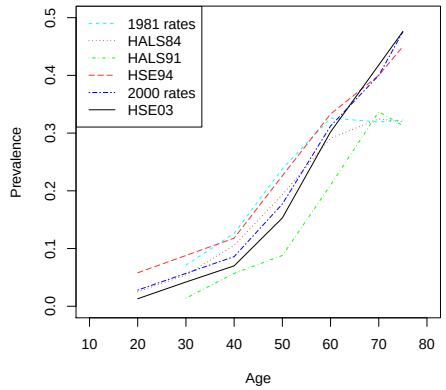

Figure 3.56: Prevalence of hypertension level 2 for females in the UK.

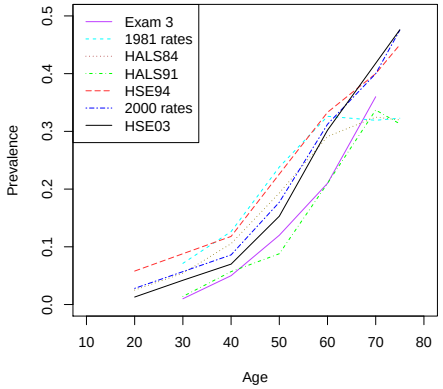

Figure 3.57: Prevalence of hypertension level 2 for females in the UK and Framingham.

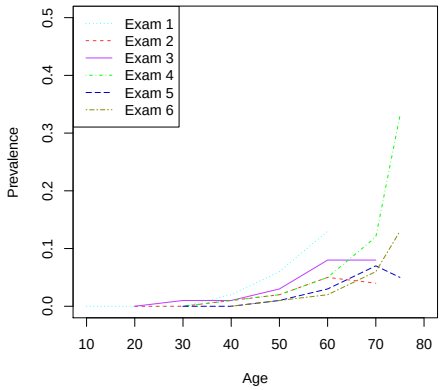

Figure 3.58: Prevalence of hypertension level 3 for females in Framingham.

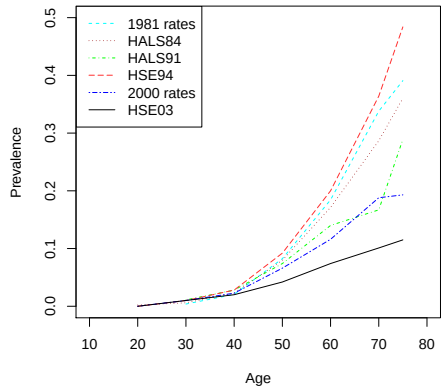

Figure 3.59: Prevalence of hypertension level 3 for females in the UK.

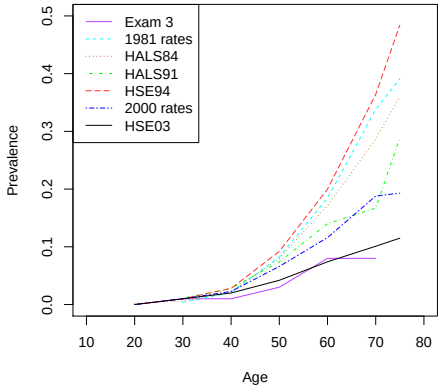

Figure 3.60: Prevalence of hypertension level 3 for females in the UK and Framingham.

3.3.4 Hypercholesterolaemia

For hypercholesterolaemia, we have one data souce from the Dietary and Nutritional Survey 1984 (DNS84). We will not use the observed prevalence rates from the dataset as it represents a small study which consists of 919 males and 856 females and would not be a reliable source for observed prevalence rates in the 1980s. The time trend is also different from HSE and the highest age in the dataset is 64. We need observed prevalence rates for higher ages as we are interested in rates for 45 to 80. So we will extrapolate the 1981 observed prevalence rates using the HSE1994 and 2003 observed prevalence rates and interpolate these rates to get the 2000 observed prevalence rates.

Figures 3.61, 3.62 and 3.63 show the observed prevalence rates for hypercholesterolaemia level 0 for males from Framingham Study Exam 1 to 6, UK data sources and UK data sources and Framingham Exam 3, respectively. The trends in the observed prevalence rates from the Framingham Study and UK data sources for level 0 are increasing as shown in Figures 3.64 and 3.65. Figure 3.63 shows the Exam 3 observed prevalence rates from the Framingham Study have the same trend but higher level as in the UK observed prevalence rates. For hypercholesterolaemia level 1, the observed prevalence rates have a decreasing trend as shown in Figures 3.64, 3.65 and 3.66 for Framingham Study Exam 1 to 6, UK data sources and UK data sources and Framingham Exam 3, respectively. We can say that Exam 3 observed prevalence rates from the Framingham Study is quite similar to the observed prevalence rates in 1980s as shown in Figure 3.66.

Figures 3.67, 3.68 and 3.69 show the observed prevalence rates for hypercholesterolaemia level 2 and Figures 3.70, 3.71 and 3.72 show the observed prevalence rates for hypercholesterolaemia level 3 from Framingham Study Exam 1 to 6, UK data sources and UK data sources and Framingham Exam 3, respectively. There is an increasing trend in the UK observed prevalence rates as shown in Figure 3.68 which is different from the trend in the Framingham Study observed prevalence rates. As shown in Figure 3.67, the observed prevalence rates are decreasing over time. Observed prevalence rates from Exam 3 in the Framingham Study are lower than the UK observed prevalence rates, shown in Figure 3.69 which is also true for level 3 shown in Figure 3.72.

Figures 3.73, 3.74 and 3.75 show the observed prevalence rates for hypercholestero-

laemia level 0 for females from Framingham Study Exam 1 to 6, UK data sources and UK data sources and Framingham Exam 3, respectively. A clear increasing trend can be seen at older ages in the UK observed prevalence rates, shown in Figure 3.74 and the 1981 UK observed prevalence rates do not have the same levels as the observed prevalence rates in the same year in the Framingham study which is shown in Figure 3.75. Figures 3.76, 3.77 and 3.78 show the observed prevalence rates for hypercholesterolaemia level 1 and Figures 3.79, 3.80 and 3.81 show the observed prevalence rates for hypercholesterolaemia level 2 from Framingham Study Exam 1 to 6, UK data sources and UK data sources and Framingham Exam 3, respectively. The observed prevalence rates from Exam 3 in the Framingham Study does not have the same level as the observed prevalence rates in the UK 1980s observed prevalence rates for both levels, shown in Figures 3.78 and 3.81. Figures 3.82, 3.83 and 3.84 show the observed prevalence rates for hypercholesterolaemia level 3 for females from Framingham Study Exam 1 to 6, UK data sources and UK data sources and Framingham Exam 3, respectively. The trend over age is similar between the observed prevalence rates from the Framingham Study and UK data sources but different levels between the observed prevalence rates from the same year.

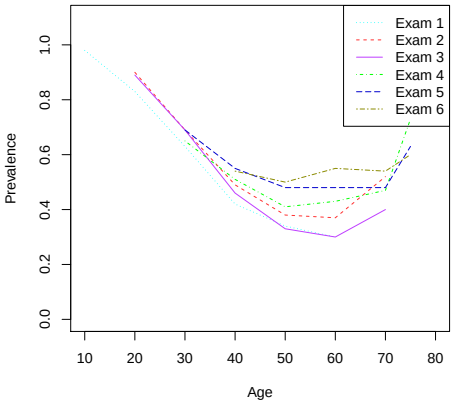

Figure 3.61: Prevalence of hypercholesterolaemia level 0 for males in Framingham.

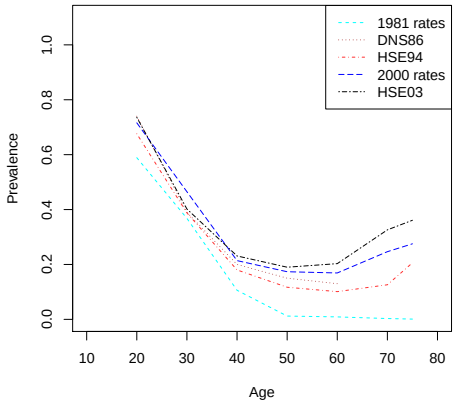

Figure 3.62: Prevalence of hypercholesterolaemia level 0 for males in the UK.

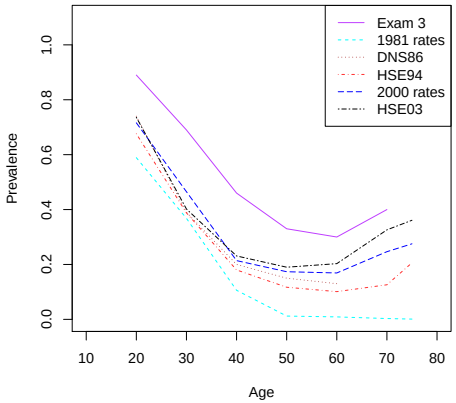

Figure 3.63: Prevalence of hypercholesterolaemia level 0 for males in the UK and Framingham.

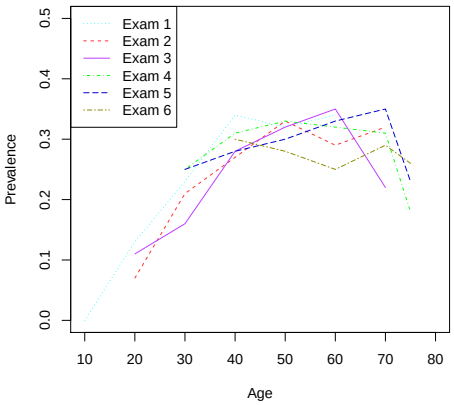

Figure 3.64: Prevalence of hypercholesterolaemia level 1 for males in Framingham.

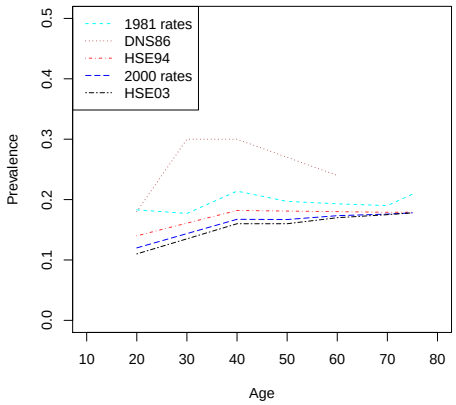

Figure 3.65: Prevalence of hypercholesterolaemia level 1 for males in the UK.

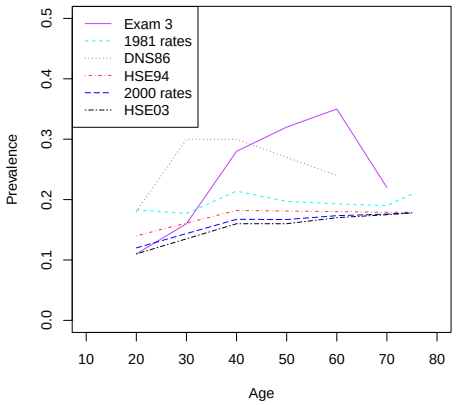

Figure 3.66: Prevalence of hypercholesterolaemia level 1 for males in the UK and Framingham.

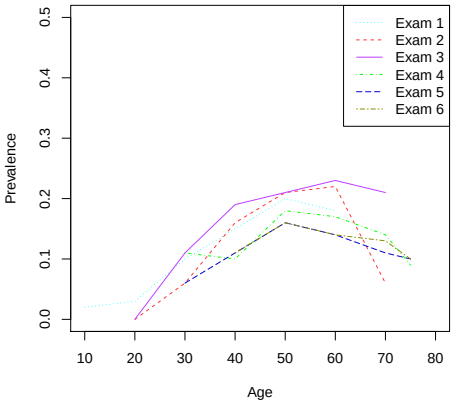

Figure 3.67: Prevalence of hypercholesterolaemia level 2 for males in Framingham.

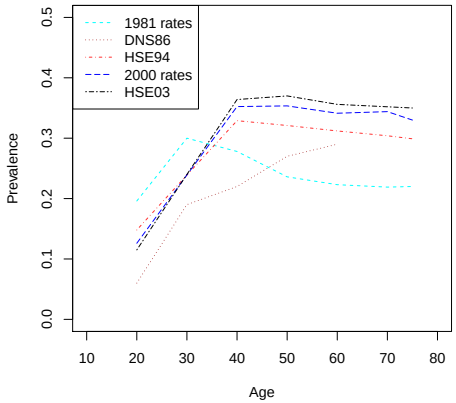

Figure 3.68: Prevalence of hypercholesterolaemia level 2 for males in the UK.

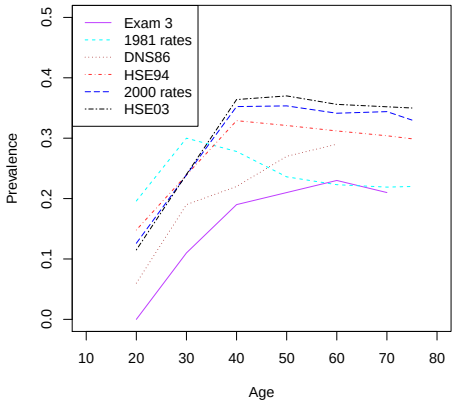

Figure 3.69: Prevalence of hypercholesterolaemia level 2 for males in the UK and Framingham.

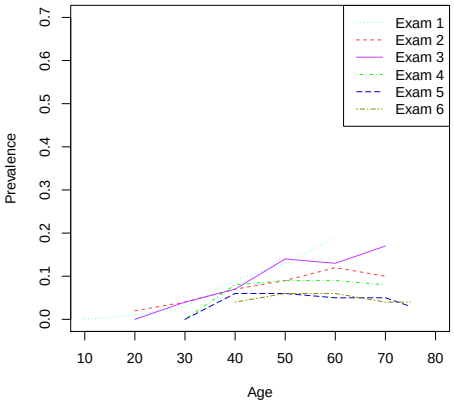

Figure 3.70: Prevalence of hypercholesterolaemia level 3 for males in Framingham.

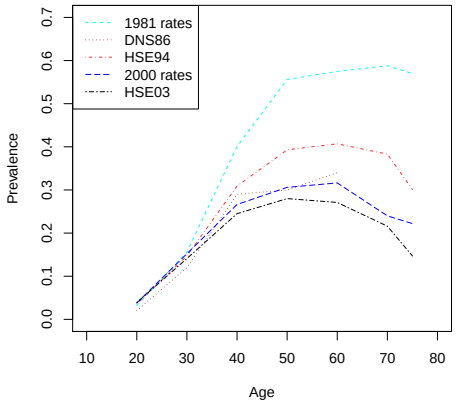

Figure 3.71: Prevalence of hypercholesterolaemia level 3 for males in the UK.

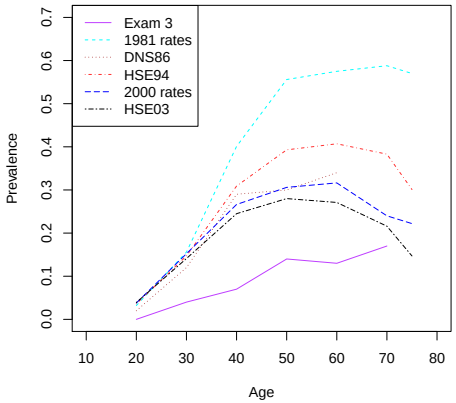

Figure 3.72: Prevalence of hypercholesterolaemia level 3 for males in the UK and Framingham.

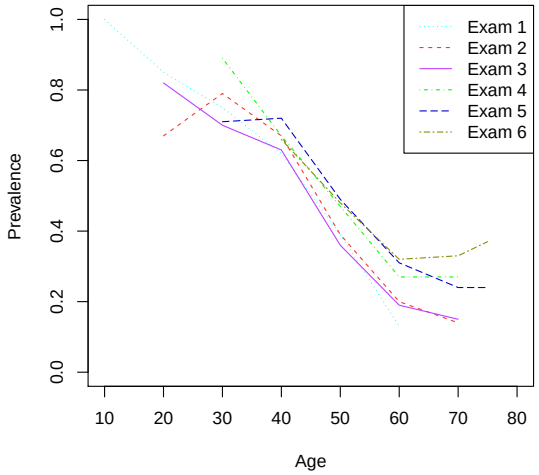

Figure 3.73: Prevalence of hypercholesterolaemia level 0 for females in Framingham.

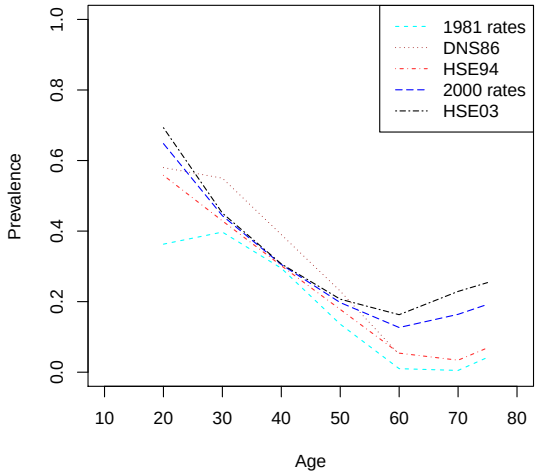

Figure 3.74: Prevalence of hypercholesterolaemia level 0 for females in the UK.

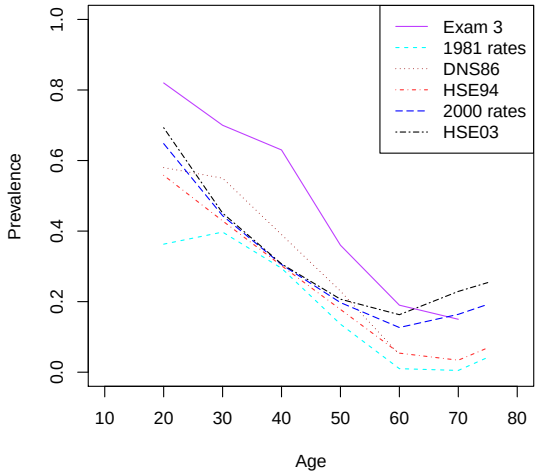

Figure 3.75: Prevalence of hypercholesterolaemia level 0 for females in the UK and Framingham.

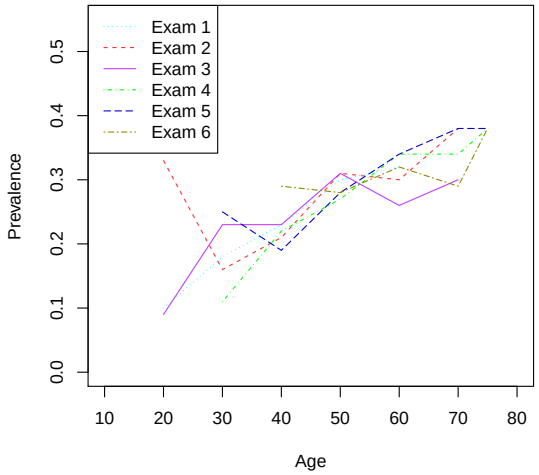

Figure 3.76: Prevalence of hypercholesterolaemia level 1 for females in Framingham.

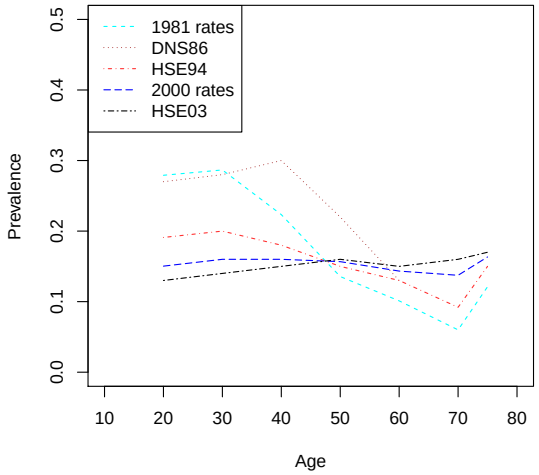

Figure 3.77: Prevalence of hypercholesterolaemia level 1 for females in the UK.

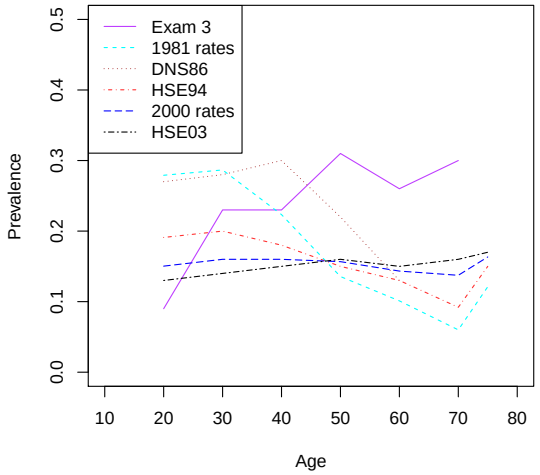

Figure 3.78: Prevalence of hypercholesterolaemia level 1 for females in the UK and Framingham.

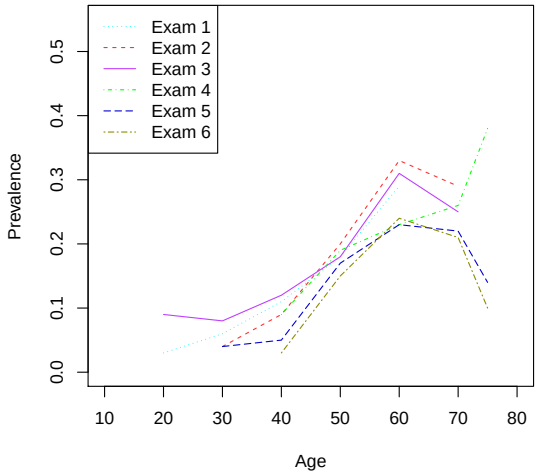

Figure 3.79: Prevalence of hypercholesterolaemia level 2 for females in Framingham.

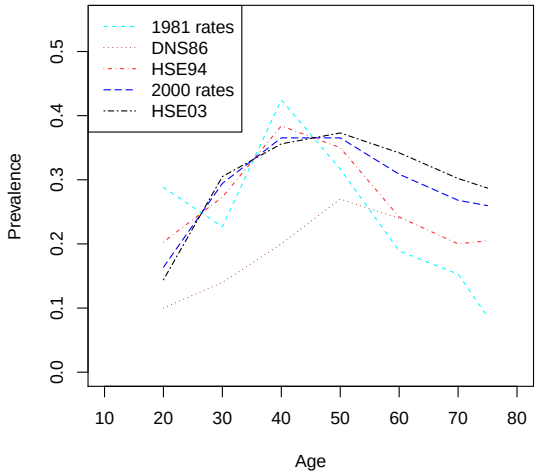

Figure 3.80: Prevalence of hypercholesterolaemia level 2 for females in the UK.

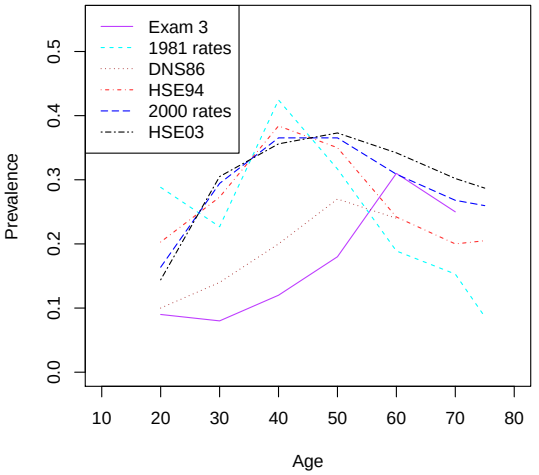

Figure 3.81: Prevalence of hypercholesterolaemia level 2 for females in the UK and Framingham.

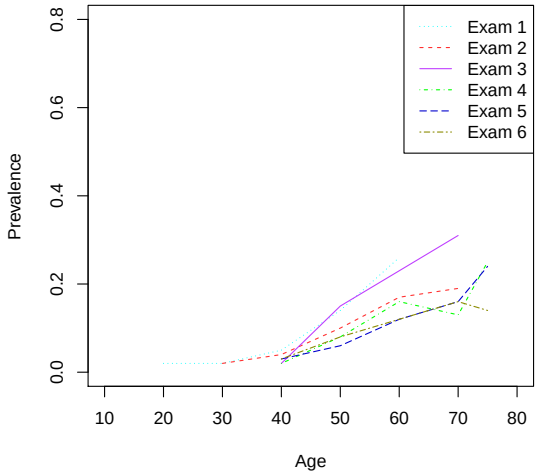

Figure 3.82: Prevalence of hypercholesterolaemia level 3 for females in Framingham.

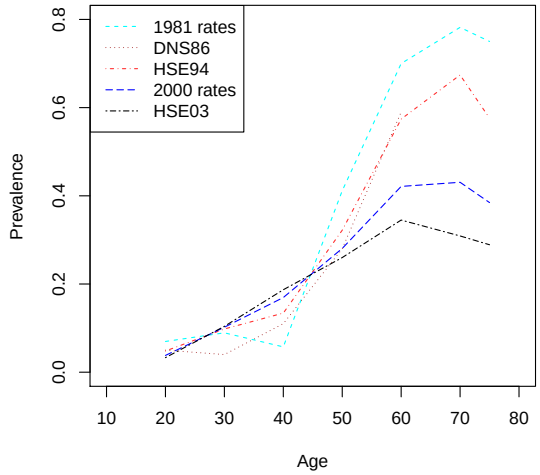

Figure 3.83: Prevalence of hypercholesterolaemia level 3 for females in the UK.

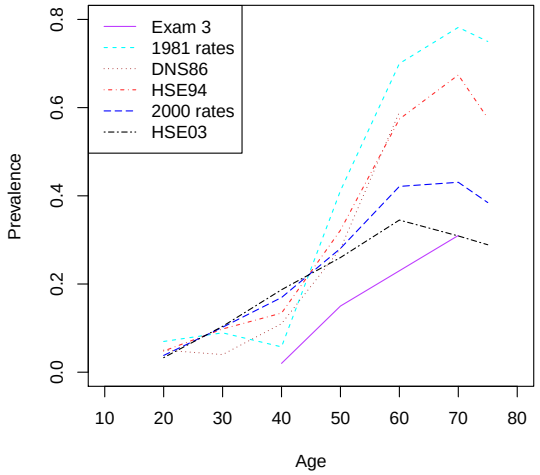

Figure 3.84: Prevalence of hypercholesterolaemia level 3 for females in the UK and Framingham.

3.3.5 IHD, Stroke and Mortality

For IHD and stroke observed prevalence rates, we calculated the 1981 and 2000 observed prevalence rates from the HSE observed prevalence rates taken from NHS (2006). We extrapolate the HSE94 and HSE06 observed prevalence rates to get the observed prevalence rates in 1981 and interpolate using the same HSE year observed prevalence rates for the observed 2000 prevalence rates. We use the English Life Tables no 14 and 16 to represent the mortality rates in 1981 and 2000. Figures 3.85, 3.86 and 3.87 show the rates for IHD, stroke and IHD and/or stroke for males. The observed prevalence rates for females are shown in Figures 3.88, 3.89 and 3.90.

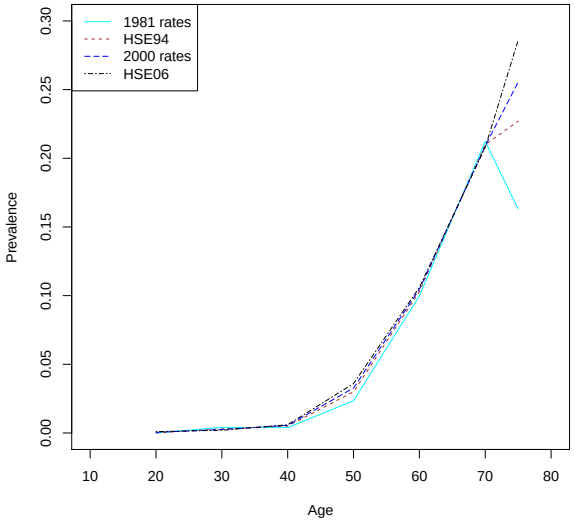

Figure 3.85: Prevalence of IHD for males in the UK.

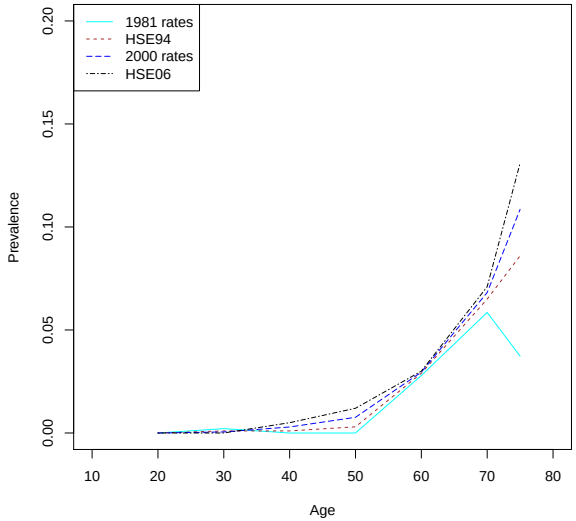

Figure 3.86: Prevalence of stroke for males in the UK.

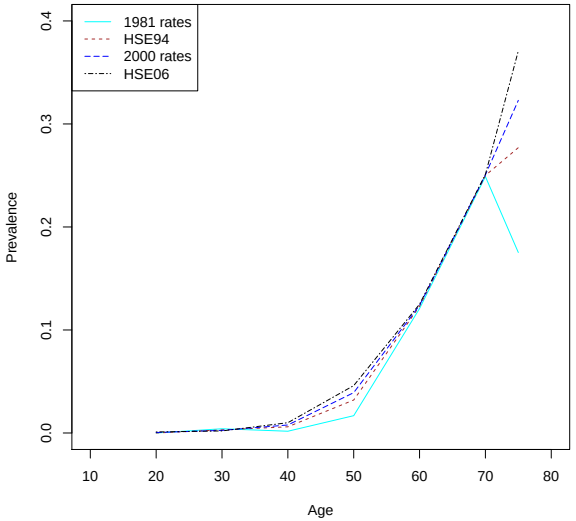

Figure 3.87: Prevalence of IHD and/or stroke for males in the UK.

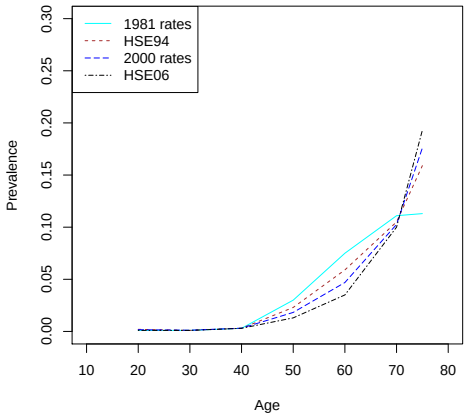

Figure 3.88: Prevalence of IHD for females in the UK.

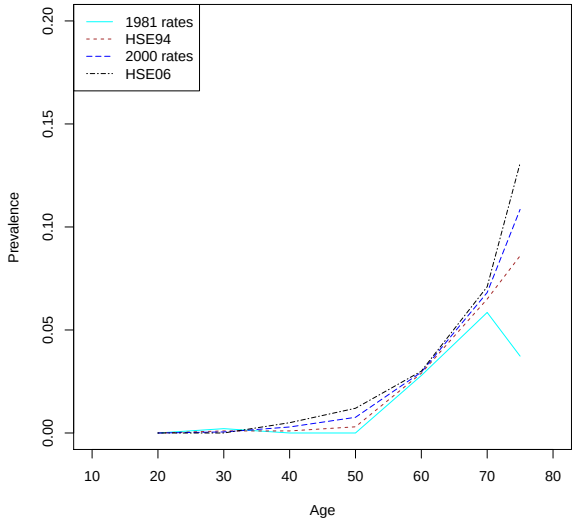

Figure 3.89: Prevalence of stroke for females in the UK.

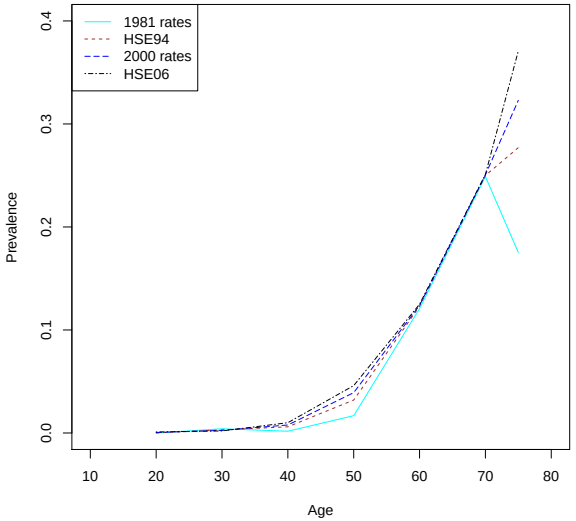

Figure 3.90: Prevalence of IHD and/or stroke for females in the UK.

3.4 Summary

The observed prevalence rates are calculated from different sources to obtain the observed prevalence rates for different years. The observed prevalence rates calculated from the UK Data Archives are consistent with the trends of the observed prevalence rates taken from the Health Survey of England except for some categories in hypertension. These rates will be used as the initial risk profiles in the HW model for years 1981 and 2000 and as the observed 1981 and 2000 prevalence rates, which will be matched by adjusting the HW model.

Chapter 4

Sudden Death Adjustments

4.1 Introduction

Before we start adjusting the transition intensities for the risk factors, we adjust the sudden death probabilities to match the sudden death observed rates in 1981 and 2000. In the HW Model, sudden death is defined as death from any cause within one month following myocardial infarction (MI) or stroke. It is a significant factor to be looked into as the crude risk of death was greatest in the first year after stroke (36% in 1989-90 and 37% in 1995-96) and particularly in the first 30 days from onset (22% in 1989-90 and 23% in 1995-96), according to Hardie *et al.* (2005), a study in Perth, Western Australia. Caro *et al.* (2005) stated that 17% of patients with myocardial infarction and 10% of patients who suffered a stroke died within the first 30 days.

Some studies define sudden death as IHD death that occured within one hour of the onset of symptoms (e.g. Fox *et al.*, 2004), while Volmink *et al.* (1998) identified sudden death as a fatal infarction where death occured before the patient could be seen by a doctor. We are interested to see how the probability of sudden death from MI or stroke has changed over the period 1981–2000. We look at studies that focus on sudden death with the same definition as for the HW Model.

4.2 Myocardial Infarction

A summary of the literature on sudden deaths following a MI is shown in Table 4.1. Studies that we had looked into suggested that the sudden death observed rates for

myocardial infarction in England and some other countries decreased over the period 1981–2000. The observed rates from the studies, where available, are shown in Figure 4.1 which includes the results calculated from the Framingham dataset. The studies referenced in Table 4.1 are discussed below.

Oxford Myocardial Infarction Incidence Study (OXMIS)

The Oxford Myocardial Infarction Incidence Study Group (OXMIS), Volmink *et al.* (1998), studied the sudden death observed rate for myocardial infarction among a population of 568, 800 in Oxfordshire, England in 1994 - 95. The OXMIS study considered the rate for overall sudden death, which is the proportion of hospitalised patients who died within 28 days of onset of symptoms and the proportion of these patients who died before reaching hospital (out of hospital case fatality rate). The overall sudden death rate declined significantly by 28% in men (from 56.7% in 1966-67 to 41.0% in 1994-95) and 32% (from 64.6% in 1966-67 to 44.1% in 1994-95) in women. The reduction in case fatality rates from hospitalised cases only are higher: for men, there is a reduction of 43.4% (from 27.2% in 1966-67 to 15.4% in 1994-95) and for women, the reduction is 52.7% (from 45.5% in 1966-67 to 21.5% in 1994-95). Volmink *et al.* (1998) suggested that the reductions in coronary events and sudden death rates are related to reductions in risk factors and improvements in medical care.

National Centre for Health Outcomes Development by NHS

Another useful study that shows the reduction in the rates of sudden deaths from MI is given by the National Centre for Health Outcomes Development (NHS, 2009). This provides a recent set of data which includes years 1999 to 2007. The National Health Service (NHS) has calculated the indirectly standardised by age and diagnosis rates for deaths from MI. The data consists of deaths in hospital and after discharge within 30 days of an emergency admission to hospital with MI. All death records are taken from the Hospital Episodes Statistics (HES 2008) and the Office for National Statistics (ONS) from ages 35 to 74. The sudden death rates are standardised using England 2002/2003 age, sex and diagnosis rates. 30-day death rates for women were higher than men in both conditions, but both have shown some improvements as shown in Figure 4.1. The 30-day death rates for MI reduced by 41% for women and

38% for men. These data include only those who had reached hospital and do not include sudden deaths at home without being referred to the hospital.

The Framingham Heart Study

Studies from other countries also suggest that there are reductions in sudden death from MI. Fox *et al.* (2004) concluded that over the period from 1950 to 1999 the sudden death rates in the Framingham Heart Study decreased by 49%. The risk of sudden death for those without prior history of IHD was 39% lower in 1990 to 1999 compared to 1950 to 1969, whereas for those with a prior history, the risk was 57% lower, comparing the same year. Reductions were also seen for smokers and non-smokers. This study defined sudden death as death within 1 hour after symptom persisted. There were 12 cases of participants who were resuscitated and survived for at least 1 hour and were excluded from the above results. Including these people, which in case of failure to resuscitate would cause them to be sudden deaths, would lower the risk of sudden death to 38% in 1990 – 1999 compared to 1950 – 1969, which suggested that part of the decline could be because of patients who survived as a result of resuscitation.

Olmsted County, Minnesota

A study of trends in the incidence of coronary disease conducted in Minnesota by Arciero *et al.* (2004) indicated that the age– and sex– adjusted incidence of sudden deaths declined over time, from 23% in the 1979 – 1983 period to 17% during the 1994 – 1998 period, a reduction of 26.1%. The definition of sudden death in this study is death that occurred out of hospital. From Table 1 in Arciero *et al.* (2004), the changes between sudden deaths for men and women are not quite significant in the second decade, between 1988-93 and 1994-98. The number of sudden deaths for men aged less than 60 is 28 in 1988-93 and 26 in 1994-98, whereas the number of sudden deaths in women has not changed between these years for the same age group. In older ages (more than 80 years old), the number of sudden deaths was 60 and 58 in 1988-93 and 1994-98 respectively, while for women the number of sudden deaths is the same between 1988-93 and 1994-98. The sudden death trend among patients in Minnesota is the same for both men and women in the second decade, which is

between 1988-93 and 1994-98.

Pennsylvania

However, there are some studies that reported no changes in sudden deaths from MI. Over 21 years of study for white males, aged 35 to 44 years old in Pennsylvania, Traven *et al.* (1995) reported no reduction in sudden deaths for IHD. This study defined sudden death as death within 24 hours of the symptoms with no history of heart disease. There was also a quite steady rate for death within one hour of onset. The proportion of sudden deaths has not changed across the two decades despite the reduction in the incidence of heart disease where the IHD mortality reduced by 60% between 1970-72 and 1988-90.

Belfast

A study on temporal trends in out of hospital sudden cardiac death (OHSCD) in Belfast by Moore *et al.* (2006) concluded that the incidence of OHSCD over the past 20 years has not fallen despite a 37% reduction in heart attack mortality in Ireland. This study defined sudden death as death within one hour of symptoms.

4.2.1 Modelling Sudden Deaths Following Myocardial Infarction

We will model the probability of sudden death following a myocardial infarction (SDMI) by using the data from the Framingham Heart Study from 1971 to 1991, which is the Original Cohort (OC). For the Offspring and Spouses Cohort (OS), there were missing data on the date of events of MI. Since the number of the cases of MI in the OS data is quite small, this should not affect our model. In the Framingham OC data, there were 179 sudden deaths following a MI from 1049 MI cases for males and females. We will model the sudden deaths using a GLM, fitted using the R statistical package, under a binomial distribution for the number of sudden deaths. The response variable which is the SDMI (D_{MI}) will take the value 0 if the individual is alive after 30 days and 1 if the individual has died within 30 days after MI. First we model the SDMI using age at MI, year of MI and sex as the explanatory variables.

Name of study	Period	Definition of sudden death	Reduction of SDMI within the given period
Oxford Myocardial Infarction Incidence Study (OXMIS) by Volmink *et al.* (1998)	1994 – 95 (compared with 1966 – 67)	Patients who died within 28 days of onset of symptoms (hospitalised and out of hospital)	Males: 28% (56.7% to 41%) Females: 32% (64.6% to 44.1%)
National Centre for Health Outcomes Development by NHS (2009)	1999 – 2007	Deaths in hospital and after discharge within 30 daysof an emergency admission to hospital with MI (hospitalised)	Males: 38% (10.22% to 6.35%) Females: 41% (12.74% to 7.49%)
The Framingham Heart Study (OC & OS) by Fox *et al.* (2004)	1950 – 1999	CHD deaths that occurred within 1 hour of the onset of symptoms (hospitalised)	Overall: 49% Males: 49% Females: 47%
Olmsted County, Minnesota by Arciero *et al.* (2004)	1979 – 1983 and 1994 – 1998	Deaths occured out of hospital due to CHD	A reduction of 26.1% (23% in 1979 – 83 to 17% in 1994 – 98) Very little change between the 2^{nd} decade, 1988 – 93 and 1994 – 98
Pennsylvania by Traven *et al.* (1995)	1970 – 1990	Deaths within 24 hours of the symptoms (hospitalised and out of hospital)	No trends of reduction in 35 – 44 years old white males
Out of hospital sudden cardiac death (OHSCD) Belfast by Moore *et al.* (2006)	2004 (compared with 1966)	Deaths within one hour of onset of symptoms	Does not appear to have fallen over the past 38 years (1966 – 2004)

Table 4.1: Literature summary for sudden deaths following a myocardial infarction

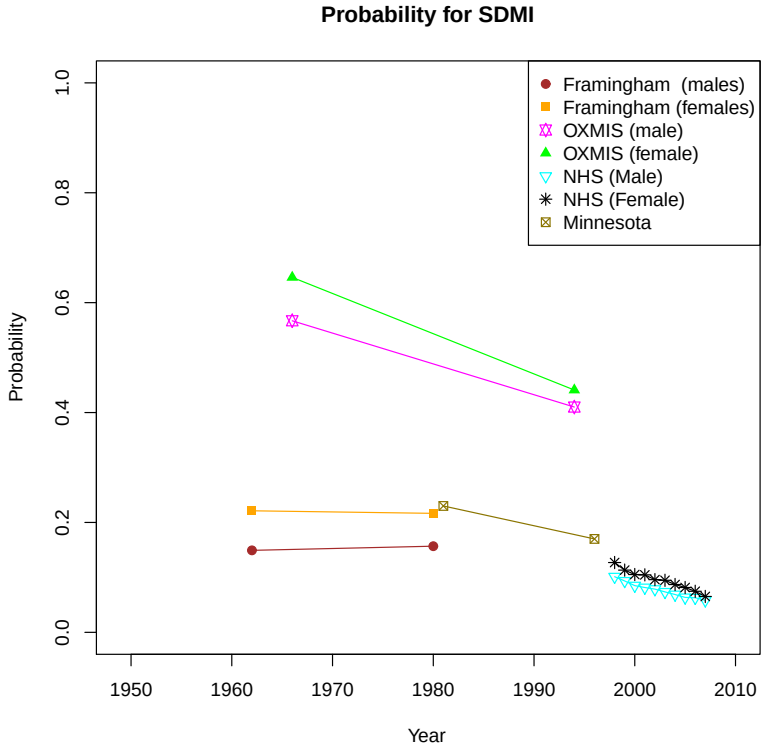

Figure 4.1: Rates of sudden death from myocardial infarction from Table 4.1

We found that age at MI and year of MI are significant explanatory variables while sex is not a significant factor for modelling the SDMI. The model is shown below and the R output is shown in Table 4.2:

$$D_{SDMI} \tilde{} Bin(1, P_{SDMI})$$

where

$$logit(P_{SDMI}) = b_0 + b_1 Age + b_2 YearMI \tag{4.1}$$

Coefficients	Estimate	Standard Error	P-value
b_0	36.83813	21.27982	0.0834
b_1	0.06241	0.01109	1.81e-08
b_2	-0.02166	0.01105	0.0499

Table 4.2: Summary of SDMI model.

Figure 4.2 shows the probability of sudden deaths from MI from the modelling for 3 different ages, 40, 71 and 80. We can see that the probability increases as age increases and there are reductions over the years for all ages. The probability is consistent with most of the literature in Table 4.1, which suggests that the sudden death rates decreased over time. The probability of sudden death following MI from the R output in Table 4.2 is shown below:

$$P_{SDMI} = \frac{\exp(36.83813 + 0.06241 \times Age - 0.02166 \times Year)}{1 + \exp(36.83813 + 0.06241 \times Age - 0.02166 \times Year)} \tag{4.2}$$

In Figure 4.2, we have the sudden death rates from the literature and we used the average age at events (age 67) in the Framingham data (shown in the graph as the red line) to compare our model. We also include the model estimated sudden death rates for ages 40 and 80 calculated from the model. The data for the UK sudden death rates are from the Oxfordshire Study (Volmink *et al.*, 1998) and The National Health Service (NHS) for males and females. The sudden death rate for the average age at MI in the Framingham Data seems to be consistent with the NHS rates for males and females in 1999 to 2007. Therefore, we will use this model without any adjustment.

4.3 Stroke

Table 4.3 shows a summary of some of the literature on sudden deaths following a stroke (SDHS). Sudden death from stroke has shown no significant improvement over time, as reported in some studies that have similar definition of SDHS with the HW Model. SDHS is defined as sudden deaths following a stroke from hospitalised and non–hospitalised cases within 30 days. Figure 4.3 shows the rates of SDHS from the studies discussed below and the sudden death rates include the results calculated from the Framingham dataset.

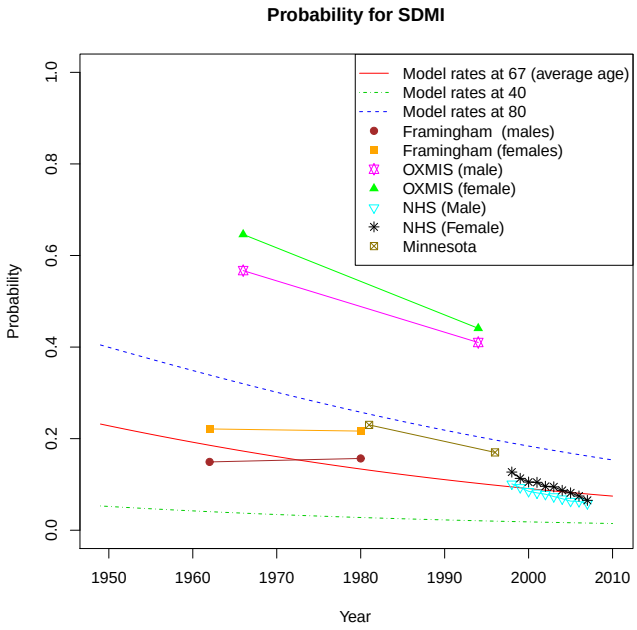

Figure 4.2: SDMI model and UK age standardised rates

Oxfordshire Study

Sudden death from stroke has shown no significant improvement over time as reported in some studies. In an Oxfordshire Study by Rothwell *et al.* (2004), the 30-day case-fatality from stroke remained the same between 1981-1984 and 2002-04, where the sudden death rates were 17.8% and 17.2% respectively, although there was a decline of 29% in incidence of stroke.

FINSTROKE Study

In a study that analyzed the case fatality from stroke in Finland, Sivenius *et al.* (2004) stated that the decrease in 28-day case fatality of stroke between 1983 and 1997 in men is from 21.7% to 18.2%, and from 22.2% to 19.2% in women. Dividing this into different types of stroke, case fatality of ischaemic stroke remained stable and similar in men and women between 1988 and 1997, while case fatality of heamorrhagic stroke decreased slightly in men and significantly in women, from 55.2% to 32.6%.

National Centre for Health Outcomes Development by NHS

The latest data (1999 to 2007) from The National Health Service (NHS, 2010) has shown some reductions in sudden deaths from stroke. The NHS has calculated rates of deaths from stroke the indirectly standardised by age and diagnosis. The data are the same as the data for MI, where it is deaths after admission to hospital or after discharge within 30 days. Figure 4.3 shows the trend of SDHS from 1999 to 2007 for men and women. Between these years, the probability of deaths within 30 days for stroke seems to be declining. Deaths within 30 days declined by 27.5% and 21% for men and women, respectively. Comparing it with the study by Rothwell *et al.* (2004) which showed no significant reduction between 1981-1984 and 2002-04, the reduction shown in these data might indicate that within recent years there may has been an improvement in treatment, as people who have strokes are more likely to survive if admitted quickly to a hospital with treatment and care provided by a specialist coordinated stroke team. Also, the NHS data relates to 1999 to 2007, which does not overlap with the period that we are interested in.

NHS Scotland Study

A study of stroke in Scotland by Lewsey *et al.* (2009) concluded that short-term case fatality for stroke is greater in women than men over the 20 – year period of study, from 1986 to 2005. From Lewsey *et al.* (2009), there was a reduction in the short-term case fatality especially for men and women less than 55 years old. This study also has a declining trend and the short-term case fatality only includes hospitalised cases, which is similar to NHS (2010).

4.3.1 Modelling Sudden Deaths Following Stroke

We will model the probability of sudden deaths following a stroke by using the same dataset and methods as used in Section 4.2.1. We will use the Framingham dataset, which includes 157 cases of sudden deaths following a stroke from 740 stroke cases for males and females. We start the modelling by including age at stroke, year of stroke and sex as the explanatory variables. However, year of stroke and sex were found to be not significant for SDHS. This can also be seen in Figure 4.4 where we can see

Name of study	Period	Definition of sudden death	Reduction of SDHS within the given period
Oxfordshire Study by Rothwell *et al.* (2004)	1981 – 2004	30 - day case fatality (hospitalised and out of hospital)	Remained the same, 17.8% in 1981 – 84 and 17.2% in 2002 – 04
The FINSTROKE Study by Sivenius *et al.* (2004)	1983 – 1997	28 - day case fatality	Males: 21.7% to 18.2% Females: 22.2% to 19.2% Notes: Decline were seen in the case fatality of heamorrhagic strokes, whereas case fatality of ischemic strokes did not change.
National Centre for Health Outcomes Development by NHS (2010)	1999 – 2007	Deaths in hospital and after discharge within 30 days of an emergency admission to hospital with stroke	Males: 29.4% to 21.2% Reduction of 27.5% Females: 30.5% to 24% Reduction of 21%
NHS Scotland by Lewsey *et al.* (2009)	1986 – 2005	30 – day case fatality (hospitalised)	$<$ 55 years old Males: 22.7% in 1986 to 11.7% in 2005 Females: 28.4% in 1986 to 12.7% in 2005 $>$ 85 years old Males: 41% in 1986 to 32% in 2005 Females: 37.3% in 1986 to 31.8% in 2005

Table 4.3: Literature summary for sudden deaths following a stroke

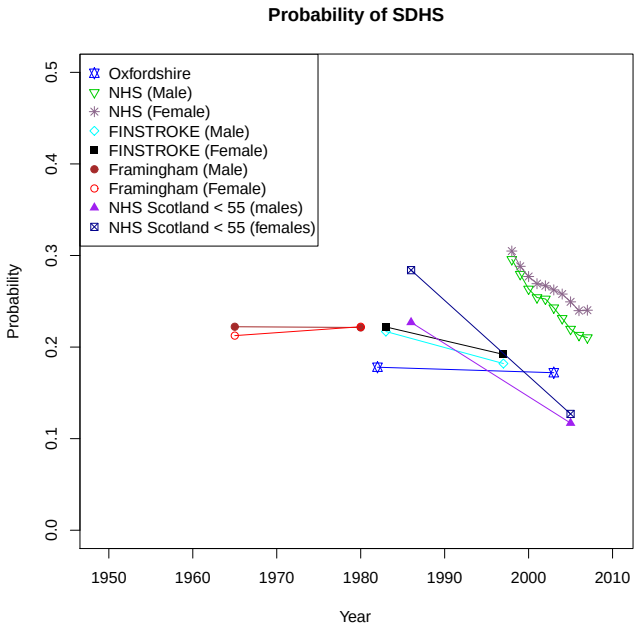

Figure 4.3: Rates of sudden death from stroke from Table 4.3

that the sudden death rates for different ages are almost the same over the years. This means that there is no calendar time effect in the sudden death rates following a stroke which is consistent with the literature in Table 4.3 that shows no improvement over time. The model is shown below and the R output is shown in Table 4.4:

$$D_{SDHS} \tilde{} Bin(1, P_{SDHS})$$

where

$$logit(P_{SDHS}) = b_0 + b_1 Age \tag{4.3}$$

Coefficients	Estimate	Standard Error	P-value
b_0	-3.625166	0.651198	2.59e-08
b_1	0.032011	0.008797	0.000274

Table 4.4: Summary of SDHS model.

As year of event is not a significant factor, our model for the sudden deaths from stroke uses only age, which can be referred to Table 4.4 and is shown below:

$$P_{SDHS} = \frac{\exp(-3.625166 + 0.032011 \times Age)}{1 + \exp(-3.625166 + 0.032011 \times Age)} \tag{4.4}$$

We compared our model with the rates of sudden death following a stroke from the studies in Table 4.3 and this is shown in Figure 4.4. From the plot, we see that the NHS sudden death rates are not in line with the sudden death rates from our model, or with the Oxfordshire and Finstroke studies. The NHS Scotland includes hospitalised and all discharges data which is similar to the NHS England data. Both NHS rates have shown that there were reductions over time for the sudden death rates from stroke whereas data from Oxfordshire and Finstroke show that there was no time trend.

We note that the Oxfordshire and Finstroke studies use a definition of SDHS consistent with our data from the Framingham Heart Study which includes all deaths (hospitalised and out of hospital) and the results from these studies show no calendar time effect. So we can use this model without any adjustment to match with the UK observed rates. Power (2004) mentioned in his article that approximately 20% of patients will die within 30 days of stroke onset in the UK. This is consistent with our result in Figure 4.4, where the purple line shows the sudden death rates from an average age at stroke using our model at approximately 20%.

4.3.2 Incidence of sudden death following stroke

A possible explanation for the reason why the rate of sudden death from stroke in the NHS England and NHS Scotland data decreased over time can be given by looking at the incidence rate for stroke over the populations. We will look at the incidence rate per 100,000 people which is available for the NHS and Oxfordshire studies and see what makes the trend in sudden death different between the studies. We would expect the incidence rate from the NHS data to be lower than in the Oxfordshire Study as the NHS only includes those who were hospitalised. Tables 4.5 and 4.6 show the incidence rate of stroke per 100,000 people for males and females from the NHS

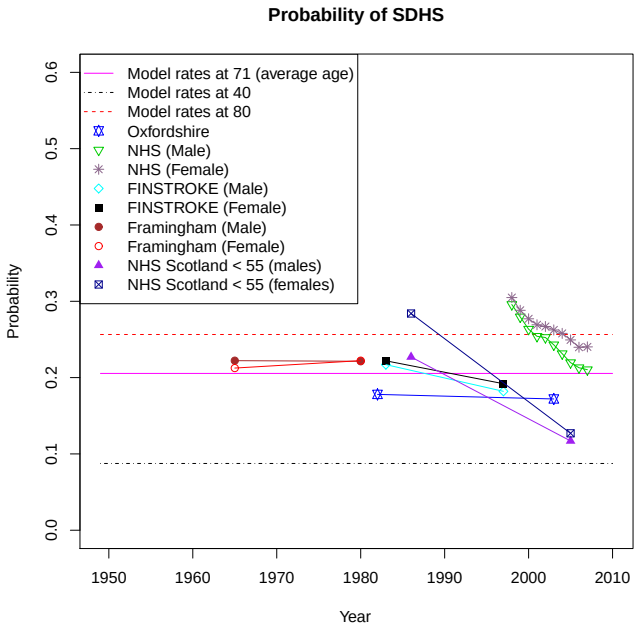

Figure 4.4: SDHS model and UK age standardised rates

and Oxfordshire studies. From the tables, we can see that indeed the incidence rates for the NHS are generally lower than for Oxfordshire.

The higher sudden death rates in the Oxfordshire study could represent the out-of-hospital cases which might explain why there were no changes over time for sudden death. The number of out of hospital cases in the Oxfordshire study would result in more sudden deaths compared to the NHS. So the reduction in the sudden death rates from hospitalised cases has been cancelled out by the out of hospital sudden death cases which probably resulted in no changes over time in sudden death rates in Oxfordshire and Finstroke.

Rothwell *et.al* (2004) stated that the incidence of stroke fell by 29% between 1981-84 and 2002-04 (from 2.27 to 1.62 per 1000 population). This can be seen in Tables 4.5 and 4.6 by comparing the incidence rates between 1983 and 2004 in the Oxfordshire sudden death rates. Rothwell *et.al* (2004) also mentioned that the decline resulted from the increased use of preventive treatment and better control of vascular risk factors. The decline is consistent with the reduction in mortality due to stroke in the absence of the reduction of sudden death.

A population-based study by Kleindorfer *et.al* (2006) in the United States mentioned that the annual incidence of hospitalised stroke did not change significantly

between 1993-94 and 1999. The incidence rate in both periods, 1993-94 and 1999 was 158 per 100,000 people. Kleindorfer *et.al* (2006) also measures the out-of-hospital incidence rate and there was a slight increase over the study period, from 186 to 206 per 100,000. The 30-day sudden death rates from this study were consistent with the Oxfordshire study where there were no significant changes over time. The 30-day sudden death rates in 1993-94 and 1999 were 13.9% and 14.7%, respectively. These rates include the hospitalised and out of hospital cases.

Using the England NHS data and estimated population data from the ONS, we calculated the age-standardised sudden death rates per 100,000 people from 1999 to 2008 for males and females. These are shown in Table 4.7. There is a slight decrease in the incidence of stroke over the time period. The NHS data includes all ages so we compared the sudden death rates with the Oxfordshire sudden death rate for all age groups. In 2004, the Oxfordshire sudden death rate per 100,000 population for all ages was 134 for males and 156 for females which is shown in Table 1 in Rothwell *et.al* (2004). Comparing these rates with the NHS sudden death rates in the same year, the NHS rates were lower than the Oxfordshire sudden death rates, 127 and 138 for males and females, respectively.

There were no changes in sudden death rates over time although there were changes in the incidence of stroke, as mentioned in the Oxfordshire study. As expected, the sudden death rate for studies that includes hospitalised and out of hospital cases are higher than hospitalised only cases. The risk of sudden death from stroke is higher for those who have not been admitted to hospital so this may cause the rate of sudden death to remain the same.

Age	NHS Scotland		Oxfordshire	
	1985	2005	1983	2004
55-64	250	250	368	214
65-74	500	450	819	678
75-84	1250	900	1772	1085
85+	1900	1300	1994	2063

Table 4.5: Incidence rate of stroke per 100,000 populations for males

Age	NHS Scotland		Oxfordshire	
	1985	2005	1983	2004
55-64	200	200	181	140
65-74	450	300	601	464
75-84	1000	750	1529	1109
85+	1600	1250	1769	1863

Table 4.6: Incidence rate of stroke per 100,000 populations for females

Year	Males	Females
1999	140	151
2000	134	147
2001	129	141
2002	130	139
2003	130	141
2004	127	138
2005	123	133
2006	121	130
2007	116	123
2008	115	119

Table 4.7: NHS incidence rate of stroke per 100,000 population for males and females

4.4 Summary

Tables 4.1 and 4.3 show a summary of several studies on sudden deaths from MI and stroke. There are more improvements in sudden deaths from MI compared to stroke. Reductions in sudden death in MI can be seen from studies in England and Framingham. Sudden death from stroke has not shown significant improvements, as mentioned in the Oxfordshire and Finland studies, but there are improvements since 1999 as shown in the NHS data. We have modelled the changes over time of sudden death in MI and stroke and built it in the HW Model. The adjustments for probability of sudden deaths following a MI is a function of age and year of MI, while for stroke it is a function of age only. The adjustments will be included in the HW Model in which the intensities for other risk factors will be adjusted to match the 1981 and 2000 observed rates. The probability of sudden deaths following a MI and a stroke will be added to the mortality rates. The probability is added to the mortality rates to assume deaths happen to new cases of MI and stroke within 30 days of the attack, thus adjusting the mortality rates.

Chapter 5

Adjustments to Other Risk Factors

5.1 Introduction

Further adjustments are needed to other risk factor intensities to match the model with 1981 and 2000 observed prevalence rates (taken from data and surveys) and here we include the sudden deaths adjustments to the HW Model as explained in the previous chapter. The risk profiles calculated from Tables 3.7 and 3.8 are put into the HW Model as the 1961 and 1981 initial risk profiles as mentioned in Section 2.3 and we run it for 19 and 20 years to get the HW Model estimated prevalence rates in 1981 and 2000. We will make adjustments to the risk factors based on the sequence of the significant risk factors table given in the HW Model (Chatterjee *et al.*, 2008a, Table 12).

Figure 5.1 is a diagram that shows how each risk factor influences other risk factors based on Table 12 in Chatterjee *et al.* (2008a). As mentioned in Chatterjee *et al.* (2008a), an obvious feature is that BMI is a significant explanatory factor for hypertension, diabetes transition from level 0 to 1 and mortality. This is graphically demonstrated in Figure 5.1 where changes in BMI affect hypertension, diabetes and mortality. Hypercholesterolaemia is a significant risk factor for mortality, IHD and stroke, as also illustrated in Figure 5.1. In Table 12 (Chatterjee *et al.*, 2008a), only age and sex affect significantly the changes in hypercholesterolaemia.

Based on Chatterjee *et al.* (2008a), we also observed the following significant effects. After age and sex, smoking is also a significant factor for transition between BMI categories, particularly for category 2 to 1, 1 to 2 and 2 to 3. Smoking is also

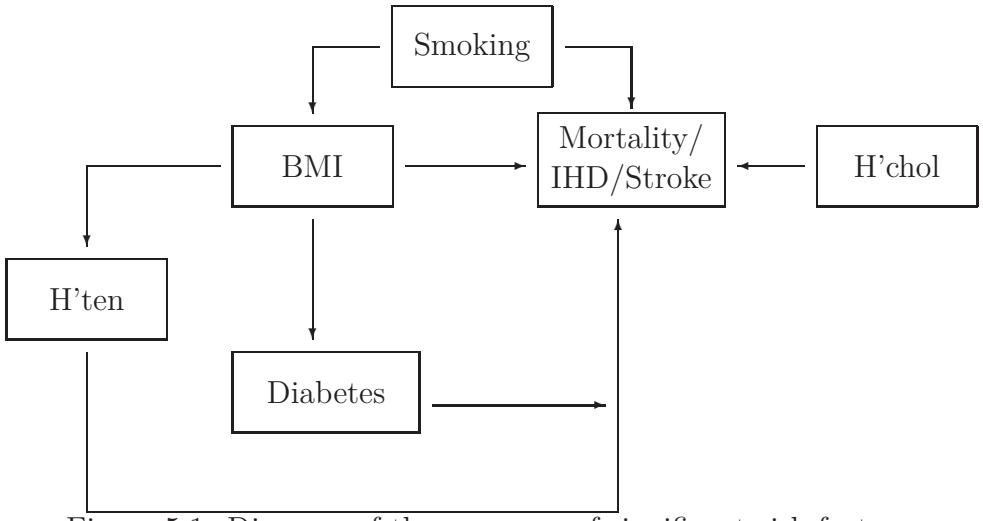

Figure 5.1: Diagram of the sequence of significant risk factors.

a significant factor that increases the risk of having IHD and stroke. BMI is then a significant factor for diabetes and hypertension. Age and sex are the significant risk factors for hypercholesterolaemia so any adjustments to other risk factors will not affect the transition between the categories of hypercholesterolaemia. All the risk factors then affect the prevalence rates of IHD, stroke and mortality.

We have applied some adjustment for the modelling of sudden death following IHD and stroke in the previous section as sudden death is dependent on age and year of event and is not influenced by the risk factors in the diagram. This is based on Chatterjee *et al.* (2008a, Section 9.3) where they used the Framingham data to model probabilities of sudden death from MI and HS and included all risk factors in their model but found only age was the significant factor for MI and that no risk factors were significant for HS. Since smoking is a deterministic factor and will influence some categories of BMI and indirectly influence diabetes and hypertension, we choose to start with the smoking factor. The definition of each risk factor is shown in Tables 2.1, 2.2, 3.5 and 3.6.

5.2 Adjustments to model intensities

We will start our adjustments with the HW Model transition intensities and include the adjustment for sudden death as mentioned in Chapter 4. First we will make adjustments by changing the transition intensities in the HW Model to match the

observed prevalence rates in 2000 and then we will obtain another set of intensities to match the observed prevalence rates in 1981. The adjustments will be done based on the following sequence: smoking, BMI, diabetes, hypertension, hypercholesterolaemia, IHD, stroke and mortality. These intensities are adjusted by hand as mentioned in Section 2.2. Using the results from the adjusted model, we calculate the prevalence rates of different levels of each risk factor for surviving males and females by using this calculation:

$$\mathcal{P}_{x|G,SP}(i_b) = \frac{f^{HW}_{x,x-t}(i_b \mid \mathcal{P}^{indYear}_{x-t}(\mathcal{I}), G, SP)}{(1 - f^{HW}_{x,x-t}(Dead \mid \mathcal{P}^{indYear}_{x-t}(\mathcal{I}), G, SP))} \tag{5.1}$$

where

$\mathcal{P}_{x|G,SP}(i_b)$: the probability of being in state i_b at age x for a given sex, G and smoking profile, SP,

$f^{HW}_{x,x-t}(i_b \mid \mathcal{P}^{indYear}_{x-t}(\mathcal{I}), G, SP)$: the probability of being in state i_b at age x for a given sex, G, smoking profile, SP, and a given initial risk profile, $\mathcal{P}^{indYear}_{x-t}(\mathcal{I})$ at age $x - t$,

$f^{HW}_{x,x-t}(Dead \mid \mathcal{P}^{indYear}_{x-t}(\mathcal{I}), G, SP)$: the probability of being dead at age x for a given sex, G, smoking profile, SP, and a given initial risk profile, $\mathcal{P}^{indYear}_{x-t}(\mathcal{I})$ at age $x - t$,

$Year$: year for the independent initial risk profiles, 1961 or 1981,

t: 20 if $Year$ is 1961 and 19 if $Year$ is 1981.

5.2.1 Confidence intervals for observed prevalence rates

As mentioned in Section 5.2, adjustments will be informed by quantifying the uncertainty in the observed prevalence rates, and therefore we provide relevant 95% confidence intervals for each of these observed prevalence rates. We note here that, as mentioned in Section 2.5, observed prevalence rates are taken from the Health Survey for England (HSE, 2006) which provides figures for the proportion of the general population, in specified age groups, with a risk factor at a specific level (where appropriate). It also provides the number of people sampled in each group. The numbers

provided in HSE (2006) only concern individual risk factors, ignoring joint prevalence of one or more of these factors. For this reason, and also for simplifying the calculation of the confidence intervals, we only consider here risk factors separately. Therefore, taking different age groups as the sampled populations under consideration, this leads to a binomial assumption for the number of people with a risk factor of two category levels, such as diabetes, IHD and stroke (and for mortality). Following the usual assumptions of independence and common probability of occurrence among subjects, 95% confidence intervals are then calculated using the common normal approximation to the binomial distribution, which gives:

$$\hat{p} \pm Z_{(\alpha/2)} \sqrt{\frac{\hat{p}(1-\hat{p})}{n}} \tag{5.2}$$

$$= \hat{p} \pm 1.96 \sqrt{\frac{\hat{p}(1-\hat{p})}{n}} \tag{5.3}$$

where $\hat{p}$ is the sample proportion of the specified age group with the risk factor and n is the relevant sample size. Similarly, for risk factors with more than 2 category levels, such as BMI, hypertension and hypercholesterolaemia, we assume a multinomial distribution and use a similar normal approximation (Goodman, 1965), giving:

$$\hat{p}_i \pm Z_{(\alpha/2k)} \sqrt{\frac{\hat{p}_i(1-\hat{p}_i)}{n}} \tag{5.4}$$

where $\hat{p}_i$, $i = 1,\ldots,$ k is the sample proportion with level i of the risk factor, and k is the number of risk factor levels. For all figures in this chapter, the total populations are the total population in the age groups explained below:

Age group 1: 44 - 54,

Age group 2: 55 - 64,

Age group 3: 65 - 74,

Age group 4: 75 - 84.

5.3 Adjusted prevalence rates for 2000

In this section we provide adjusted prevalence rates for 2000, which are derived as described in Section 5.2.

5.3.1 Smoking

Smoking is a deterministic factor in the HW Model so we will determine the patterns of smoking in the population based on the available data from the General Household Survey 2006 (Goddard, 2006) and we will have different scenarios to be applied to the model. The smoking scenarios are explained below:

(i) Never smoked

This group consists of non–smokers who never smoke throughout their lifetime.

(ii) Smokers

This group started smoking at ages shown in Table 5.1 and smoke throughout their lifetime. Specifically Table 5.1 shows the percentages of people who started smoking regularly at different ages in 2000 for males and females from Goddard (2006). From the table, we can see that many smokers started to smoke before age 16, so we assumed that people who smoke have started smoking at the age of 15.

(iii) Ex-smokers

For ex-smokers, we assumed that they have started smoking at the age of 15 and gave up smoking between 1980 and 2000. We assumed that the smokers quit smoking uniformly between the two years of reference, so that the middle of the interval (1990) is taken as the time of quitting.

We will run the HW Model based on different smoking scenarios and include the adjustment for sudden deaths, as explained in the previous chapter. The prevalence rates for each smoking scenario are weighted by the smoking prevalence for England and Wales populations in 2000 from the Office for National Statistics (ONS), as shown in Tables 3.2, 3.3 and 3.4. These give the estimated prevalence of the risk factors for

Age group	% of Male	% of Female
under 16	43	33
16 - 17	27	27
18 - 19	15	19
20 - 24	11	12
25+	5	8

Table 5.1: Age started smoking regularly in 2000, by sex.

each category in 2000. As we have determined the smoking scenario, we will calculate the prevalence of different categories of BMI in 2000 using the model and compare it with the observed prevalence rates.

5.3.2 BMI

Using the 1981 independent risk profiles, we run the HW Model by projecting forward for 19 years to get the HW model estimated prevalence rates in 2000. The prevalence rates for different smoking scenarios are then weighted by the smoking prevalence, as mentioned in the previous section. The BMI model that we used is Model 1 in Chatterjee *et al.*, (2008b) which does not allow for changes in the prevalence of obesity over calendar time.

Figures 5.2, 5.3, 5.4, 5.5 and 5.6 show the comparison between the HW model estimated prevalence rates before and after adjustments and the observed prevalence rates for each category of BMI for males for each age group. From the graphs, the prevalence rates from the model before adjustments for BMI levels 0, 2 and 4 in Figures 5.2, 5.4 and 5.6 are similar to the observed prevalence rates and lie within the 95% confidence limits of the observed prevalence rates whereas from Figures 5.3 and 5.5 for males, we can see that the HW model estimated prevalence rates before adjustment from the HW Model are significantly different from the observed prevalence rates. The trend over age is almost the same as for the observed prevalence rates for all levels. In Figure 5.3, the estimated prevalence rates from the HW Model are higher than the observed prevalence rates whereas in Figure 5.5, the HW model estimated prevalence rates are lower than the observed prevalence rates. So we need to adjust the forward and backward transition from levels 2 and 3, mostly at the intercepts.

The adjustments that were made to the BMI transition intensities are shown in Table 5.2. The changes shown in the table are the changes in the coefficient of the

variables stated in the table. The estimated prevalence rates from the HW Model after adjustments are shown in Figures 5.2 to 5.6. We can see that after adjustments, the HW model estimated prevalence rates lie within the confidence intervals of the observed prevalence rates.

Transition	Variables	Changes	
		From	To
BMI01	intercept	−2.0093	−2.0393
BMI12	intercept	−2.5725	−2.3625
	age^2	−0.000075	−0.000025
BMI23	intercept	−3.3188	−2.9788
BMI21	intercept	−3.9435	−3.9735
BMI10	intercept	−7.5065	−7.0065

Table 5.2: Adjustments in BMI intensities for males.

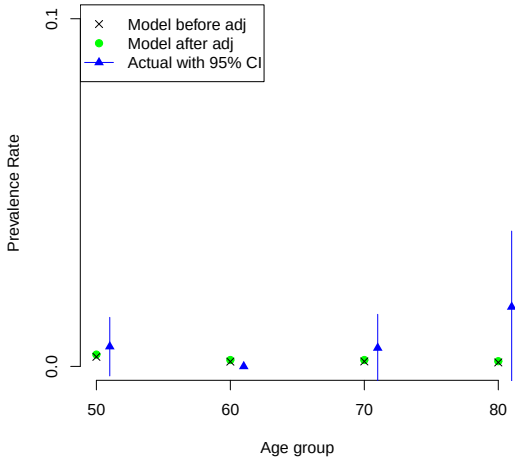

Figure 5.2: Prevalence of BMI level 0 in 2000 (males).

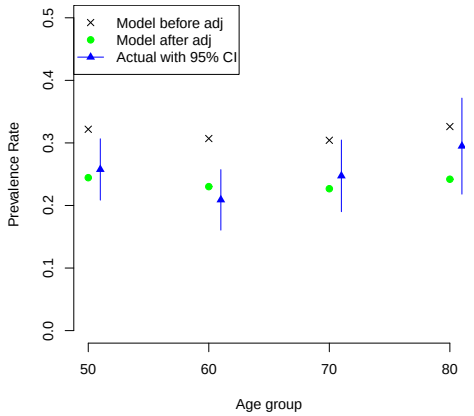

Figure 5.3: Prevalence of BMI level 1 in 2000 (males).

Figures 5.7, 5.8, 5.9, 5.10 and 5.11 show the comparison for females. The adjustments for females involved all levels. The adjustments made are listed in Table 5.3.

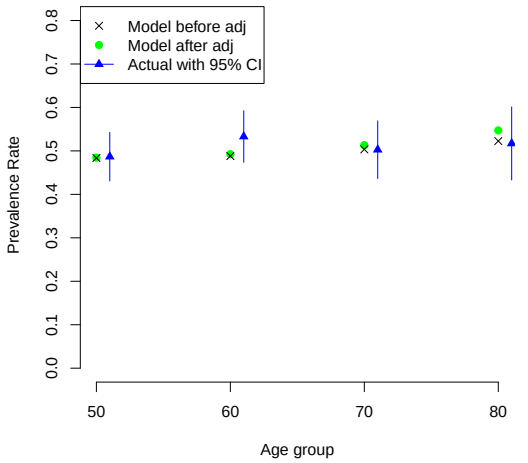

Figure 5.4: Prevalence of BMI level 2 in 2000 (males).

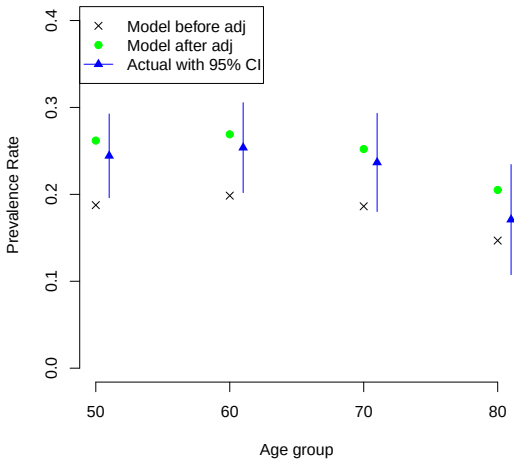

Figure 5.5: Prevalence of BMI level 3 in 2000 (males).

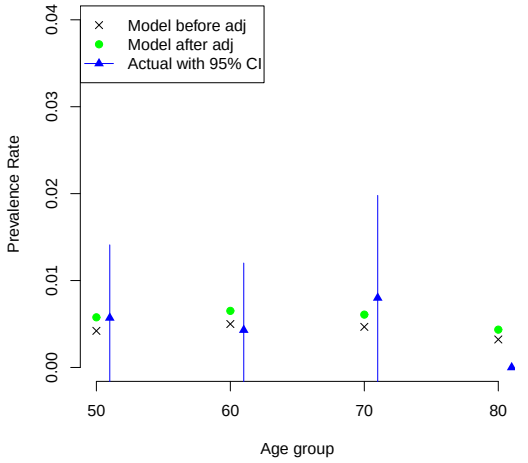

Figure 5.6: Prevalence of BMI level 4 in 2000 (males).

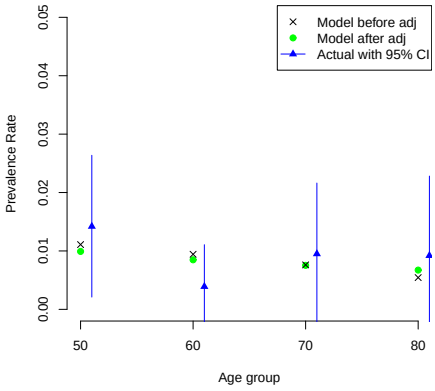

Figure 5.7: Prevalence of BMI level 0 in 2000 (females).

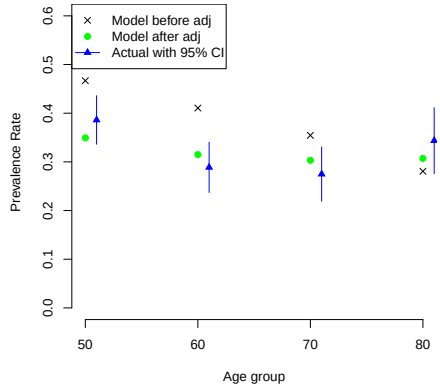

Figure 5.8: Prevalence of BMI level 1 in 2000 (females).

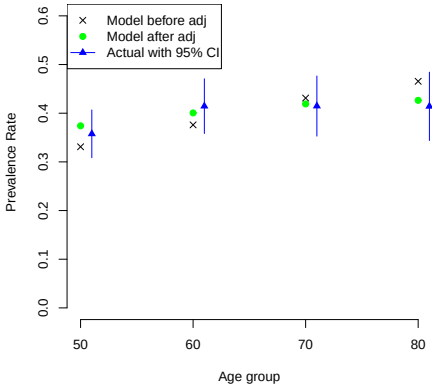

Figure 5.9: Prevalence of BMI level 2 in 2000 (females).

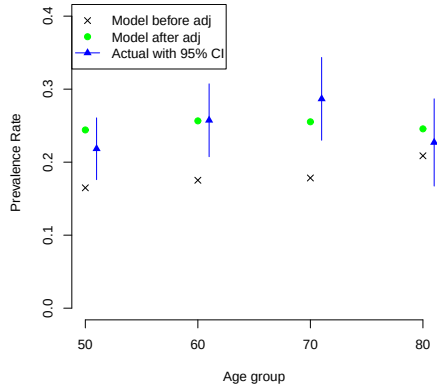

Figure 5.10: Prevalence of BMI level 3 in 2000 (females).

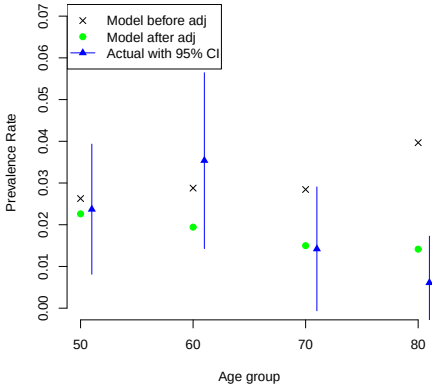

Figure 5.11: Prevalence of BMI level 4 in 2000 (females).

The trend over age group for levels 1, 2 and 3 is the same as for the observed prevalence rates but not for level 4. We added an age^2 term to some of the transitions to adjust the model. More adjustments were made to females compared to males. The HW model estimated prevalence rates are shown in Figures 5.7 to 5.11 and we can see that the model estimated prevalence rates lie within the 95% confidence limits for the observed prevalence rates.

Transition	Variables	Changes	
		From	To
BMI01	intercept	-2.0093	-1.7093
BMI12	intercept	-2.5725	-2.2225
	age^2	-0.000075	-0.000055
	intercept female	-1.3913	-1.3992
	intercept female ex$-$smoker	-3.4373	-3.4073
	age female	0.02196	0.04996
	age^2 female	0.000025	0.000005
BMI23	intercept	-3.3188	-2.4488
	age^2	-0.000075	-0.000055
	intercept female	0.5096	0.3296
	age^2 female	0.000025	0.000005
BMI34	intercept female	1.7403	2.4903
	add age female		-0.02525
BMI43	intercept	-3.035	-2.611
BMI32	intercept	-3.5036	-2.1636
	add age		-0.007
	add age^2		0.0001
BMI21	intercept female	0.2572	2.19
	add age		-0.007
	add age^2		0.0003
BMI10	intercept	-7.5065	-7.0065
	intercept female	1.5701	1.5901

Table 5.3: Adjustments in BMI intensities for females.

5.3.3 Diabetes

We then run the HW Model by including the previous adjustments. We made one adjustment to the diabetes intensities for males to get the HW model estimated

prevalence rates to be within the confidence interval for the observed prevalence rates. The observed prevalence rates are shown in Figures 3.32 and 3.35 for males and females. We adjusted the transition for diabetes from level 0 to 1 (DIAB01) for the intercept, from -13.1194 to -13.2194 to reduce the transition from level 0 to 1. The diabetes estimated rates from the HW model after the BMI adjustments and before any further adjustments were made are shown in Figure 5.12 for males. The HW model estimated prevalence rates after adjustment and the 2000 observed prevalence rates for males are also shown in the same figure.

For females, the transition from 0 to 1 is adjusted by increasing the intercept. The coefficients for age and age^2 are also adjusted to increase the estimated prevalence rates over age and at older ages as shown in Figure 5.13. The adjustments are shown in Table 5.4 and the HW model estimated prevalence rates are shown in Figure 5.13. By looking at the minimal adjustments for diabetes, it can be said that the adjustments for BMI have affected the estimated prevalence rates for diabetes and this shows the relationship between the changes in diabetes with BMI.

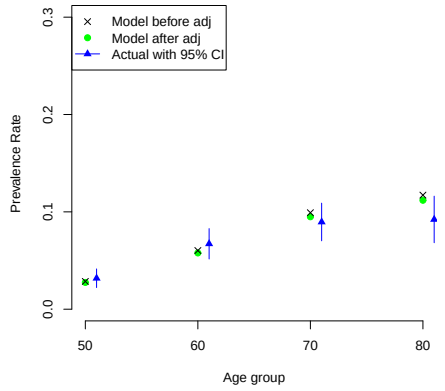

Figure 5.12: Prevalence of diabetes in 2000 (males).

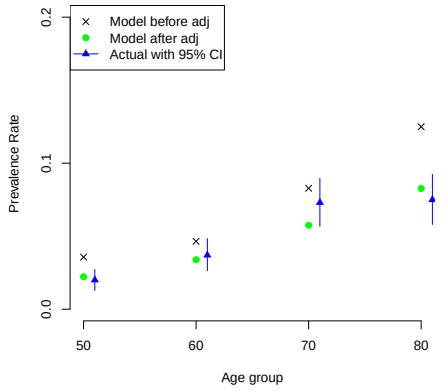

Figure 5.13: Prevalence of diabetes in 2000 (females).

Transition	Variables	Changes	
		From	To
DIAB10	intercept	−5.7628	−4.4628
	age	0.08451	0.07451
	age^2	−0.00007309	−0.00006809

Table 5.4: Adjustments in diabetes intensities for females.

5.3.4 Hypertension

The adjustments are continued with the hypertension risk factor. The 2000 observed prevalence rates are shown in Figures 3.38, 3.41, 3.44 and 3.47 for males and 3.50, 3.53, 3.56 and 3.59 for females. The trend over age group from the estimated prevalence rates for all hypertension levels is the same as in observed prevalence rates as shown in Figures 5.14 to 5.17 so we only need to adjust by reducing the transition intensities between the levels. Adjustments for males are shown in Table 5.5. The estimated prevalence rates after adjustments are shown in the same figures as the observed prevalence rates.

For females, more adjustments were made compared to males. The HW model estimated prevalence rates before adjustments are shown in Figures 5.18 to 5.21. From Figures 5.18, 5.19 and 5.20, we can see that levels 0, 1 and 2 are different from the observed prevalence rates. The HW Model estimated a higher rate of hypertension level 0 for younger ages for females in 2000 and it decreased steeply against age. This is not the case for the observed prevalence rates as the rate for level 0 decreases slightly with age. The Health Survey for England 2003 (Sproston & Primatesta, 2004) reported that the prevalence of hypertension (level 1, 2 and 3) increased steeply with age for both males and females. This leads to a slight decrease in hypertension level 0 as we can see in the observed prevalence rates in Figure 5.18. The model estimates that a lower percentage of younger people (ages 40 and 50) in 2000 have hypertension. This could be because the model has estimated lower obesity rates at younger ages and this has reduced the hypertension rates for the same group as BMI levels could effect hypertension rates. Mokdad *et al.* (2003) reported that those with BMI greater than 30 (level 3 and 4) were found to have a higher risk for diabetes and hypertension with age-adjusted odds-ratio of 3.66 and 3.72, respectively, compared to those with normal BMI.

The adjustments for the transition intensities for hypertension for females are

shown in Table 5.6. The adjustments were made to the transitions between all levels of hypertension, mostly to the intercepts and age^2. We also add an age^2 term to HTEN32, HTEN21 and HTEN10 to make adjustments for older ages. The HW model estimated prevalence rates after adjustments are shown in Figures 5.18 to 5.21.

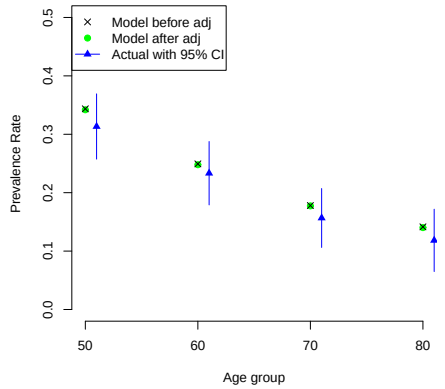

Figure 5.14: Prevalence of h'ten level 0 in 2000 (males).

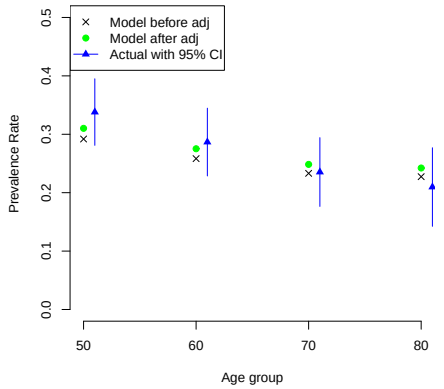

Figure 5.15: Prevalence of h'ten level 1 in 2000 (males).

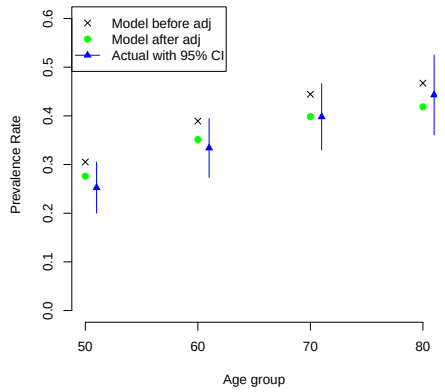

Figure 5.16: Prevalence of h'ten level 2 in 2000 (males).

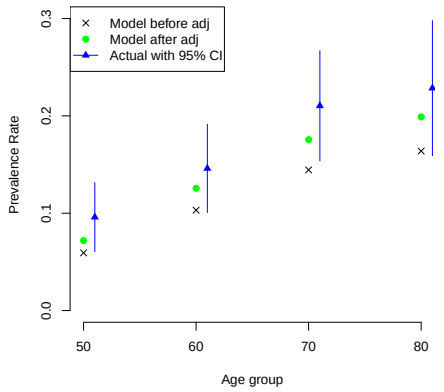

Figure 5.17: Prevalence of h'ten level 3 in 2000 (males).

Transition	Variables	Changes	
		From	To
HTEN23	intercept	−6.107	−5.807
HTEN21	intercept	−1.5793	−1.3793

Table 5.5: Adjustments in h'ten intensities for males.

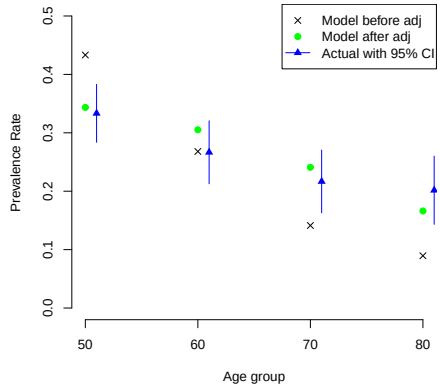

Figure 5.18: Prevalence of h'ten level 0 in 2000 (females).

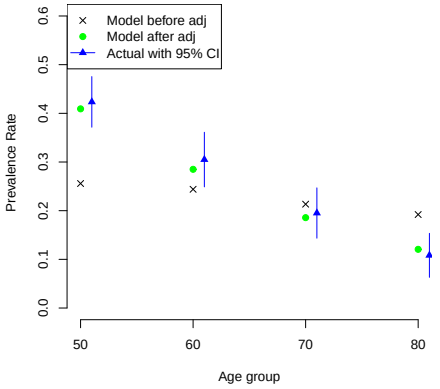

Figure 5.19: Prevalence of h'ten level 1 in 2000 (females).

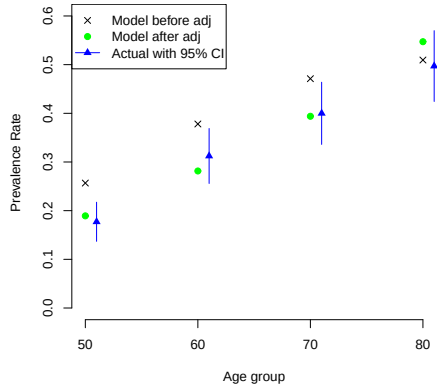

Figure 5.20: Prevalence of h'ten level 2 in 2000 (females).

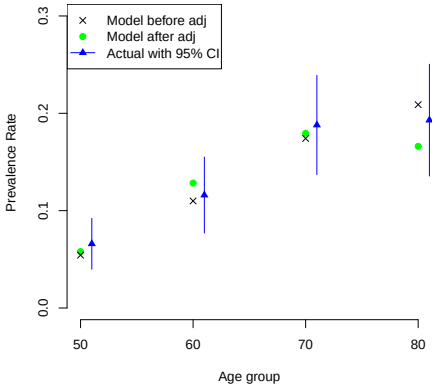

Figure 5.21: Prevalence of h'ten level 3 in 2000 (females).

Transition	Variables	Changes	
		From	To
HTEN01	intercept female	−2.2040	6.6956
	age female	0.06351	−0.07454
	age^2 female	−0.0004287	0.0006254
HTEN12	intercept female	−0.1456	1.8886
	age^2 female	0.00006362	0.0007594
	add age female		−0.06396
HTEN23	intercept female	0.1204	−3.30396
	add age female		−0.06978
	add age^2 female		−0.001118
HTEN32	intercept	−1.4509	−2.2745
	age	−0.00757	0.004882
	add age^2		0.0000754
HTEN21	intercept	−1.5793	1.3806
	age	−0.01088	−0.03879
	add age^2		−0.0000006
HTEN10	intercept female	0.3378	2.4998
	age^2 female	−0.00008308	−0.0000129
	add age female		−0.0000129

Table 5.6: Adjustments in h'ten intensities for females.

5.3.5 Hypercholesterolaemia

For hypercholesterolaemia, more adjustments need to be made, compared to BMI, diabetes and hypertension, as hypercholesterolamia is not related to changes in any of these factors. For levels 0 and 3, the modelled trend over age is different than the actual trend as shown in Figures 5.22 and 5.25. The HW model estimated prevalence rates for level 1 in Figure 5.23 are higher than the observed prevalence rates whereas for level 2 in Figure 5.24, the model estimated prevalence rates are lower than the observed prevalence rates. We need to change the coefficients for age and age^2 to adjust the trend. We also need to adjust the intercepts to match the model estimated prevalence rates with the observed prevalence rates. The adjustments for transitions between categories of hypercholesterolaemia are shown in Table 5.7. The estimated prevalence rates from the HW model are shown in Figures 5.22 to 5.25.

For females, the HW model estimated prevalence rates before any adjustments of the transition intensities for hypercholesterolaemia are shown in Figures 5.26 to 5.29. Hypercholesterolaemia levels 0 and 3, shown in Figures 5.26 and 5.29 respectively,

have similar trends but need some adjustments to the model estimated prevalence rates. The adjustments are shown in Table 5.8. Adjustments are made to the transitions between all levels of hypercholesterolaemia. These involve mainly changes to the intercept and age^2 to increase or decrease the model estimated prevalence rates and some adjustments to the coefficients for age to adjust the trends. The model estimated prevalence rates after adjustments are shown in the same figures as the model estimated prevalence rates before adjustments.

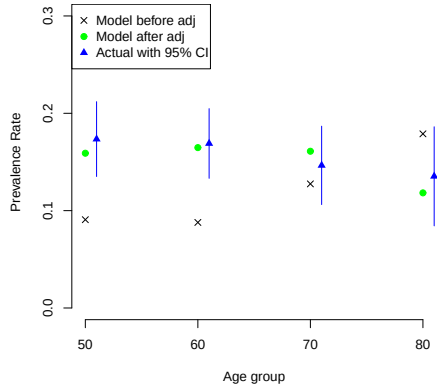

Figure 5.22: Prevalence of h'chol level 0 in 2000 (males).

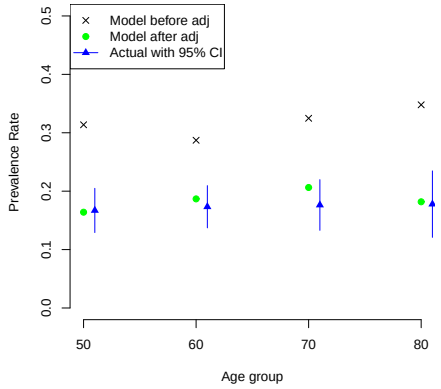

Figure 5.23: Prevalence of h'chol level 1 in 2000 (males).

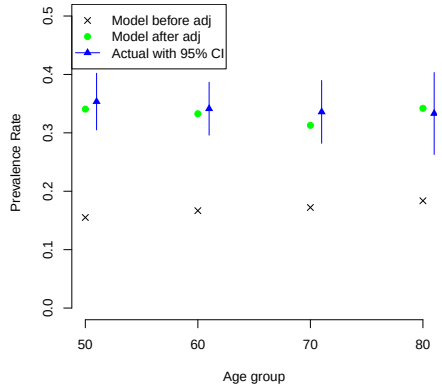

Figure 5.24: Prevalence of h'chol level 2 in 2000 (males).

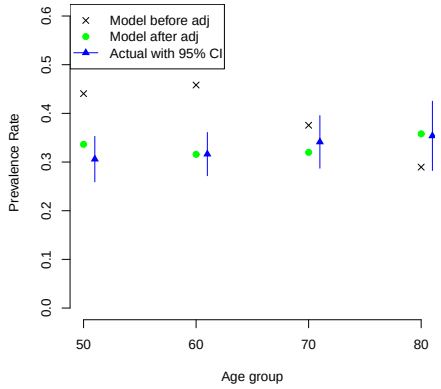

Figure 5.25: Prevalence of h'chol level 3 in 2000 (males).

Transition	Variables	Changes	
		From	To
HCHOL01	intercept	-5.6141	-0.8141
	age	-1.699	0.0005
	age^2	-0.001643	-0.0000000001
HCHOL12	intercept	-4.9372	-0.5372
	age	0.1109	0.0059
	age^2	-0.001279	-0.001079
HCHOL23	intercept	-4.0056	-0.0056
	age	0.1305	-0.035
HCHOL32	intercept	-3.2804	-5.1804
HCHOL21	intercept	-3.5572	-4.0572
	age^2	-0.0004721	-0.0007821
HCHOL10	intercept	-5.2261	-1.1261
	age	0.09142	0.01842
	age^2	-0.0007403	-0.0002403

Table 5.7: Adjustments in h'chol intensities for males.

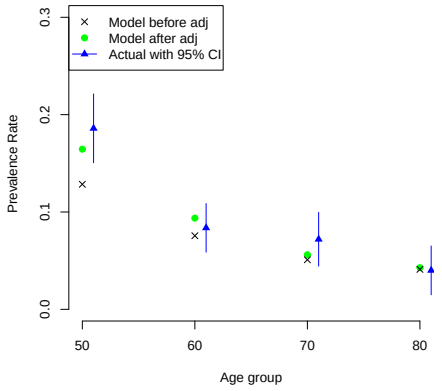

Figure 5.26: Prevalence of h'chol level 0 in 2000 (females).

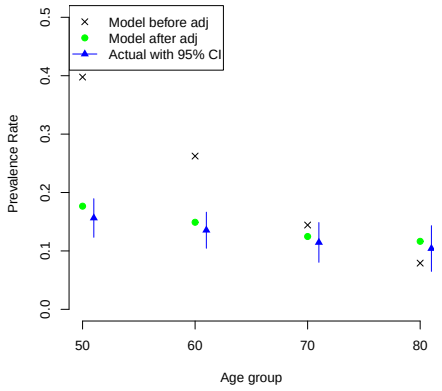

Figure 5.27: Prevalence of h'chol level 1 in 2000 (females).

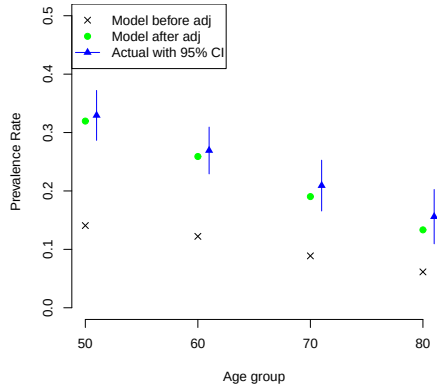

Figure 5.28: Prevalence of h'chol level 2 in 2000 (females).

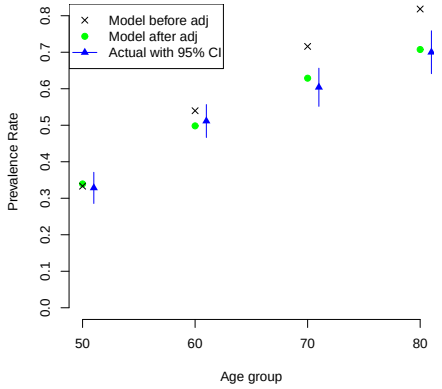

Figure 5.29: Prevalence of h'chol level 3 in 2000 (females).

Transition	Variables	Changes	
		From	To
HCHOL01	intercept female	−0.7676	3.3207
	age female	0.0147	−0.1528
	age^2 female	−0.0000375	0.001638
HCHOL12	intercept female	−3.0015	2.6730
	age female	0.062	−0.08472
	age^2 female	−0.0000411	0.0011035
HCHOL23	intercept female	−1.3449	−9.8716
HCHOL32	intercept female	−0.4248	−0.0158
HCHOL21	intercept female	−0.2666	1.61003
	add age female		−0.08474
	add age^2 female		0.0009442
HCHOL10	intercept female	2.9518	6.1203
	age female	−0.1051	−0.1765
	age^2 female	0.0008393	0.0013596

Table 5.8: Adjustments in h'chol intensities for females.

5.3.6 IHD, stroke and IHD and/or stroke

After some adjustments were made in the transition intensities for four risk factors, we look into the prevalence of IHD, stroke and IHD and/or stroke. As we can see in Figures 5.30, 5.31 and 5.32, the estimated prevalence rates for males from the HW model are within the confidence intervals of the observed prevalence rates except for the prevalence of IHD and/or stroke. Some adjustments were made and are shown in Table 5.9. We adjust the parameter for age^2 in angina pectoris (AP) and transient ischemic attack (TIA) to lower the prevalence at older ages in IHD and/or stroke. We also adjust the intercept and age parameters. The prevalences after adjustments are also shown in Figures 5.30, 5.31 and 5.32.

Adjustments for IHD, stroke and IHD and/or stroke intensities for females are shown in Table 5.10. There is only one transition that is adjusted, since as we can see in Figures 5.33, 5.34 and 5.35, the model estimated prevalence rates before any adjustments to the intensities are close to the observed prevalence rates in 2000. Adjustments are made to the transition to MI by changing the intercept and coefficient for age. The estimated prevalence rates after adjustments from the HW Model are also shown in Figures 5.33, 5.34 and 5.35.

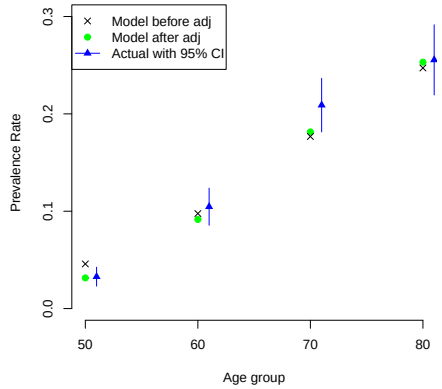

Figure 5.30: Prevalence of IHD in 2000 (males).

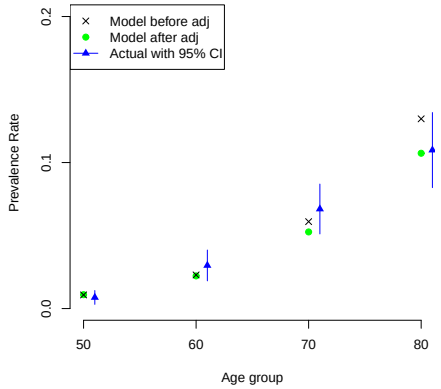

Figure 5.31: Prevalence of stroke in 2000 (males).

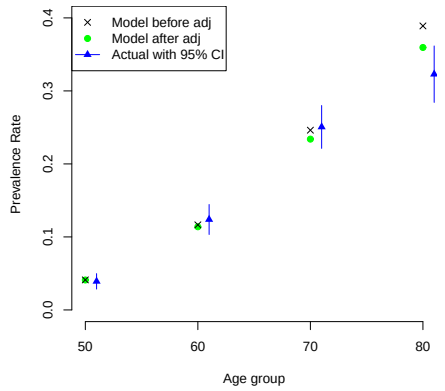

Figure 5.32: Prevalence of IHD and/or stroke in 2000 (males).

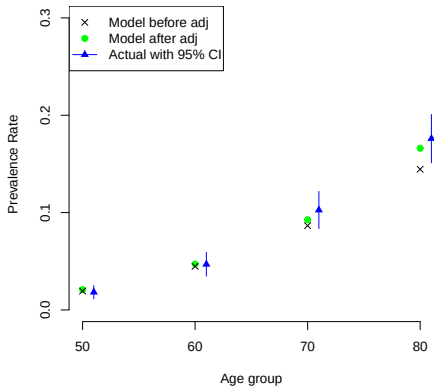

Figure 5.33: Prevalence of IHD in 2000 (females).

Transition	Variables	Changes	
		From	To
MI	intercept	-10.8973	-1.8973
	age	0.06967	-0.48567
AP	intercept	-15.83	-16.07
	age	0.3003	0.3073
	age^2	0.002252	0.002203
CI	age	0.04473	0.02273
TIA	intercept	-21.18	-21.58
	age	0.3201	0.3901
	age^2	-0.001708	-0.002908

Table 5.9: Adjustments in IHD, stroke and IHD and/or stroke intensities for males.

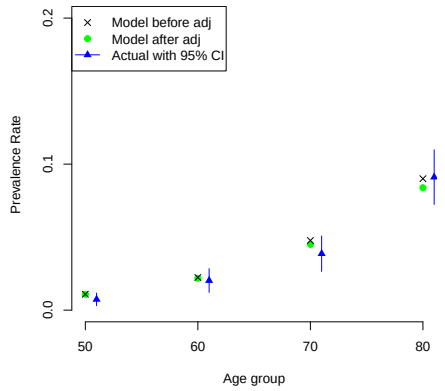

Figure 5.34: Prevalence of stroke in 2000 (females).

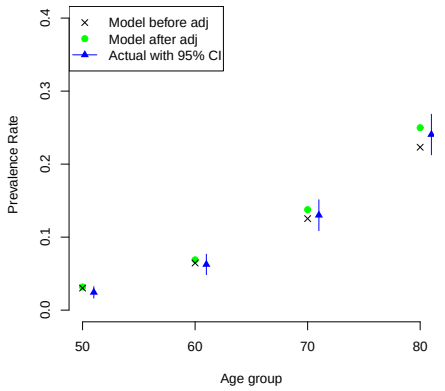

Figure 5.35: Prevalence of IHD and/or stroke in 2000 (females).

Transition	Variables	Changes	
		From	To
MI	intercept	−10.8973	−11.0973
	age	0.06967	0.07967

Table 5.10: Adjustments in IHD, stroke and IHD and/or stroke intensities for females.

5.3.7 Mortality

We run the HW Model with all the adjustments performed earlier for eight factors including sudden deaths and calculate the estimated mortality rates in 2000. The model estimated rates are compared with the rates from ELT16 (ONS, 2009), the English Life Table No 16 which covers years from the middle of 2000 to mid 2002. The HW model estimated rates are shown in Figures 5.36 and 5.37. As shown, the estimated mortality rates from the HW Model are within the confidence intervals of the observed mortality rates from ELT16 and these are achieved without any adjustment to the mortality intensities. The confidence intervals are calculated using the number of exposed to risk given in the ELT16 methodology (ONS, 2009) as the sample size, n. As the previous risk factors mentioned have an effect on mortality, the adjusted intensities might have influenced the mortality intensities so that no further adjustment is needed.

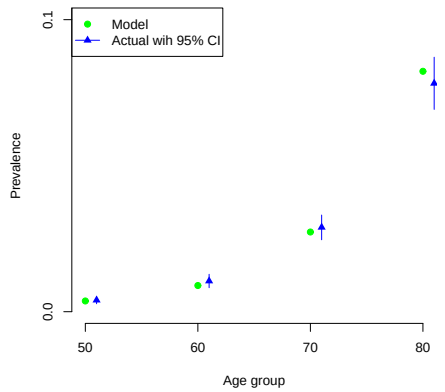

Figure 5.36: Mortality rates in 2000 (males).

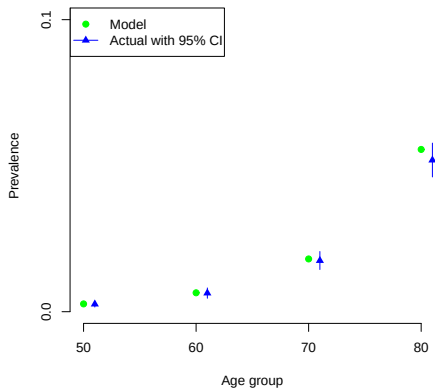

Figure 5.37: Mortality rates in 2000 (females).

5.4 Adjusted prevalence rates for 1981

Having parameterised a model that matches the 2000 observed prevalence rates (HW Model estimated 2000 prevalence rates), we then make adjustments to find a parameterisation that match the 1981 observed prevalence rates. We would need the HW model estimated prevalence rates to be used to find the effect of changes in risk factors between 2000 and 1981. We will use the parameters that matches the 1981 observed prevalence rates with the model that matches the 2000 observed prevalence rates in order to quantify the changes. The 1981 observed prevalence rates are shown in Chapter 3. We use the risk profiles for 1961 (see Table 3.7) as our starting point and then run the model for 20 years to calculate prevalences for different age groups as at 1981.

5.4.1 Smoking

We use the same smoking scenarios as explained in Section 5.3.1. The estimated prevalence rates from the model are weighted using the 1981 smoking prevalence which is calculated using interpolation with the available observed prevalence rates from ONS. The observed prevalence rates are shown in Tables 3.2, 3.3 and 3.4 for males and females.

5.4.2 BMI

For BMI, we adjust the original (2003) intensities to match the 1981 observed prevalence rates. The 1981 observed prevalence rates are interpolated between observed prevalence rates from HWS80 and HALS84 as mentioned in Section 3.3. The observed prevalence rates are shown in Figures 3.2, 3.5, 3.8, 3.11 and 3.2 for males and Figures 3.17, 3.20, 3.23, 3.26 and 3.17 for females. Table 5.11 shows the adjustments that were made to the BMI transition intensities for males. The HW model estimated prevalence rates after adjustments are shown in Figures 5.38 to 5.42. The HW model estimated prevalence rates are adjusted to be within the 95% confidence interval of the observed prevalence rates as shown in the figures.

For females, the adjustments are shown in Table 5.12. The adjustments are fewer than for males as we started the adjustments by using the 1981 adjusted intensities

for males. The HW model estimated prevalence rates are shown in Figures 5.43 to 5.47.

Transition	Variables	Changes	
		From	To
BMI01	intercept	−2.0093	−1.3093
	add age		0.011948
	add age^2		−55.002855
BMI12	intercept	−2.5725	−1.9734
	add age		−0.611948
	delete age^2		
BMI23	intercept	−3.3188	−2.4718
	age	−0.00425	0.00875
	delete age^2		
BMI34	intercept	−5.9188	−8.4188
	add age		0.08275
	add age^2		2.104805
BMI32	intercept	−3.5036	−1.5636
	add age		0.613
	add age^2		1.7561
BMI21	intercept	−3.9435	−2.9735
	add age		0.413
BMI10	intercept	−7.5065	−5.1065
	add age		0.08275
	add age^2		2.104805

Table 5.11: Adjustments in BMI intensities for males.

5.4.3 Diabetes

For diabetes, we have data from the Health and Lifestyle Survey 1984-1985 (HALS84) and HSE1991 and we extrapolate the 1981 observed prevalence rates using these observed prevalence rates from HALS84 and HSE1991. The observed prevalence rates are shown in Figures 3.32 and 3.35. We adjust the intensities to match the extrapolated observed prevalence rates that we have calculated before. The adjustments for

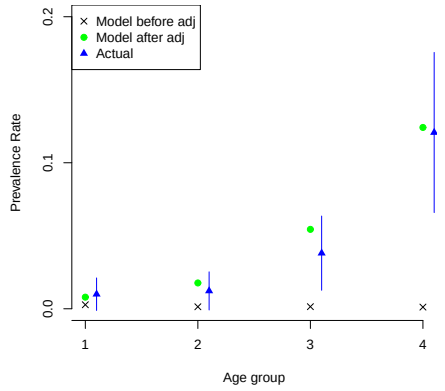

Figure 5.38: Prevalence of BMI level 0 in 1981 (males).

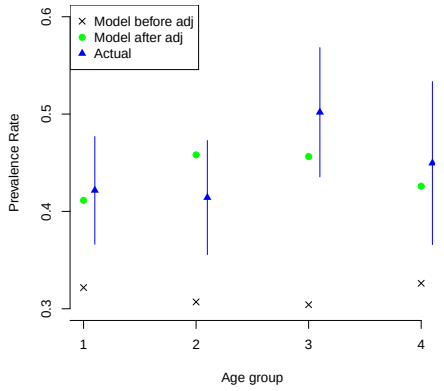

Figure 5.39: Prevalence of BMI level 1 in 1981 (males).

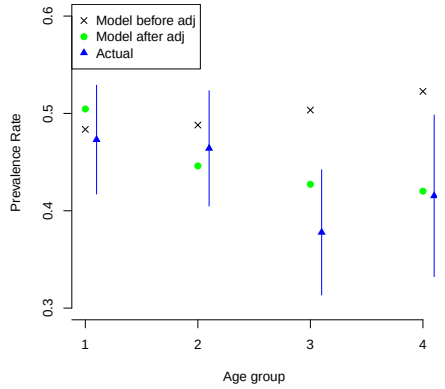

Figure 5.40: Prevalence of BMI level 2 in 1981 (males).

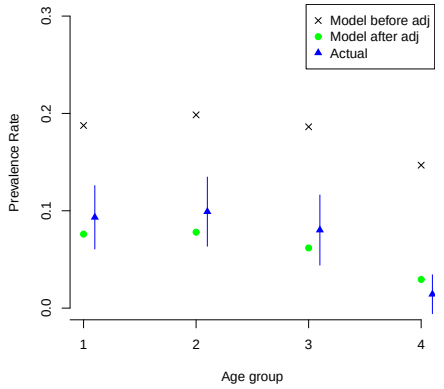

Figure 5.41: Prevalence of BMI level 3 in 1981 (males).

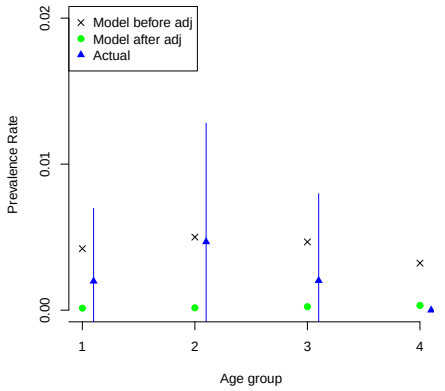

Figure 5.42: Prevalence of BMI level 4 in 1981 (males).

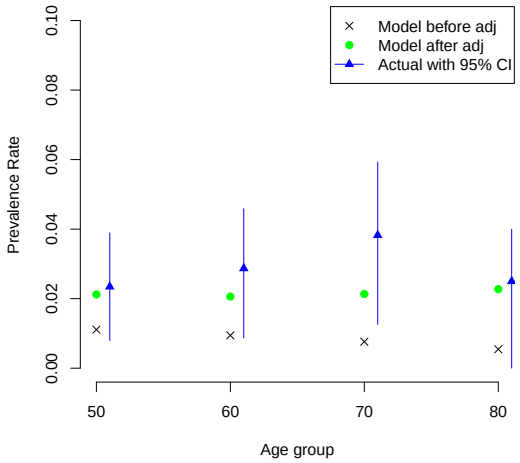

Figure 5.43: Prevalence of BMI level 0 in 1981 (females).

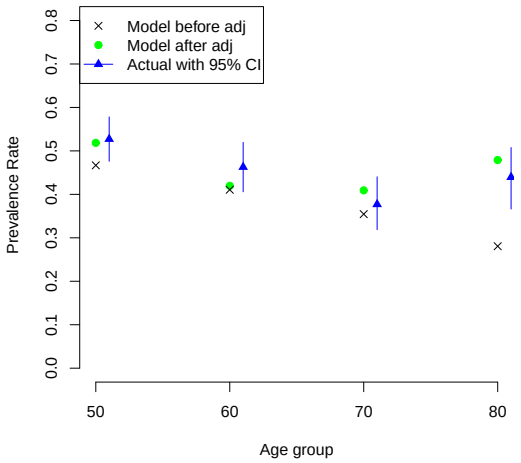

Figure 5.44: Prevalence of BMI level 1 in 1981 (females).

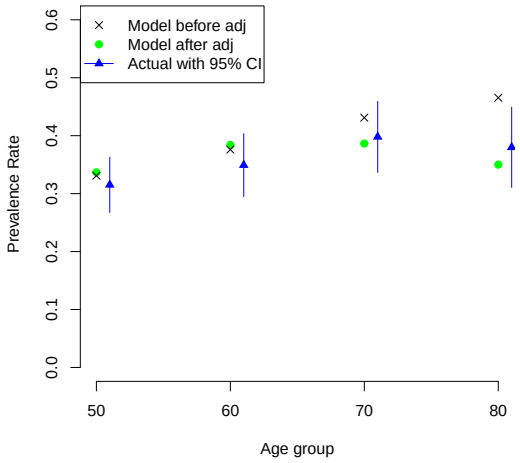

Figure 5.45: Prevalence of BMI level 2 in 1981 (females).

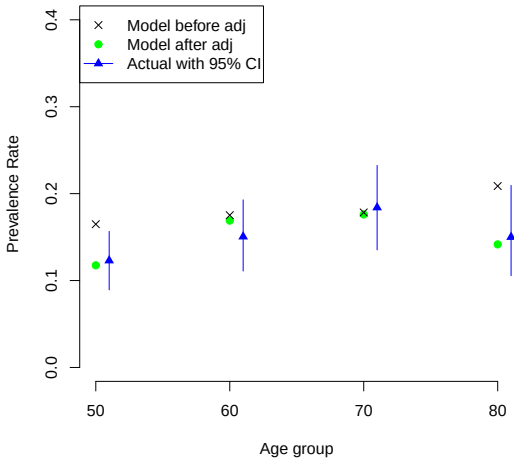

Figure 5.46: Prevalence of BMI level 3 in 1981 (females).

Transition	Variables	Changes	
		From	To
BMI01	intercept	−1.3093	−1.7093
	age	0.011948	−0.711948
	delete age^2		
BMI12	intercept	−1.9734	−1.9034
	intercept female age	0.02196	2.56426
	intercept female age^2	0.000025	−1.04805
BMI34	intercept female	−1.7403	−4.891
BMI32	intercept	−1.5636	−3.0636
BMI21	intercept female	0.2752	−1.0535
BMI10	intercept	−5.1065	−6.5065

Table 5.12: Adjustments in BMI intensities for females.

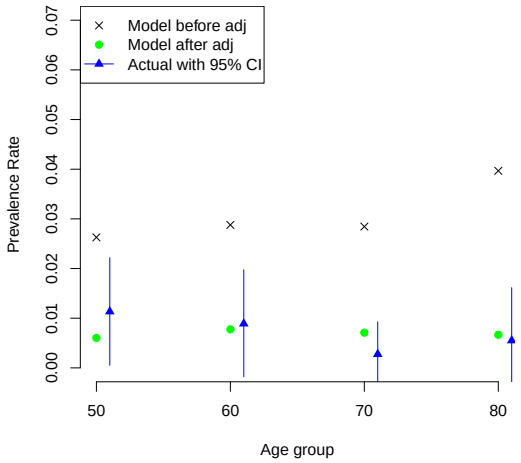

Figure 5.47: Prevalence of BMI level 4 in 1981 (females).

males are shown in Table 5.13. Figure 5.48 shows the estimated diabetes rates that match the observed prevalence rates in 1981.

The adjustments for females are shown in Table 5.14. The adjustments are made only to the forward transition from level 0 to 1. The estimated prevalence rates are shown in Figure 5.49 together with the 1981 observed prevalence rates for diabetes.

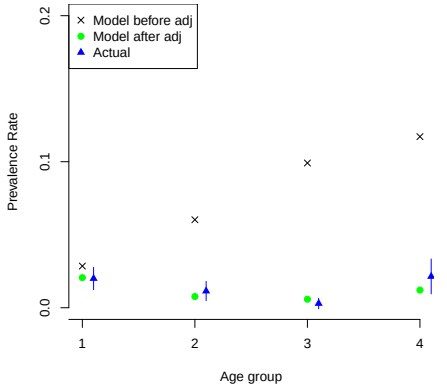

Figure 5.48: Prevalence of diabetes in 1981 (males).

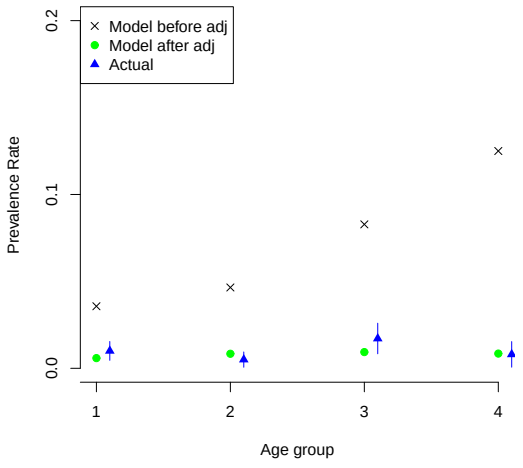

Figure 5.49: Prevalence of diabetes in 1981 (females).

Transition	Variables	Changes	
		From	To
DIAB01	intercept	−13.1194	−6.8894
	age	0.2171	0.3971
	age^2	−0.00143	−2.80423
DIAB10	age	0.08451	4.19902
	age^2	−0.0007309	−1.1043

Table 5.13: Adjustments in diabetes intensities for males.

Transition	Variables	Changes	
		From	To
DIAB01	intercept	−13.1194	−6.8394
	age	0.2171	2.2971

Table 5.14: Adjustments in diabetes intensities for females.

5.4.4 Hypertension

For hypertension, we calculate the observed prevalence rates in 1981, which are shown in Figures 3.38, 3.41, 3.44 and 3.47 for males and 3.50, 3.53, 3.56 and 3.59 for females by using extrapolation between HALS84 and HALS91. The adjustments to the intensities to match the 1981 observed prevalence rates are shown in Table 5.15 for males. The HW model estimated prevalence rates after adjustments are shown in Figures 5.50 to 5.53.

The adjustments for hypertension for females are shown in Table 5.16. The HW model estimated prevalence rates are shown in Figures 5.54 to 5.57.

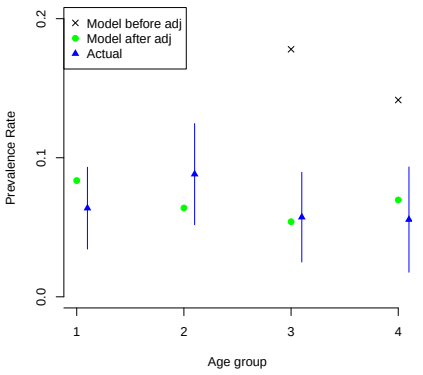

Figure 5.50: Prevalence of h'ten level 0 in 1981 (males).

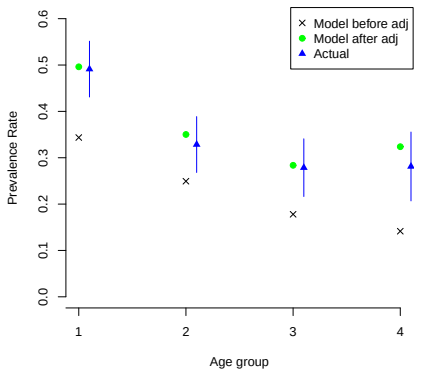

Figure 5.51: Prevalence of h'ten level 1 in 1981 (males).

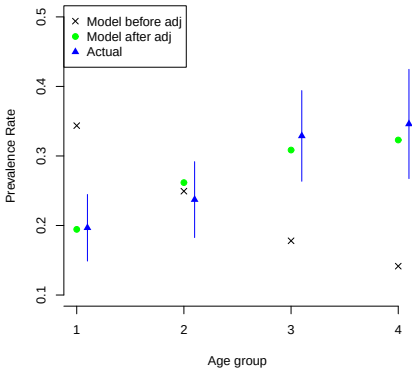

Figure 5.52: Prevalence of h'ten level 2 in 1981 (males).

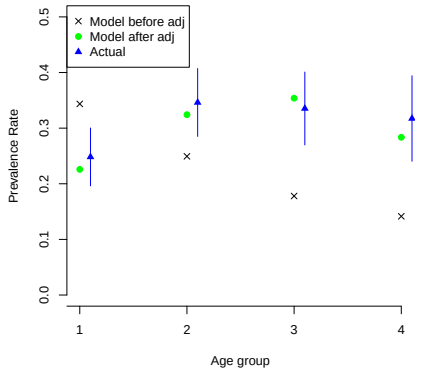

Figure 5.53: Prevalence of h'ten level 3 in 1981 (males).

Transition	Variables	Changes	
		From	To
HTEN01	intercept	−5.225	−1.7735
	delete age		
	age^2	−0.0005662	−0.5441
HTEN12	intercept	−5.4559	−3.01365
	age	0.1102	2.05219
	age^2	−0.0008271	−2.4948
HTEN23	intercept	6.107	−1.6595
	age	0.09257	0.22323
	age^2	−0.0006924	−1.06539
HTEN32	intercept	−1.4509	−1.9994
	age	−0.00757	−0.00467
	delete age^2		
HTEN21	intercept	−1.5793	−2.5233
	age	−0.01088	−0.03728
	delete age^2		
HTEN10	intercept	−2.0782	−3.031025
	age	−0.009779	−0.00054
	delete age^2		

Table 5.15: Adjustments in h'ten intensities for males.

Transition	Variables	Changes	
		From	To
HTEN01	intercept female	0.6956	1.7585
	age female	−0.07454	1.02225
	age^2 female	0.0006254	1.03688
HTEN12	intercept female	1.8886	−1.32445
	age female	−0.06396	0.223542
	age^2 female	−0.0007594	−0.8650998
HTEN23	age female	−0.06978	3.45167
	age^2 female	−0.001118	−2.13997
HTEN21	intercept	1.3806	−0.660175
HTEN10	intercept female	2.4998	1.41625
	age female	−0.0000129	−2.007218
	age^2 female	−0.0.0000129	1.13997

Table 5.16: Adjustments in h'ten intensities for females.

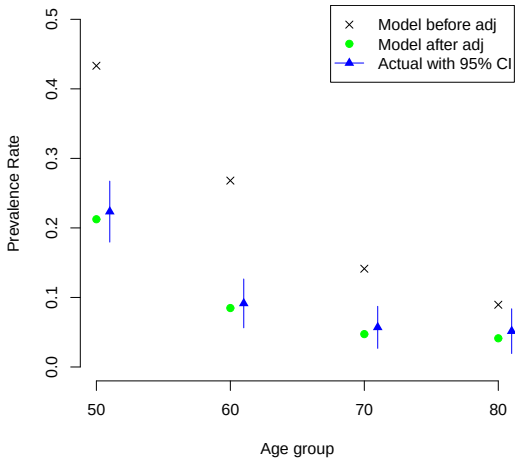

Figure 5.54: Prevalence of h'ten level 0 in 1981 (females).

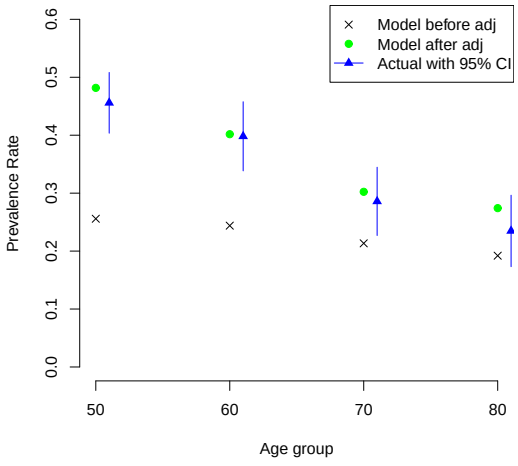

Figure 5.55: Prevalence of h'ten level 1 in 1981 (females).

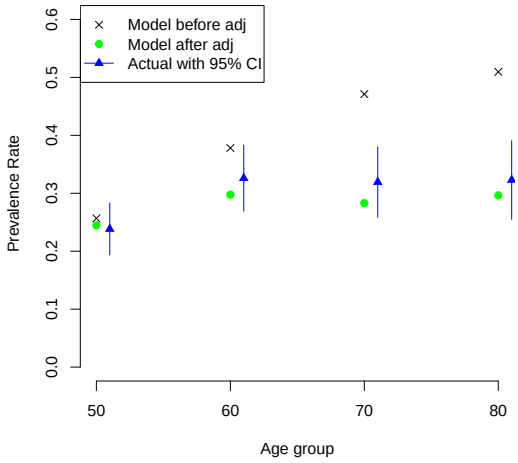

Figure 5.56: Prevalence of h'ten level 2 in 1981 (females).

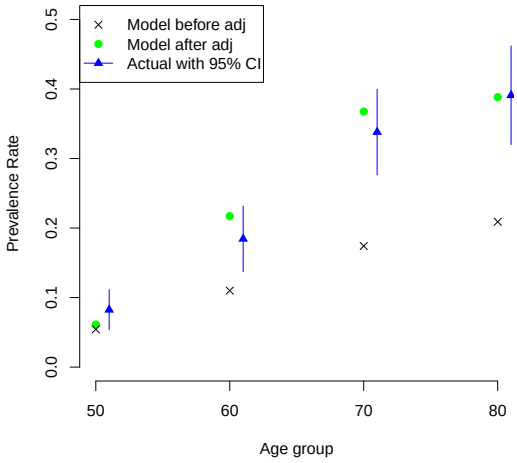

Figure 5.57: Prevalence of h'ten level 3 in 1981 (females).

5.4.5 Hypercholesterolaemia

We make adjustments to the transition intensities to match the hypercholesterolaemia observed prevalence rates in 1981. The 1981 observed prevalence rates are calculated from HSE 1994 and 2003 and are explained in Chapter 3. The adjustments are shown in Table 5.17 for males. The estimated prevalence rates from the adjusted model with the observed prevalence rates are shown in Figures 5.58 to 5.61 for males. We used the 2000 adjusted intensities as the starting intensities to adjust the model to match the 1981 observed prevalence rates for females. The HW model estimated prevalence rates are shown in Table 5.18. Figures 5.62 to 5.65 show the adjusted rates estimated from the HW model for females.

5.4.6 IHD, stroke and IHD and/or stroke

For IHD and stroke, we only have data from HSE. So we used the observed prevalence rates from 1994 and 2006 to extrapolate the 1981 observed prevalence rates. The adjustments to the transition intensities for males are shown in Table 5.19. The

Transition	Variables	Changes	
		From	To
HCHOL01	intercept	−0.8141	−1.0141
	age	0.0005	2.51305
	age^2	−0.0000000001	6.00496
HCHOL12	intercept	−0.5372	−3.7172
	delete age		
	age^2	−0.001079	−15.436
HCHOL23	intercept	−0.0056	−2.3056
	age	−0.035	0.0305
	delete age^2		
HCHOL32	age	0.04828	0.14828
	age^2	−0.0004436	1.436
HCHOL21	intercept	−4.0572	−3.4972
	delete age		
	delete age^2		
HCHOL10	intercept	−1.1261	−3.6261
	delete age		
	delete age^2		

Table 5.17: Adjustments in h'chol intensities for males.

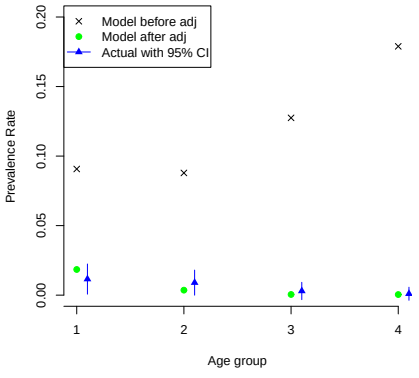

Figure 5.58: Prevalence of h'chol level 0 in 1981 (males).

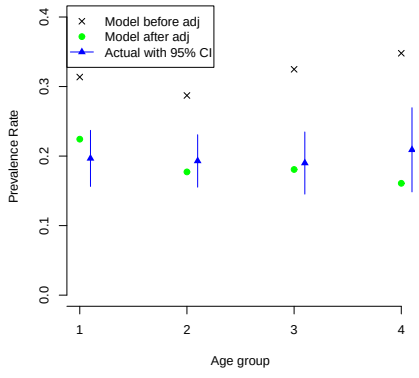

Figure 5.59: Prevalence of h'chol level 1 in 1981 (males).

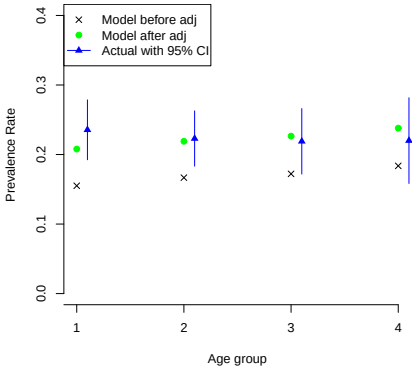

Figure 5.60: Prevalence of h'chol level 2 in 1981 (males).

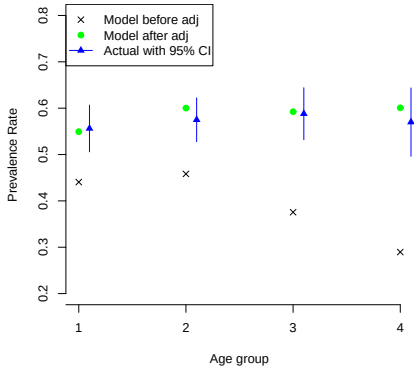

Figure 5.61: Prevalence of h'chol level 3 in 1981 (males).

Transition	Variables	Changes	
		From	To
HCHOL01	intercept female	3.3207	−0.85295
	age female	−0.1528	4.91305
	age^2 female	0.001638	−3.0549605
HCHOL12	intercept female	2.6730	−0.80395
	age female	−0.08472	0.00559
	age^2 female	0.0011035	−0.58621
HCHOL23	intercept female	−9.8716	−1.3205
	age female	−0.01509	2.08671
	age^2 female	0.00075	−1.08621
HCHOL32	intercept female	−0.0158	−2.1912
HCHOL21	age female	−0.08474	1.35057
	delete age^2 female		
HCHOL10	age female	−0.1765	−1.21718
	age^2 female	0.0013596	3.595139

Table 5.18: Adjustments in h'chol intensities for females.

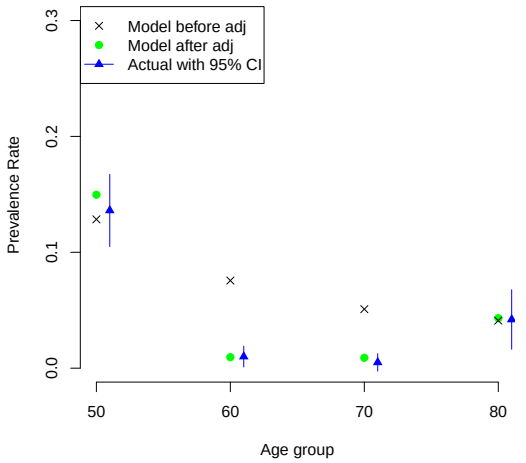

Figure 5.62: Prevalence of h'chol level 0 in 1981 (females).

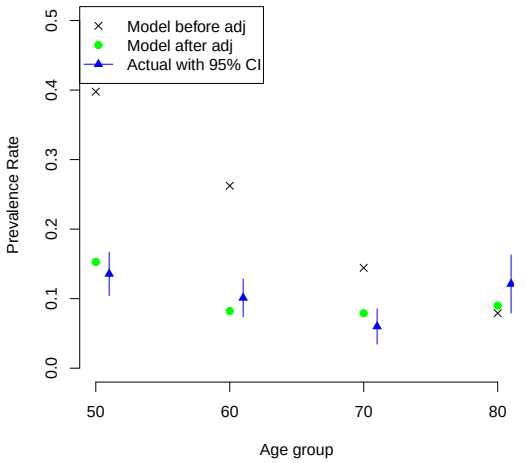

Figure 5.63: Prevalence of h'chol level 1 in 1981 (females).

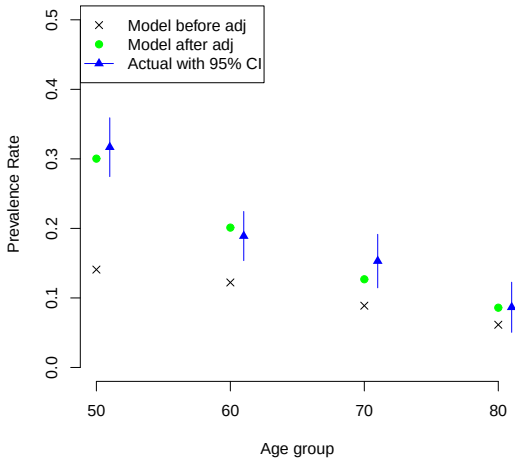

Figure 5.64: Prevalence of h'chol level 2 in 1981 (females).

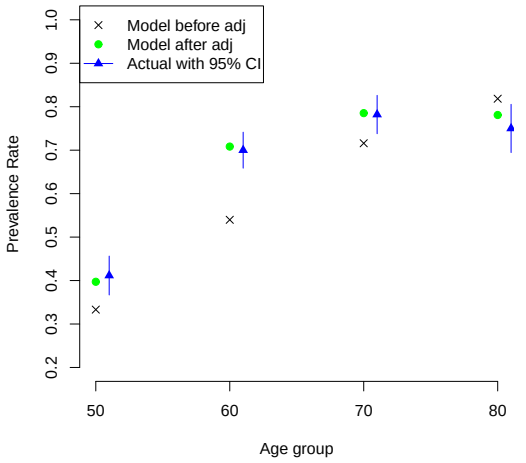

Figure 5.65: Prevalence of h'chol level 3 in 1981 (females).

estimated prevalence rates from the adjusted model are shown in Figures 5.66, 5.67 and 5.68 for males.

Table 5.20 shows the adjustments that have been made to the IHD and stroke intensities to match the HW model estimated prevalence rates with 1981 observed prevalence rates for females. Figures 5.69, 5.70 and 5.71 show the estimated and observed prevalence rates for females.

Transition	Variables	Changes	
		From	To
MI	intercept	−10.8973	−8.0138
	age	0.06967	8.46977
	add age^2		−9.164172
AP	intercept	−15.83	−6.645
	age	0.3003	2.0281
	age^2	0.002252	−3.164172
Stroke	intercept	−11.8289	−9.0694
	age	0.08779	12.72149
	add age^2		−14.764172
TIA	age	0.3201	5.9283
	age^2	−0.001708	−17.641388

Table 5.19: Adjustments in IHD and stroke intensities for males.

5.4.7 Mortality

For mortality of males, we use ELT14 as the 1981 observed mortality rates. Only one adjustment was needed to increase the model estimated rates at higher ages. The adjustment is made to the age coefficient, from 1.85535 to 2.25535. Figure 5.72 shows the model estimated rates with the observed mortality rates in 1981.

For females, a similar adjustment to the age coefficient is made to the female mortality intensities. The estimated mortality rates from the adjusted model and the observed 1981 rates are shown in Figure 5.73.

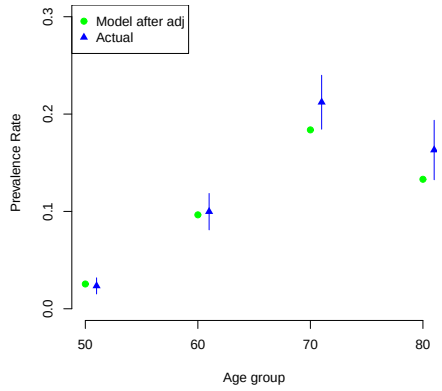

Figure 5.66: Prevalence of IHD in 1981 (males).

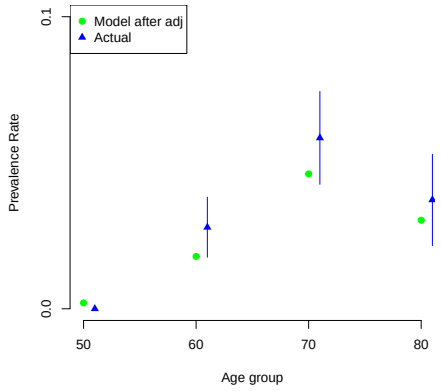

Figure 5.67: Prevalence of stroke in 1981 (males).

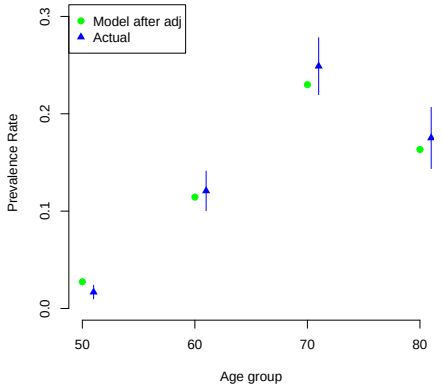

Figure 5.68: Prevalence of IHD and/or stroke in 1981 (males).

Transition	Variables	Changes	
		From	To
MI	intercept	−10.8773	−7.0138
	age	0.06967	8.46977
	add age^2		−8.654172
AP	intercept female	−0.4767	−6.645
	add age female		2.0281
	add female age^2		6.164172
CI	intercept female	−0.7155	−15.46475
	add age female		0.300663
Stroke	intercept	−11.8289	−8.7694
TIA	age^2	−0.001708	−3.641388

Table 5.20: Adjustments in IHD, stroke and IHD and/or stroke intensities for females.

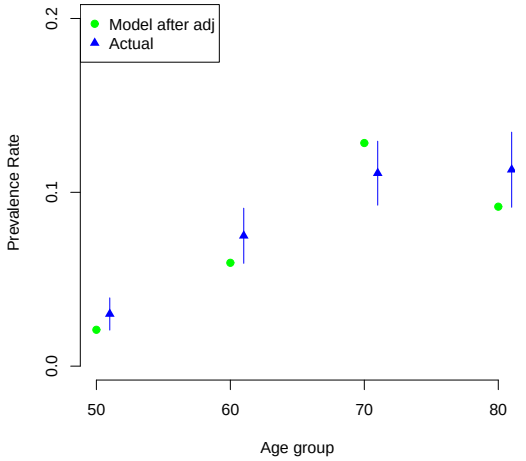

Figure 5.69: Prevalence of IHD in 1981 (females).

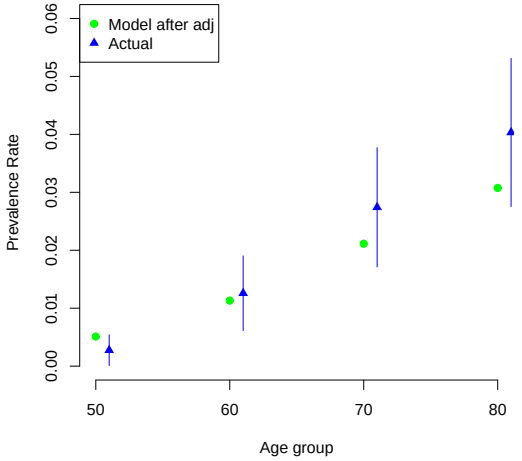

Figure 5.70: Prevalence of stroke in 1981 (females).

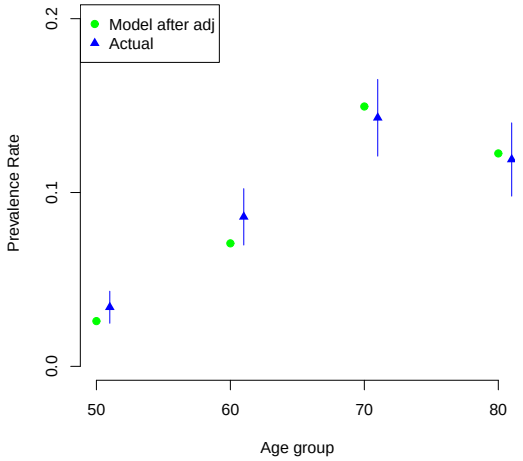

Figure 5.71: Prevalence of IHD and/or stroke in 1981 (females).

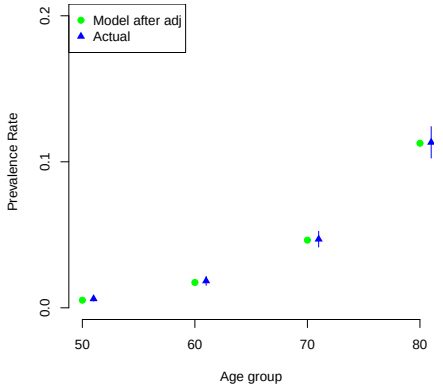

Figure 5.72: Mortality rates in 1981 (males).

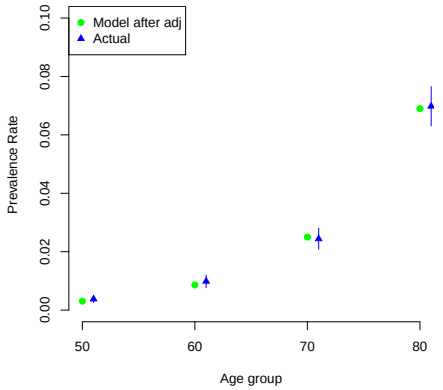

Figure 5.73: Mortality rates in 1981 (females).

5.5 Summary

Adjustments are based on the sequence of the significant risk factors as explained in Section 5.1. A factor that has more influence on other risk factors requires more adjustments as we can see in BMI. From what we have done, BMI has more adjustments than diabetes for males and females. For hypercholesterolaemia, as this risk factor is not affected by changes in other risk factors, there were more adjustments for males and females. The 1981 and 2000 adjusted models will be used to find the effect on IHD, stroke and mortality if the risk factor rates in 2000 were the same as in 1981.

Chapter 6

Effect of Changes

6.1 Introduction

The IMPACT Model calculates the extent to which deaths have reduced between 1981 and 2000 due to changes in cardiovascular risk factors and medical and surgical treatments. Unal *et al.* (2005) stated that there were 68,230 fewer IHD deaths in 2000, of which 58% (35,944) are the results of changes in cardiovascular risk factors. The factor that contributes the most to the reduction is smoking. We will carry out similar calculations using our adjusted HW Model. We find out which factors contribute the most to the reduction and by how much. We are also interested to see how these changes affect the number of IHD and stroke incidents in 2000.

For the HW Model, we now have two parameterisations, one that is consistent with 1981 prevalences and one consistent with 2000 prevalences. For the HW model with the 1981 parameterisation, we use the 1960 observed prevalence rates as the initial risk profiles and for the HW model with the 2000 parameterisation, we use the 1981 observed prevalence rates as the initial risk profiles. We are interested to see what would have happened if the intensities in 1981 for the risk factors remained the same in 2000. The effect of changes will be explored by changing the factors one at a time and also by combining such changes one by one. The sequence of risk factors that we will use to calculate the effect will follow the order suggested by Figure 5.1, i.e. we will apply the IHD, stroke and mortality rates to the England and Wales population in 2000 and see how the risk factor changes affect these rates. We focus on ages from 45 to 84 and divide these ages into four age groups. Table 6.1 shows

the age structure of the 2000 (ONS, 2004) population of England and Wales in each age group for males and females. The percentage of change is calculated using the formula

$$((Fixed\ factor\ results - 2000\ results)\ /2000\ results) \times 100 \tag{6.1}$$

where the fixed factor result is the total expected number of deaths for the total population of England and Wales in 2000 from ages 45 to 84 from the model estimated prevalence rates calculated using the HW Model for which either one factor or a combination of factors has been kept fixed to 1981 intensities and the changes are over all age groups with other factors using 2000 intensities. 2000 results are total expected number of deaths for total population of England and Wales in 2000 from ages 45 to 84 from the model estimated prevalence rates calculated using the HW Model with intensities consistent with 2000 observed prevalence rates which will be identified as the 2000 HW model. The difference is divided by the 2000 results as we would like to see what would have happened to the 2000 model estimated prevalence rates if one or more risk factors had been the same as in 1981. For the fixed factor results and the 2000 results, we will use the Heriot-Watt model with the 1981 risk profiles as the initial risk profiles.

Age group	Male	Female
45-54	3,412,800	3,468,000
55-64	2,687,900	2,758,900
65-74	2,040,200	2,332,100
75-84	1,148,500	1,758,300

Table 6.1: Population of England and Wales by age group in 2000.

6.2 Single factor effects

6.2.1 Smoking

We start to investigate the effect of changes to the numbers of IHD, stroke and mortality cases by using the smoking factor. Using the 2000 HW model with intensities that match the 2000 observed prevalence rates and 1981 observed prevalence rates as the initial risk profiles, we calculate the changes by replacing the 2000 smoking rates with 1981 smoking rates. Table 6.2 shows the differences and the percentage of changes between the HW model with the 1981 smoking rates with other intensities consistent with 2000 observed prevalence rates and the HW model with everything consistent with 2000 observed prevalence rates. Both are using the same initial risk profiles which are the 1981 observed prevalence rates. As an example, the difference in mortality for males is 20,462, as shown in Table 6.2. This means that there is a higher number of deaths when we use the 1981 smoking rates compared to using the 2000 smoking rates in the HW model with other risk factors retaining the 2000 intensities and using 1981 observed prevalence rates as the initial risk profiles. This represents a 11.85% change when compared with the 2000 HW model. In other words, we can say that if the 1981 smoking rates for males continued to persist in 2000, there would have been a higher number of deaths by 11.85%.

Males

With the HW Model, we used the 2000 intensities with 1981 smoking rates to calculate what would have happened if smoking rates had not changed since 1981. We start by changing the 2000 smoking rates in the 2000 HW Model to the 1981 smoking rates. The model estimated prevalence rates when we fixed one or more factor with the 1981 intensities are shown in blue, in Figure 6.1 for 1981 smoking rates, whereas the model estimated prevalence rates from all factors consistent with 2000 intensities are shown in red. The observed smoking rates are shown in Tables 3.2, 3.3 and 3.4. With other risk factors intensities consistent with 2000 observed prevalence rates, the 1981 smoking prevalences will increase the mortality rates for our age groups by up to 12.5% for males as seen in Figure 6.1 where the highest change is from 0.02452 to 0.02759 for age group 65-74. Table 6.2 shows the changes in the number of IHD cases, stroke

and death in percentages. Smoking rates were higher in 1981 and this has increased the number of stroke incidents and deaths by 8.70% and 11.85%, respectively. Higher mortality rates for smokers with IHD has caused the number of IHD cases to reduce by 0.88%.

Females

For females, similar changes as for males happen to stroke and mortality where the model estimated prevalence rates increase by 2.75% and 6.46%, respectively, as there are higher smoking rates in 1981. The IHD rates are higher when we fix smoking to 1981 smoking rates. Although smoking rates were higher in 1981, the IHD rates are higher than the IHD rates from the 2000 HW model as the IHD rates are higher in 1981 than in 2000 as shown in Figures 3.88 and 6.2. The IHD rates are higher by 3.41% compared to the 2000 model with 2000 smoking rates as the mortality rates are lower for females. This is different from males where IHD rates have reduced due to higher mortality rates compared to females. The changes for females are shown in Table 6.2.

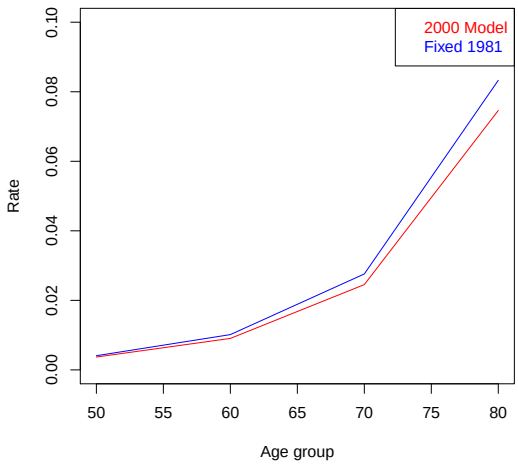

Figure 6.1: Mortality rates in 2000 (males): model (red) and with 1981 smoking rates (blue).

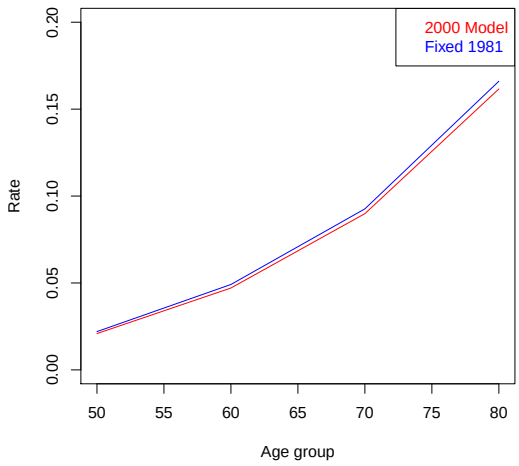

Figure 6.2: IHD rates in 2000 (females): model (red) and with 1981 smoking rates (blue).

Cases	Male		Female	
	Difference	% changes	Difference	% changes
IHD	−8962	−0.88	23770	3.41
Stroke	28196	8.70	9533	2.75
Mortality	20462	11.85	10277	6.46

Table 6.2: Changes when using 1981 smoking rates for total population in 2000 for males and females.

6.2.2 BMI

Males

The definition of each BMI level is shown in Table 2.2. To see what would have happened if BMI rates followed the same level as in 1981, we ran the 2000 Model for 19 years with 1981 BMI intensities. The results for males show that this will reduce the rates of diabetes as there are lower rates of obesity. These can be seen in Figures 6.3 and 6.4. The prevalence rate for obesity has the highest effect on age group 75-84 where it is 86% lower if the 1981 levels continue to 2000 as we can see in Figure 6.3. It also reduces diabetes rates by up to 14%, as we can see in Figure 6.4 where the highest changes happen in age group 65-74.

Lower levels of BMI will tend to reduce the prevalence of diabetes and lower the levels of hypertension (Chatterjee *et. al*, 2008(a), Tables 5 and 7). These, in turn, will tend to reduce the prevalence of IHD and stroke (Chatterjee *et. al*, 2008(a), Table 9) which will then tend to reduce mortality. However, BMI has a direct U-shaped effect on mortality (Chatterjee *et. al*, 2008(a), Table 11) so that the overall effect of lower levels of BMI is an increase in the number of deaths. A slight decrease in hypertension has reduced the IHD and stroke rates by 0.73% and 2.16%, respectively as shown in Table 6.3. In the HW Model, an increase in hypertension levels 1, 2 and 3 will increase the IHD and stroke rates by a different factor. Hypertension level 3 has the highest factor that will increase the IHD and stroke rates, so reduction in hypertension will slightly reduce these rates. Mortality rates are slightly higher than the adjusted model when we fix BMI as we can see in Figure 6.5. Higher prevalence of lightweight has increased the mortality rates by up to 8%. We can see that the BMI level 0 and 1 are decreasing over time in Figures 3.2 and 3.5. In our model, a lower level of BMI reduces the mortality rates by a factor lower than a higher level of BMI. This means that a lower BMI level has higher mortality rates than a higher

BMI level. The number of deaths would increase by 7.17% in 2000 if BMI had not changed from 1981. Table 6.3 shows the percentage of changes for IHD, stroke and mortality when 1981 BMI rates are considered.

Females

A similar trend in the percentage of changes for IHD, stroke and mortality occurs for females when 1981 BMI intensities are considered in the 2000 Heriot-Watt model. These changes are shown in Table 6.3. Lower obesity rates in 1981 have reduced the IHD and stroke rates by 1.16% and 1.56%, respectively. We can see in Figures 3.23 and 3.26 that the observed prevalence rates for BMI levels 2 and 3 are increasing over time. Higher lightweight rates for BMI has increased the number of deaths for females by 1.51%. This is illustrated in Figure 6.6, although the differences are too small to be seen clearly.

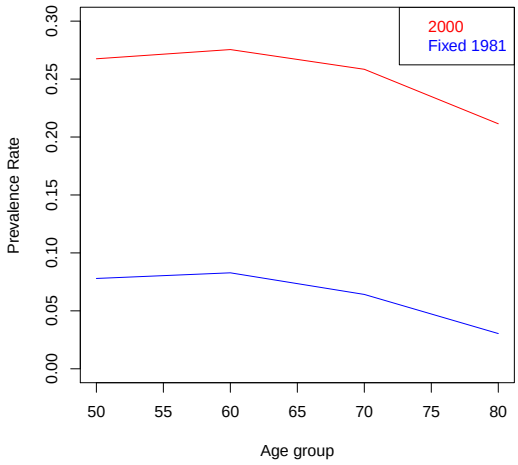

Figure 6.3: Prevalence of obesity in 2000 (males): model (red) and with 1981 BMI rates (blue).

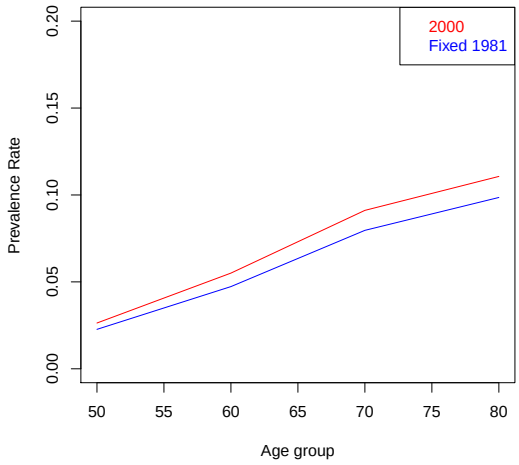

Figure 6.4: Prevalence of diabetes in 2000 (males): model (red) and with 1981 BMI rates (blue).

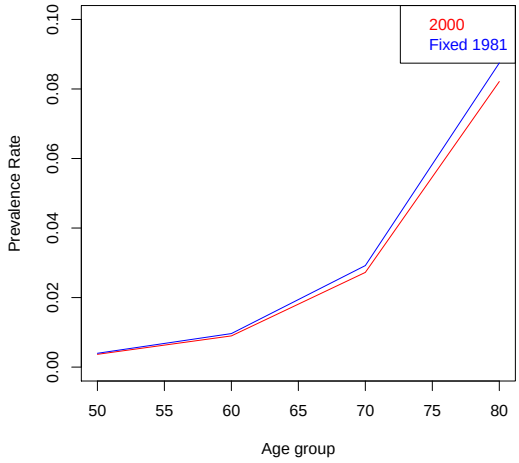

Figure 6.5: Mortality rates in 2000 (males): model (red) and with 1981 BMI rates (blue).

Cases	Male		Female	
	Difference	% changes	Difference	% changes
IHD	−7448	−0.73	−8067	−1.16
Stroke	−7001	−2.16	−5400	−1.56
Mortality	12374	7.17	2397	1.51

Table 6.3: Changes when using 1981 BMI for total population in 2000 for males and females.

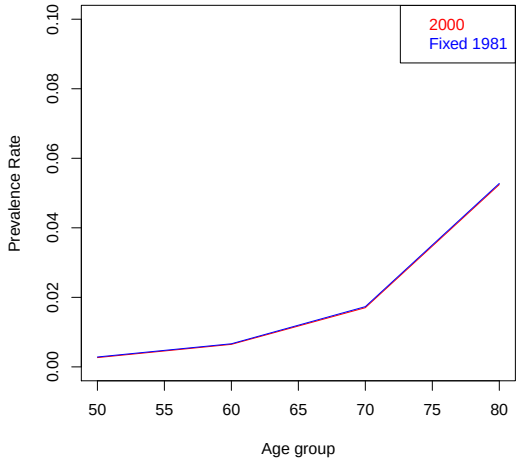

Figure 6.6: Mortality rates in 2000 (females): model (red) and with 1981 BMI rates (blue).

6.2.3 Diabetes

Males

We ran the HW Model with 1981 diabetes intensities to see what would have happened if diabetes rates followed the same intensities as in 1981. The prevalence of diabetes

Cases	Male		Female	
	Difference	% changes	Difference	% changes
IHD	−232	−0.02	−4911	−0.71
Stroke	1205	0.37	598	0.17
Mortality	−3677	−2.13	−2408	−1.51

Table 6.4: Changes when using 1981 diabetes for total population in 2000 for males and females.

with 1981 diabetes intensities is lower than the 2000 model estimated prevalence rates as shown in Figure 6.7. This then reduces the number of deaths by 2.13% as shown in Table 6.4 and the mortality rates are shown in Figure 6.8. The effect is different than in the previous section, as here the BMI model estimated prevalence rates are based on the oserved prevalence rates in 2000 which have a lower lightweight level as explained in Section 6.2.2 and lower diabetes rates would reduce the mortality rates. 1981 diabetes intensities have a small effect on hypertension, IHD and stroke. It reduces the number of IHD cases by 0.02%. There is a small increase in stroke as higher levels of obesity increase the hypertension rates slightly. Diabetes has a direct effect on IHD and mortality, but not on stroke (Chatterjee *et. al*, 2008(a), Tables 9 & 11). Hence, lower prevalence of diabetes will tend to reduce the prevalence of IHD and reduce the number of deaths. A reduced number of deaths will increase the prevalence of stroke. These can be seen in Table 6.4.

Females

Table 6.4 shows the percentage of changes for IHD, stroke and mortality for females when we considered 1981 diabetes intensities in the 2000 HW model. The changes are similar to the males. The diabetes rates are lower in 1981 as we can see in Figure 3.35 and these have reduced the IHD and mortality rates by 0.71% and 1.51%, respectively. The mortality rates are also lower than the 2000 HW model as we are using the 2000 BMI intensities that have lower lightweight rates as mentioned for males. The stroke rates have increased slightly by 0.17% as the hypertension rates are slightly higher due to higher rates of obesity.

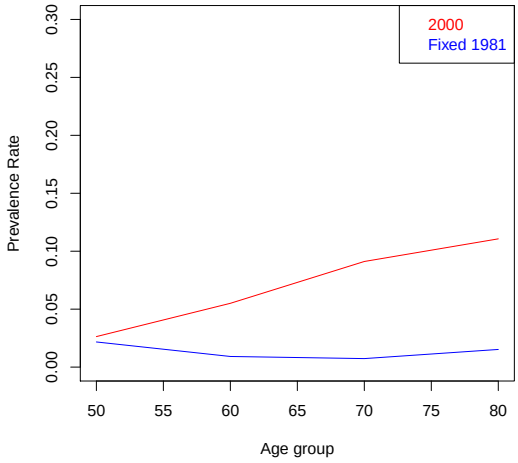

Figure 6.7: Prevalence of diabetes in 2000 (males): model (red) and with 1981 diabetes rates (blue).

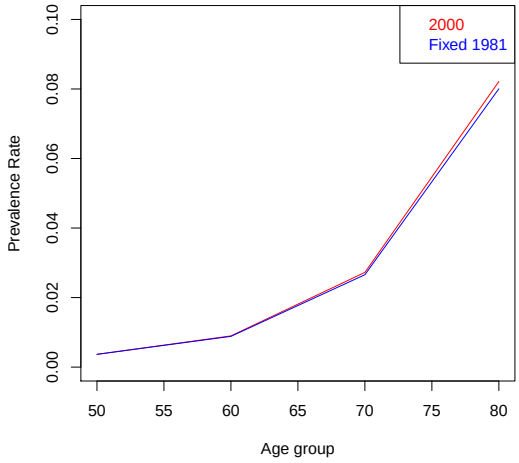

Figure 6.8: Mortality rates in 2000 (males): model (red) and with 1981 diabetes rates (blue).

6.2.4 Hypertension

Males

After diabetes, we then use the 2000 HW model with 1981 hypertension intensities. The hypertension rates in 2000, if there are no changes in hypertension since 1981, are generally higher than the model estimated prevalence rates. This is shown in Figure 6.9 where the model estimated prevalence rates increase by up to 19% for age groups 45-54, 55-64 and 65-74 but there is a slight decrease for age group 75-84. Hypertension is defined as a combination of levels 2 and 3 where the definition of each level is shown in Table 3.5. Hypertension has a direct effect on IHD, stroke and mortality (Chatterjee *et. al*, 2008(a), Tables 9 & 11). Increasing the levels of hypertension to 1981 levels will tend to increase the prevalence of IHD and stroke and the number of deaths. This can be seen in Figures 6.10, 6.11 and 6.12 where the model estimated prevalence rates with the adjusted intensities are higher than the model estimated prevalence rates from the 2000 HW model. Table 6.5 shows a higher percentage of changes in IHD and stroke compared to previous risk factors. 1981 hypertension intensities have increased the numbers of IHD and stroke cases by 6.06% and 12.98%, respectively. It also increases the number of deaths by 7.26%. We can see in Figures 3.47 for males and 3.59 for females that the hypertension level 3 rates are higher in 1981 than in 2000.

Cases	Male		Female	
	Difference	% changes	Difference	% changes
IHD	61712	6.06	34899	5.01
Stroke	42082	12.98	46044	13.28
Mortality	12530	7.26	9497	5.97

Table 6.5: Changes when using 1981 h'ten for total population in 2000 for males and females.

Females

Similar changes can be seen for females in Table 6.5. The number of IHD and stroke cases increases by 5.01% and 13.28%, respectively, when the hypertension intensities in 2000 are similar to the 1981 intensities. The number of deaths has also increased by 5.97%.

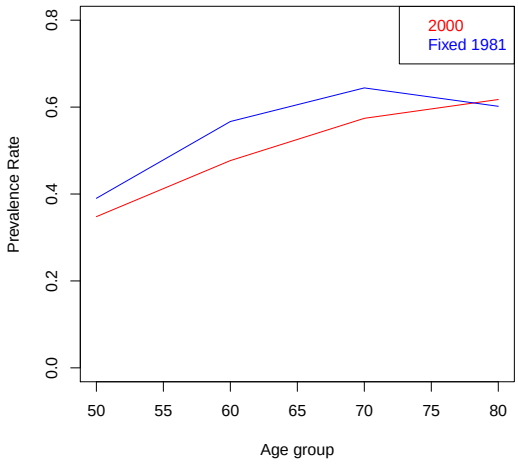

Figure 6.9: Prevalence of h'ten in 2000 (males): model (red) and with 1981 h'ten rates (blue).

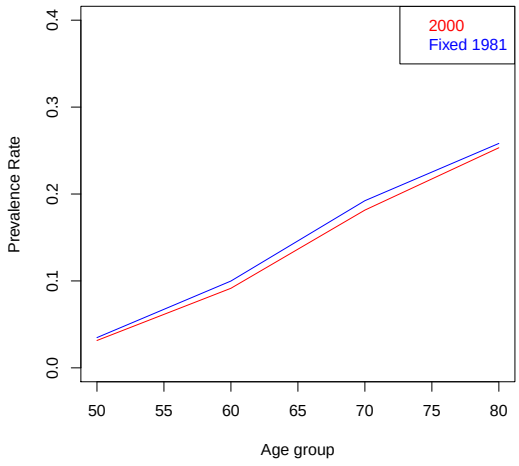

Figure 6.10: Prevalence of IHD in 2000 (males): model (red) and with 1981 h'ten rates (blue).

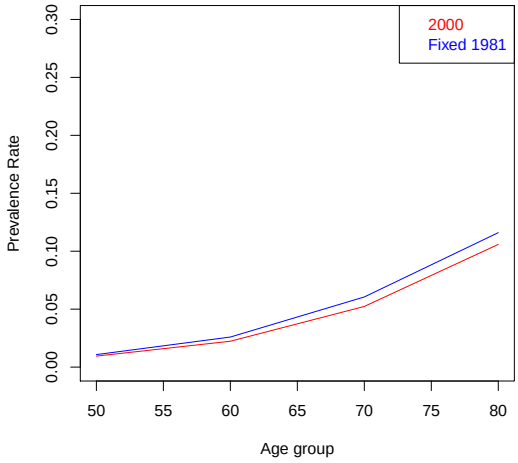

Figure 6.11: Prevalence of stroke in 2000 (males): model (red) and with 1981 h'ten rates (blue).

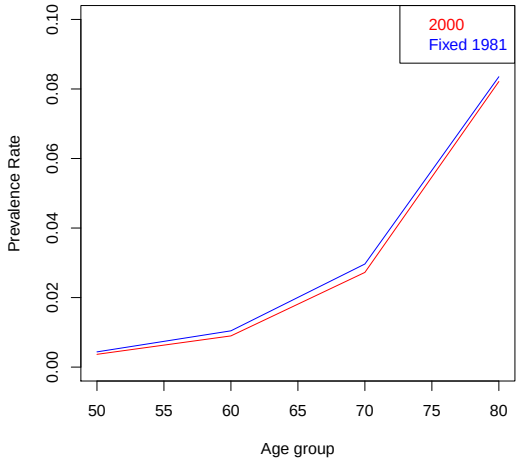

Figure 6.12: Mortality rates in 2000 (males): model (red) and with 1981 h'ten rates (blue).

6.2.5 Hypercholesterolaemia

Males

The next factor to be fixed in the 2000 HW Model is hypercholesterolaemia. The model estimated prevalence rates, if we use the 1981 hypercholesterolaemia intensities, are higher than the model estimated prevalence rates from the 2000 HW model. This is shown in Figure 6.13 which refers to a combination of hypercholesterolaemia levels 1, 2 and 3. The definition of each level is shown in Table 3.6. Hypercholesterolaemia has a direct effect on IHD but not on stroke (Chatterjee *et. al*, 2008(a), Table 9). It has a mixed effect on mortality (Chatterjee *et. al*, 2008(a), Table 11). The hypercholesterolaemia rates increase by up to 19% especially in age group 64-74 as shown in Figure 6.13. IHD and stroke rates have increased slightly when we use the 1981 hypercholesterolaemia intensities. Table 6.6 shows there is a small effect on IHD, stroke and mortality where the percentages of changes are between -0.80% to 0.28%. A higher level of hypercholesterolaemia (levels 1, 2 and 3) has slightly increased the IHD and stroke rates but reduced the mortality rates. This is because when hypercholesterolaemia is fixed to 1981 observed prevalence rates, the hypercholesterolaemia rates in levels 1 and 3 are higher than the 2000 model estimated prevalence rates which will reduce the mortality rates.

Females

For females, only IHD has the same positive change as males where it increases the number of IHD cases by 2.63% as the hypercholesterolaemia rates are higher in 1981 than 2000. Higher 1981 hypercholesterolaemia rates have also increased the number of deaths by 1.18%. Increasing hypercholesterolaemia to 1981 levels increases the prevalence of IHD, particularly for females, but has little effect on the prevalence of stroke or the numbers of deaths. There is a slight reduction in the number of stroke cases when we fixed hypercholesterolaemia as for females, although there is a decreasing trend over time, the 1981 hypercholesterolaemia rates for age group 80 are lower than the 2000 model estimated prevalence rates as we can see in Figure 6.14. The percentage changes for females are shown in Table 6.6.

Cases	Male		Female	
	Difference	% changes	Difference	% changes
IHD	1340	0.13	18302	2.63
Stroke	905	0.28	−863	−0.25
Mortality	−1388	−0.80	1877	1.18

Table 6.6: Changes when using 1981 h'chol for total population in 2000 for males and females.

6.2.6 IHD

Males

We then calculate the effect of changes in IHD and include the adjustments for sudden deaths in 1981. In Figures 6.15 and 6.16, the model estimated prevalence rates for IHD and stroke with IHD intensities being consistent with 1981 intensities are lower than the 2000 model estimated prevalence rates. This has decreased the number of IHD cases by 29.33%, as shown in Table 6.7 and has reduced stroke cases by 4.29%. When we fix IHD, the number of deaths increases by 8.99% and we can see in Figure 6.17 that the model estimated prevalence rates with fixed IHD intensities are higher than

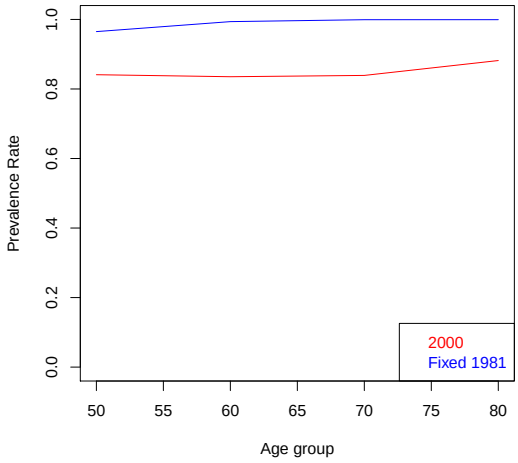

Figure 6.13: Prevalence of h'chol in 2000 (males): model (red) and with 1981 h'chol rates (blue).

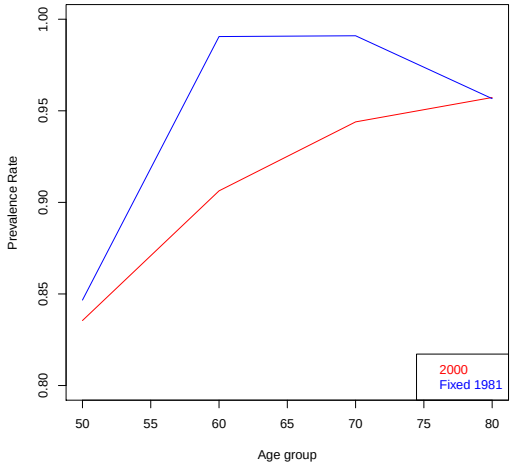

Figure 6.14: Prevalence of h'chol in 2000 (females): model (red) and with 1981 h'chol rates (blue).

the 2000 model estimated prevalence rates. The mortality rates are higher although the IHD and stroke rates have decreased. This is due to the rates of sudden deaths from IHD are much higher in 1981. The difference in mortality for males are higher than for females, as shown in Table 6.7. For sudden deaths following a myocardial infarction model, sex is not an explanatory variable as explained in Section 4.2.1. The IHD observed rates are lower in 1981 than in 2000 for males but the observed prevalence rates are slightly higher than females over time, shown in Figures 3.85 and 3.88. This could explained why the difference for the number of deaths are higher for males.

Females

If we change the 2000 IHD intensities with the 1981 IHD intensities and also include the changes for sudden deaths in 1981, the number of IHD cases for females are higher than in the 2000 HW model. This is because there is a decreasing trend over time for IHD rates for females as shown in Figure 3.88 especially at younger age groups. So higher IHD rates in 1981 have increased the number of IHD cases by 2.74% especially for age groups 60 and 70. The number of stroke cases and number of deaths have similar changes as for males. As shown in Table 6.7, the number of stroke cases reduced by 1.64%. This slight decrease in stroke rates is due to a slight decrease

in IHD rates for age groups 50 and 80. The number of deaths increased by 0.86% because of higher IHD rates in 1981 which will increase the number of sudden deaths following a myocardial infarction.

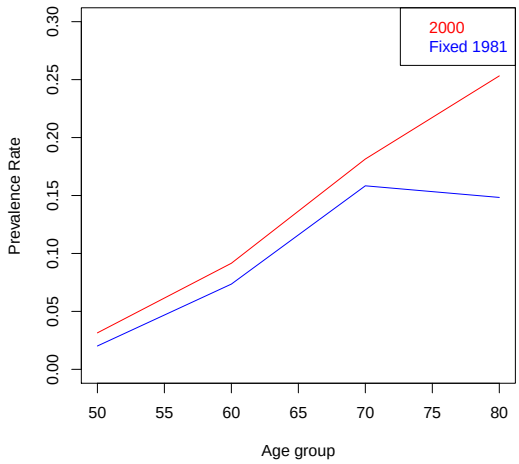

Figure 6.15: Prevalence of IHD in 2000 (males): model (red) and with 1981 IHD rates (blue).

Cases	Male		Female	
	Difference	% changes	Difference	% changes
IHD	−298616	−29.33	19102	2.74
Stroke	−13919	−4.29	−5687	−1.64
Mortality	15532	8.99	1374	0.86

Table 6.7: Changes when using 1981 IHD for total population in 2000.

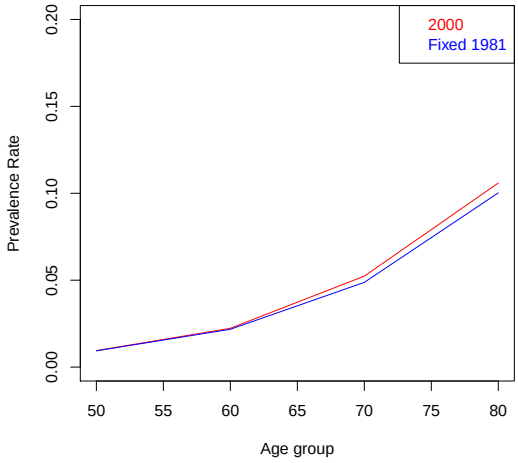

Figure 6.16: Prevalence of stroke in 2000 (males): model (red) and with 1981 IHD rates (blue).

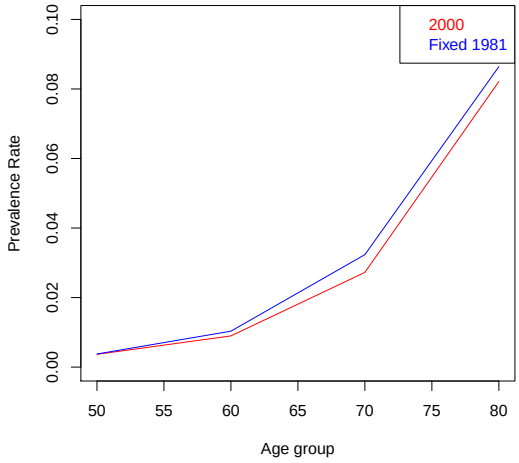

Figure 6.17: Mortality rates in 2000 (males): model (red) and with 1981 IHD rates (blue).

6.2.7 Stroke

Males

After IHD, we calculate the effect of changes in stroke. If stroke intensities are the same as in 1981, the model estimated prevalence rates with fixed 1981 stroke intensities for stroke are lower than the 2000 model estimated prevalence rates as shown in Figure 6.18. With other factors being equal to the observed prevalence rates in 2000, the intensities of stroke in 1981 have reduced stroke cases by 54.53% and this will affect mortality by reducing it by 10.11%, as shown in Table 6.8 and Figure 6.19. The increasing trend over time in IHD rates has caused the IHD cases to increase by 2.54%. When we fixed the stroke intensities to 1981 intensities, the IHD and other risk factors intensities are the 2000 intensities with higher model estimated prevalence rates for diabetes, hypertension level 3 and hypercholesterolaemia level 3.

Females

The changes for females are also similar to males for IHD, stroke and mortality. The number of IHD cases has increased by 1.03% if the 1981 stroke rates remain in 2000 which is similar to males. The number of stroke cases and the number of deaths will reduce by 60.47% and 6.61%, respectively when stroke is fixed to 1981 observed prevalence rates. These changes are shown in Table 6.8.

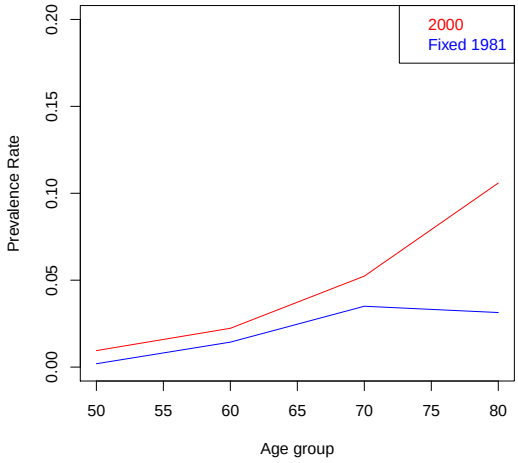

Figure 6.18: Prevalence of stroke in 2000 (males): model (red) and with 1981 stroke rates (blue).

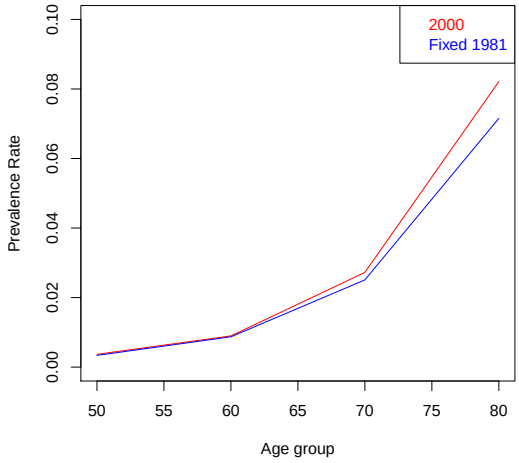

Figure 6.19: Mortality rates in 2000 (males): model (red) and with 1981 stroke rates (blue).

Cases	Male		Female	
	Difference	% changes	Difference	% changes
IHD	25864	2.54	7180	1.03
Stroke	−176749	−54.53	−209602	−60.47
Mortality	−17458	−10.11	−10516	−6.61

Table 6.8: Changes when using 1981 stroke for total population in 2000 for males and females.

6.2.8 Mortality

Males

The final factor that we consider here is mortality. Using the 1981 mortality intensities has caused mortality to be higher than the estimated rates from the 2000 HW model especially at older ages. This is shown in Figure 6.21. The number of deaths will increase by 28.16% if the mortality intensities in 1981 continue to 2000. There are slight reductions in the prevalence of obesity, diabetes and hypertension and these have caused the number of IHD and stroke cases to reduce by 0.49% and 5.01%, respectively. The model estimated rates for stroke are shown in Figure 6.20 where

the differences are mostly at older ages.

Females

Table 6.9 shows the percentage of changes for IHD, stroke and mortality for females. When we fixed mortality with the 1981 intensities, the number of deaths increased by 30.81%. With other risk factors consistent with the 2000 intensities, the numbers of IHD and stroke cases have reduced by 2.71% and 2.46%, respectively.

Cases	Male		Female	
	Difference	% changes	Difference	% changes
IHD	−4968	−0.49	−18841	−2.71
Stroke	−16228	−5.01	−8522	−2.46
Mortality	48632	28.16	48998	30.81

Table 6.9: Changes when using 1981 mortality for total population in 2000 for males and females.

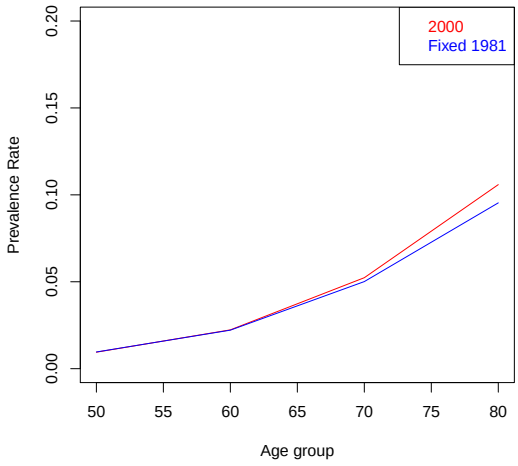

Figure 6.20: Prevalence of stroke in 2000 (males): model (red) and with 1981 mortality rates (blue).

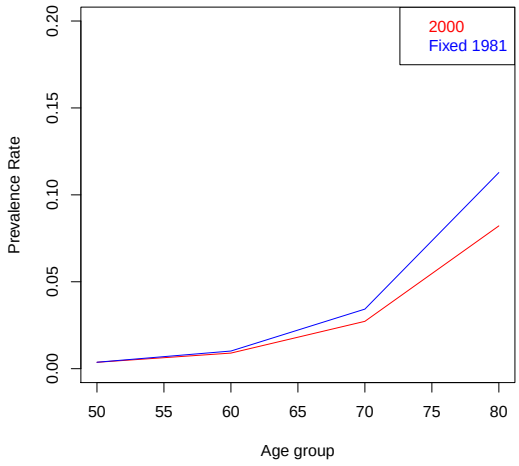

Figure 6.21: Mortality rates in 2000 (males): model (red) and with 1981 mortality rates (blue).

6.2.9 Conclusions

From the results in these sections, we see that hypertension has a higher effect on IHD and stroke for males, where if the intensities are similar to 1981, there will be higher prevalence of IHD and stroke by 6.06% and 12.98%, respectively. This is also the same for females; hypertension has the highest effect on IHD and stroke and the number of IHD cases increased by 5.01% and the number of stroke cases increased by 13.28%. If IHD rates in 2000 had the same level as in 1981, there would be 29.33% less cases of IHD in males. There is a similar effect with stroke where the number of strokes would be reduced by 54.5%. For females, there is a positive change for IHD as IHD rates in 1981 are higher than in 2000. The number of stroke cases for females reduces by 60.47% if stroke intensities in 2000 have similar intensities as in 1981. Higher observed prevalence rates for sudden deaths following MI in 1981 have increase the mortality for males and females when IHD is fix. Beside mortality itself, smoking has the highest effect on mortality for males where deaths have reduced by 20462 with the reduction in smoking rates between 1981 and 2000. This is consistent with the IMPACT Model where smoking is the biggest contributor in reducing the number of IHD deaths by 29,715. For females, changes in smoking between 1981 and 2000 will reduce the number of deaths by 10,277. The risk factor with the least influence on mortality rates for males and females is hypercholesterolaemia.

6.3 Effects of combinations of factors

In this section, we will combine the risk factors one by one to see how these combinations of 1981 risk factors intensities affect the number of IHD cases, stroke cases and mortality in 2000. We add risk factors to the considered combinations based on the order of influence suggested in Figure 5.1. We started with BMI in Section 6.2.2 and we will add diabetes in the following section.

6.3.1 BMI and diabetes

Males

We first fix the BMI and diabetes 1981 intensities and run the model with 2000 intensities for the other factors. With 1981 BMI and diabetes intensities, there will

be lower obesity and diabetes rates. These are not surprising as we would expect the model estimated prevalence rates to be similar to the model estimated prevalence rates shown in Figures 6.3 and 6.7. Mortality rates are higher than model estimated rates in 2000, when we use 1981 BMI and diabetes intensities as shown in Figure 6.22. Higher prevalence of lightweight has increased the mortality rates but the increase in mortality rates is lower than when we use the model with 1981 BMI intensities only which is shown in Table 6.3 in Section 6.2.2. The combination of 1981 BMI intensities with the 1981 diabetes intensities has reduced the increment of mortality rates as diabetes rates are lower than actual in 2000. The numbers of IHD and stroke cases have reduced slightly due to the decrease in BMI, diabetes and hypertension by 0.75% and 1.81% respectively, but the number of deaths increased by 5.18% as shown in Table 6.10.

Females

This is also similar to males where the number of IHD and stroke cases decreased by 1.82% and 1.40%, respectively for the same reason as males. The number of deaths increased slightly by 0.09%. The percentage changes are shown in Table 6.10.

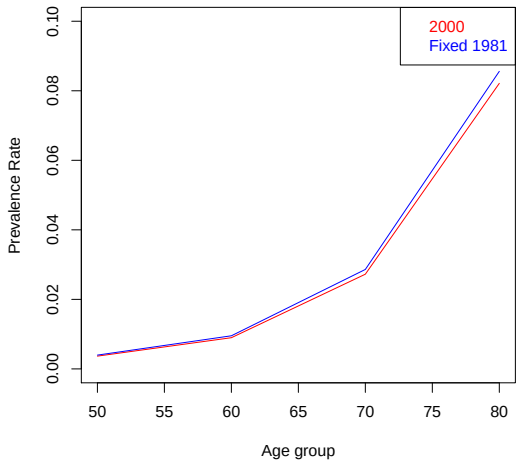

Figure 6.22: Mortality rates in 2000 (males): model (red) and with 1981 BMI and diabetes rates (blue).

Cases	Male		Female	
	Difference	% changes	Difference	% changes
IHD	−7649	−0.75	−12642	−1.82
Stroke	−5882	−1.81	−4836	−1.40
Mortality	8937	5.18	143	0.09

Table 6.10: Changes when using 1981 BMI and diabetes for total population in 2000 (males).

Cases	Male		Female	
	Difference	% changes	Difference	% changes
IHD	56122	5.51	24688	3.55
Stroke	35633	10.99	42800	12.35
Mortality	22007	12.74	9958	6.26

Table 6.11: Changes when using 1981 BMI, diabetes and h'ten for total population in 2000 for males and females.

6.3.2 BMI, diabetes and hypertension

Males

The next factor that we add to the previous combination is hypertension. When BMI, diabetes and hypertension intensities are consistent with 1981, there will be lower obesity and diabetes rates and a slight increase in the hypertension rates. The increase in hypertension has a big effect on IHD, stroke and mortality; it increases IHD by 5.51% and stroke by 10.99%. These can be seen in Figures 6.23, 6.24 and 6.25. The number of deaths has also increased by 12.74%. These figures are shown in Table 6.11 and the mortality rates are shown in Figure 6.26.

Females

The trend over time for BMI, diabetes and hypertension for females is similar to males so the percentage of changes for IHD, stroke and mortality are all positive, as shown in Table 6.11. When we fixed BMI, diabetes and hypertension with 1981 observed prevalence rates, the number of IHD cases, number of stroke cases and number of deaths increase by 3.55%, 12.35% and 6.26%, respectively.

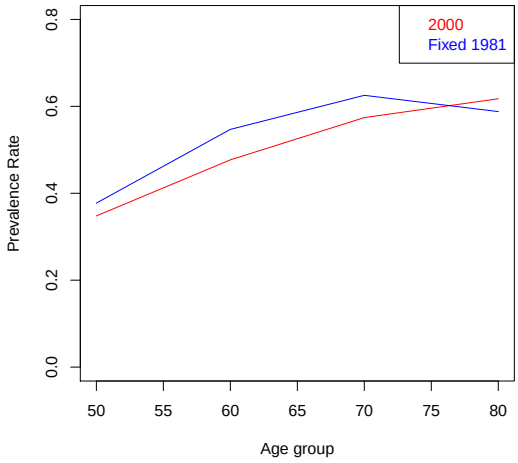

Figure 6.23: Prevalence of h'ten in 2000 (males): model (red) and with 1981 BMI, diabetes and h'ten rates (blue).

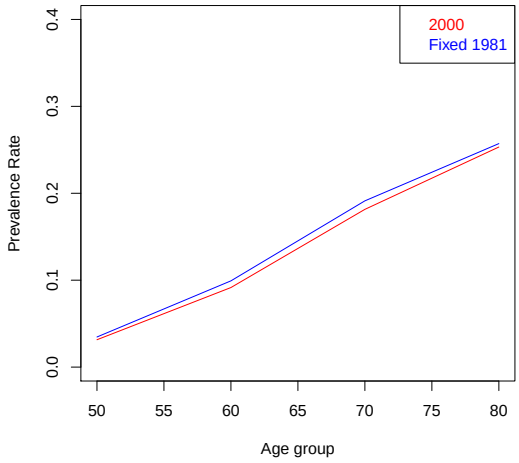

Figure 6.24: Prevalence of IHD in 2000 (males): model (red) and with 1981 BMI, diabetes and h'ten rates (blue).

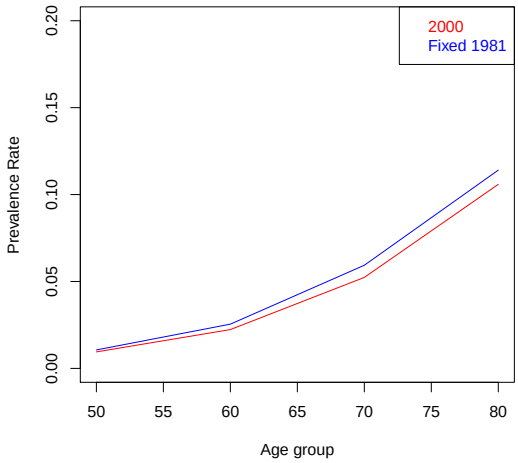

Figure 6.25: Prevalence of stroke in 2000 (males): model (red) and with 1981 BMI, diabetes and h'ten rates (blue).

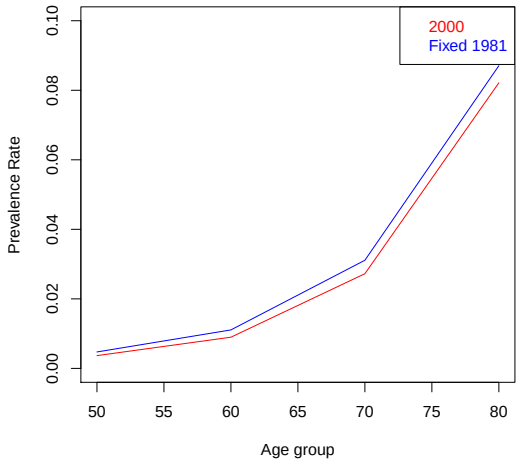

Figure 6.26: Mortality rates in 2000 (males): model (red) and with 1981 BMI, diabetes and h'ten rates (blue).

6.3.3 BMI, diabetes, hypertension and hypercholesterolaemia

Males

We then combine the previous factors with hypercholesterolaemia. With a combination of 1981 hypercholesterolaemia intensities, the IHD and stroke rates are slightly higher than for the previous combination, as shown in Figures 6.27 and 6.28, while mortality rates, shown in Figure 6.29, have also increased, though the increase,

11.84%, is less than for BMI, diabetes and hypertension (12.74%). This is consistent with what is shown in Section 6.2.5 where 1981 hypercholesterolaemia intensities have reduced the mortality rates slightly due to increases in hypercholesterolaemia levels 1 and 3 in 2000. The percentage of changes can be seen in Table 6.12.

Females

Table 6.12 also shows the percentage of changes for IHD, stroke and mortality for females. For females, adding hypercholesterolaemia has increased the number of deaths from 6.26% to 7.05% from the previous combination due to the increase in IHD rates. This combination has increased the number of IHD cases by 6.23% and reduced the number stroke cases by 12.05%.

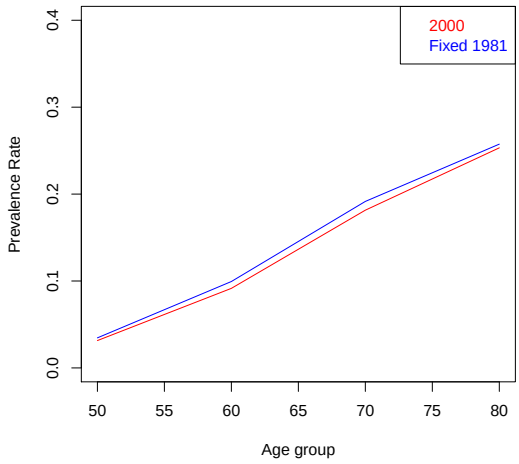

Figure 6.27: Prevalence of IHD in 2000 (males): model (red) and with 1981 BMI, diabetes, h'ten and h'chol rates (blue).

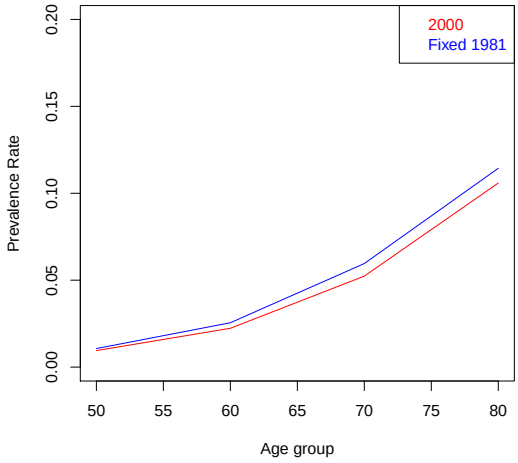

Figure 6.28: Prevalence of stroke in 2000 (males): model (red) and with 1981 BMI, diabetes, h'ten and h'chol rates (blue).

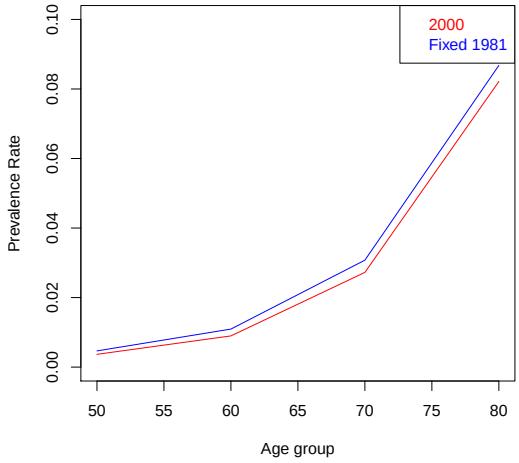

Figure 6.29: Mortality rates in 2000 (males): model (red) and with 1981 BMI, diabetes, h'ten and h'chol rates (blue).

Cases	Male		Female	
	Difference	% changes	Difference	% changes
IHD	57367	5.63	43394	6.23
Stroke	36726	11.33	41777	12.05
Mortality	20440	11.84	11924	7.5

Table 6.12: Changes when using 1981 BMI, diabetes, h'ten and h'chol for total population in 2000 for males and females.

6.3.4 BMI, diabetes, hypertension, hypercholesterolaemia and IHD

Males

We then add IHD to the combination of BMI, diabetes, hypertension and hypercholesterolaemia. This has caused the IHD rate to be lower than actual with an effect similar to that shown in Figure 6.15; IHD cases reduced by 25.47%, which is shown in Table 6.13. Adding IHD has also lowered the change in the number of stroke cases as shown in Table 6.13 where the cases increase by 6.43%, as compared to 11.33% in Table 6.12. It increased the number of deaths by an additional of 10.3% (from 11.84% to 22.14%) compared to the previous combination. The prevelance of IHD is lower but there is a large increase in mortality. This is due to the rates of sudden deaths as explained in Section 6.2.6. The mortality rates are shown in Figure 6.30 where the model estimated prevalence rates from this combination are higher than the 2000

model estimated prevalence rates.

Females

For females, this combination has increased the number of IHD cases from 6.23% to 11.44%. This is due to the decreasing trend over time for IHD rates for females. The 1981 IHD rates are higher than 2000 model estimated prevalence rates for most age groups. It has reduced the number of stroke cases from the previous combination to 9.88% and increased the number of deaths to 9.18%. These changes are shown in Table 6.13.

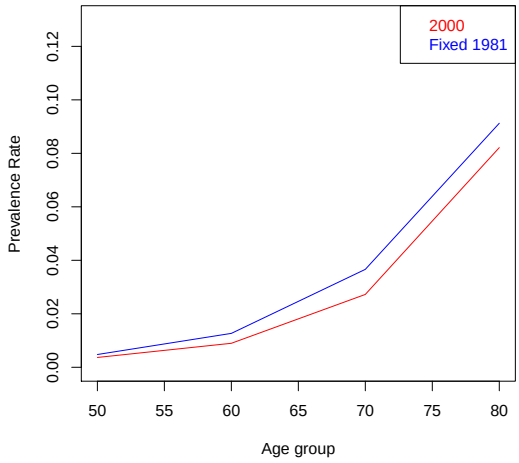

Figure 6.30: Mortality rates in 2000 (males): model (red) and with 1981 BMI, diabetes, h'ten, h'chol and IHD rates (blue).

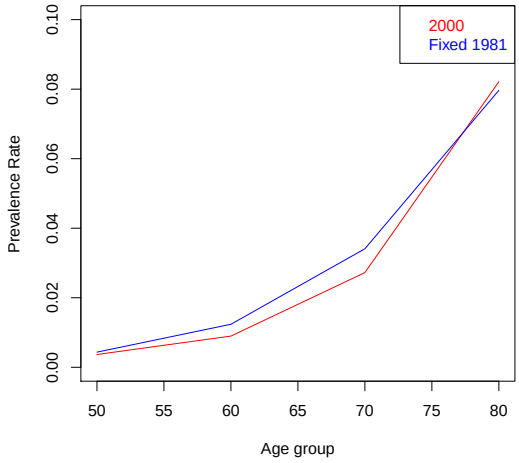

Figure 6.31: Mortality rates in 2000 (males): model (red) and with 1981 BMI, diabetes, h'ten, h'chol, IHD and stroke rates (blue).

Cases	Male		Female	
	Difference	% changes	Difference	% changes
IHD	−259304	−25.47	79606	11.44
Stroke	20846	6.43	34255	9.88
Mortality	38232	22.14	14602	9.18

Table 6.13: Changes when using 1981 BMI, diabetes, h'ten, h'chol and IHD for total population in 2000 for males and females.

6.3.5 BMI, diabetes, hypertension, hypercholesterolaemia, IHD and stroke

Males

The next factor to be added is stroke. IHD and stroke rates in 1981 are lower compared to 2000 model estimated prevalence rates, as seen in Figures 6.15 and 6.18, so there are reductions in the numbers of IHD and stroke cases as shown in Table 6.14. Using this combination, the number of stroke cases reduced by 52.81%. Because stroke cases are reduced by more than 50%, the change in the number of deaths has reduced from 22.14% in the previous combination to 10.47%. We can see in Figure 6.31 that the mortality rates for this combination are slightly lower than the 2000 model estimated prevalence rates at age group 80 and this has also contributed to the reduction in changes in the number of deaths.

Females

Adding stroke in the combination for females has increased the IHD rates slightly by 12.08%. It has reduced the number of stroke cases by 56.99% and reduced the number of deaths to 1.10% from the previous combination. Table 6.14 shows the percentage of changes for females.

Cases	Male		Female	
	Difference	% changes	Difference	% changes
IHD	−247802	−24.34	84082	12.08
Stroke	−171155	−52.81	−197522	−56.99
Mortality	18087	10.47	1747	1.10

Table 6.14: Changes when using 1981 BMI, diabetes, h'ten, h'chol, IHD and stroke for total population in 2000 for males and females.

6.3.6 BMI, diabetes, hypertension, hypercholesterolaemia, IHD, stroke and mortality

Males

The last factor to be included in the combination is mortality. Mortality rates in 1981 are higher than in 2000. This can be seen from Figure 6.32. Using this combination, the whole set of intensities is consistent with the 1981 observed prevalence rates. IHD and stroke rates are lower compared to 2000 model estimated prevalence rates, so there are reductions in the number of IHD and stroke cases as shown in Table 6.15 and the changes are slightly higher than for the previous combination. The mortality rates from this combination are close to the observed mortality rates in 1981. The only difference from the 1981 observed mortality rates is that the smoking rates used are the observed rates in 2000. If the same mortality level continued with all 1981 intensities for other factors, there would be 40.84% more deaths.

Females

Table 6.15 shows the percentage of changes for females when the whole set of intensities is consistent with 1981 observed rates. The number of IHD cases increased by 7.37% and the number of stroke cases further decreased by 58.01%. With 1981 mortality intensities added to the combination, the changes in the number of deaths increased from 1.10% to 32.87%.

Cases	Male		Female	
	Difference	% changes	Difference	% changes
IHD	−279821	−27.48	51283	7.37
Stroke	−181035	−55.85	−201069	−58.01
Mortality	70527	40.84	52271	32.87

Table 6.15: Changes when using 1981 BMI, diabetes, h'ten, h'chol, IHD, stroke and mortality for total population in 2000 (males).

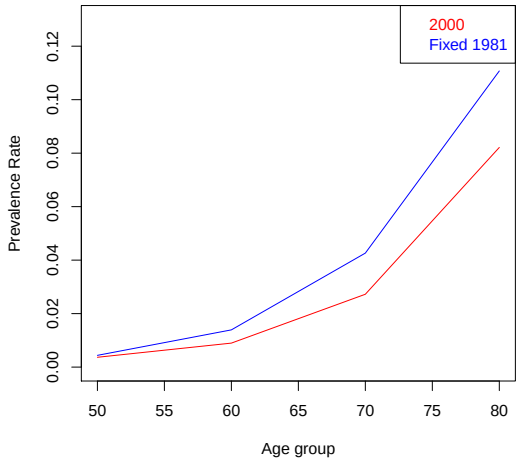

Figure 6.32: Mortality rates in 2000 (males): model (red) and with 1981 BMI, diabetes, h'ten, h'chol,IHD, stroke and mortality rates (blue).

6.3.7 Conclusions

When we add the risk factors sequentially, hypertension and hypercholesterolaemia have increased the IHD and stroke rates for males, as these intensities are higher in 1981. Beside mortality itself, the highest increment happens when we add IHD where the mortality rates increased by 10.3% from the previous combination and reduced by 11.67% when stroke is added. Mortality in males would increase by 40.84% if the intensities of all risk factors in 2000 were the same as in 1981 except for smoking.

For females, adding hypertension and hypercholesterolaemia to the combination has a similar effect as for males where the IHD and stroke rates are higher than the 2000 observed prevalence rates. 1981 IHD intensities have increased the number of IHD cases compared to the 2000 model estimated prevalence rates. This happens as 1981 IHD rates are higher than 2000 observed prevalence rates in most age groups for females. Adding stroke to the combination for females has reduced the number of deaths from 14602 to 1747 and having all risk factors' levels fixed to 1981 observed prevalence rates except for smoking would increase the number of deaths by 32.87%.

Tables 6.16 and 6.19 show the expected number of deaths for each age group as the factors are held one by one at the 1981 levels for males and females, respectively.

The labels in the Tables 6.16, 6.17, 6.18, 6.19, 6.20, 6.21 and Figures 6.33 to 6.36 are explained below and labels with $*$ indicating that 1981 smoking rates are included in the combination, and also "fixed" implies "fixed to 1981 intensities":

a: 2000 model estimated prevalence rates with smoking fixed
b: 2000 model estimated prevalence rates with BMI fixed
c: 2000 model estimated prevalence rates with BMI and diabetes fixed
d: 2000 model estimated prevalence rates with BMI, diabetes and hypertension fixed
e: 2000 model estimated prevalence rates with BMI, diabetes, hypertension and hypercholesterolaemia fixed
f: 2000 model estimated prevalence rates with BMI, diabetes, hypertension, hypercholesterolaemia and IHD fixed
g: 2000 model estimated prevalence rates with BMI, diabetes, hypertension, hypercholesterolaemia, IHD and stroke fixed
h: 2000 model estimated prevalence rates with BMI, diabetes, hypertension, hypercholesterolaemia, IHD, stroke and mortality fixed
i: 2000 model estimated prevalence rates with smoking, BMI, diabetes, hypertension, hypercholesterolaemia, IHD, stroke and mortality fixed

In Tables 6.16 to 6.21, the difference with the previous combination is calculated by finding the difference between the total expected deaths in the combination with the total deaths from the previous combination. For combination a, it is the difference between the total expected deaths in combination a with the total expected deaths using the 2000 model estimated prevalence rates.

From Table 6.16 for males, we can see that the expected number of deaths in 1981 is higher than in 2000. If smoking rates were the same as in 1981 (a), there would be more deaths in all age groups and changes in smoking have the highest effect on deaths among the risk factors. It is a similar story for females as shown in Table 6.19, where the number of deaths due to 1981 smoking rates has increased by 10277 (169302−159025). When we fixed BMI (b), it has given the most effect on the oldest age group where there are 6000 (91514−85689) more deaths than the 2000 model estimated prevalence rates for males. For females, the increment is not as high as for males. Adding diabetes to the combination, we can see fewer deaths in all age groups for males and females.

The combination of factors with hypertension further increases the number of

deaths by 13069 and 9815 for males and females, respectively. Hypercholesterolaemia has the least effect on mortality where by adding it to the combination, it reduces the number of deaths for males by 1567. A different effect is observed for females where the number of deaths increases by 1966 when hypercholesterolaemia is added to the combination.

As for events, IHD has the highest effect on mortality where it increases deaths for males by 38231 (210910−172679), compared to the 2000 model estimated prevalence rates. This is also similar to females, where it increases deaths by 14602 (173627−159025) compared to the 2000 model estimated prevalence rates. If all factors and events including mortality are not changed from 1981, there will be an additional 70527 (243206−172679) deaths for males, and 52271 (211296−159025) deaths for females in 2000, (this is the difference between the total of expected deaths in combination h and the 2000 model estimated prevalence rates). Column i in Tables 6.16 and 6.19 shows the number of deaths when smoking is also added in the combination with other 1981 risk factors intensities. The numbers of deaths increase by 101157 (273836−172679) and 64924 (223949−159025) for males and females, respectively, and are close to the 1981 model estimated prevalence rates. Figure 6.33 shows the mortality rates for each combination and we can see that the mortality rates are closer to 1981 as we add in more factors to the combination. Overall, mortality rates have decreased from 1981 to 2000 while the prevalence of IHD for males has changed very little over this period. However, if we take out the changes in other risk factors, the prevalence of IHD would have increased (Table 6.7). This worsening morbidity has been more than offset, in terms of mortality, by the reduction in the probability of sudden deaths which occur probably due to better medical treatments.

When we add smoking at the start of our combinations, we can see in Tables 6.17 and 6.20 that it increases the figures in all age groups and in each combination as smoking rates are higher in 1981. By including smoking, it has given the highest effect to the combinations in which we add BMI and hypertension where the difference for males with the case where smoking is not included is 1049 (13423−12374) and 1693 (14762−13069) deaths, respectively. These are calculated by finding the difference between the difference with previous combination in column b in Table 6.16 and column b* in Table 6.17 for combination with BMI and between column d in Table

6.16 and column d* in Table 6.17 for combination with hypertension. It also affects mortality by increasing the number of deaths by 5553 (57993−52440) for males and 2486 (53010−50524) for females when smoking is included. Figures 6.34 and 6.36 show the mortality rates for each combination in which we add smoking at the beginning of the combination for males and females, respectively. The model estimated mortality rates for each combination are higher than the model estimated mortality rates shown in Figures 6.33 and 6.35 in which 1981 smoking rates are added at the end of the combination.

Until now, we have used the 1981 risk profiles as the intial risk profiles to run the HW model. We can also run the model using the 1961 risk profiles. Tables 6.18 and 6.21 show the expected number of deaths when we use 1961 risk profile as the initial risk profile to run the HW Model for males and females. With the 1961 initial risk profile, there are higher expected deaths in all combinations compared to Tables 6.16 and 6.19 that use the 1981 observed prevalence rates. The highest difference with the previous combination is in combination b where the difference is 19586 (Table 6.18) compared to 12374 (Table 6.16) when we used 1981 risk profile for males. In combination e, hypercholestrolaemia prevalence in 1961 risk profiles has increased the expected deaths for males from previous combination which is different from the the result in Table 6.16. In column i, we can see that the expected number of deaths is very close to the result from the 1981 model estimated prevalence rates for males and females.

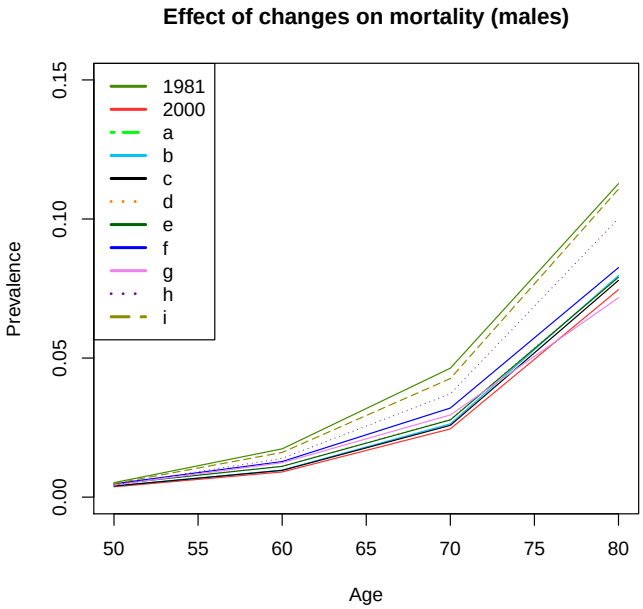

Figure 6.33: Effect of changes on mortality (males).

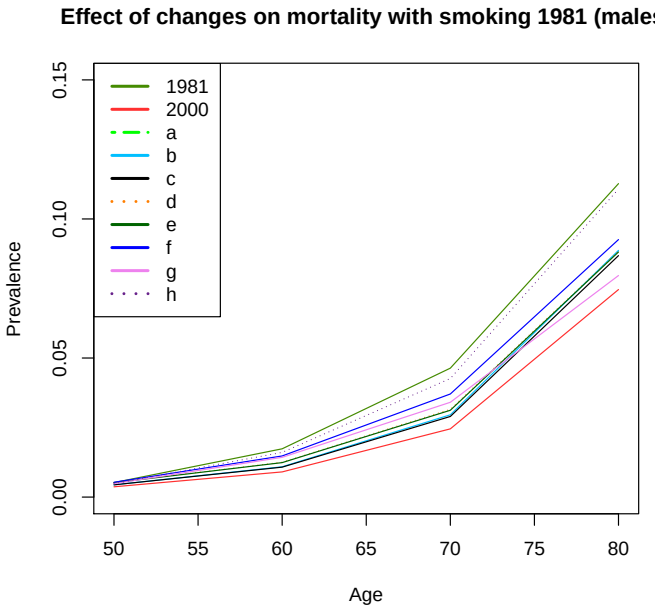

Figure 6.34: Effect of changes on mortality with 1981 smoking (males).

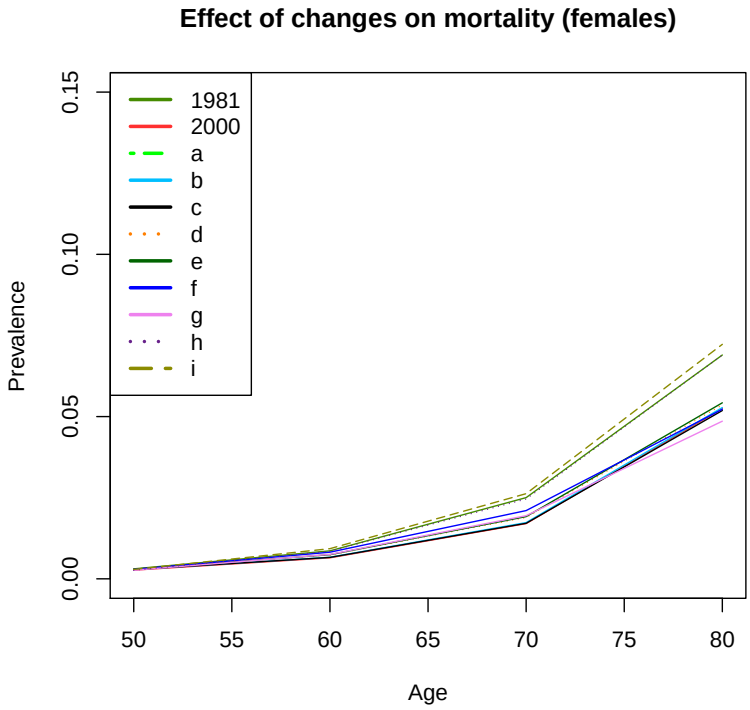

Figure 6.35: Effect of changes on mortality (females).

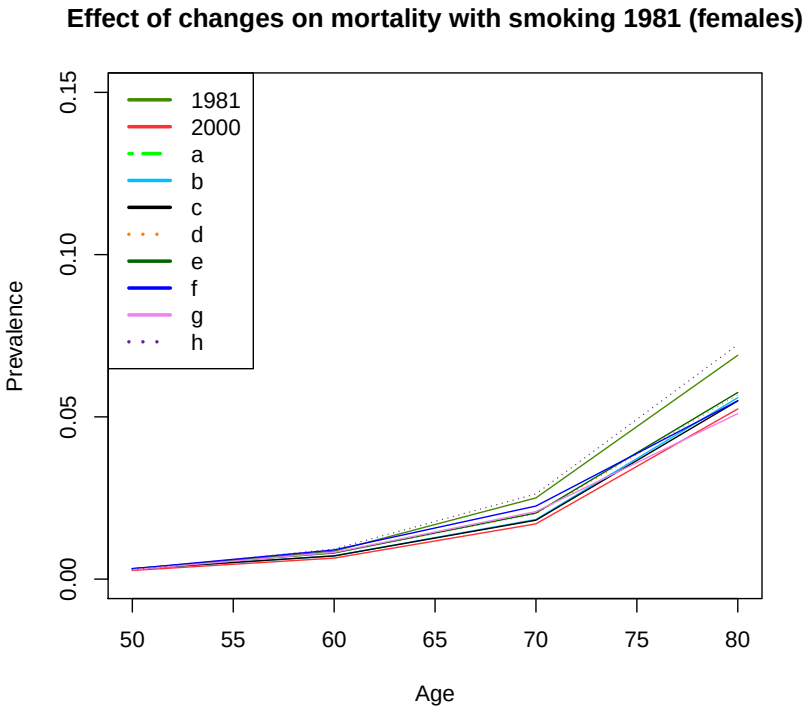

Figure 6.36: Effect of changes on mortality with 1981 smoking (females).

Age group	**2000**	a	b	c	d	e	f	g	h	i	**1981**
45-54	12620	13921	13648	13629	16252	16001	16404	14874	14986	16517	17779
55-64	24327	27272	26142	25831	30056	29704	34374	33254	37418	43171	46668
65-74	50042	56293	53749	52645	57280	56630	65345	60297	75756	86966	94573
75-84	85689	95654	91514	89511	91098	90784	94787	82341	115046	127182	129434
Total	172679	193140	185053	181616	194685	193118	210910	190766	243206	273836	288454
Difference with previous combination		20462	12374	−3437	13069	−1567	17792	−20144	52440	30630	14617

Table 6.16: Expected number of deaths (males).

Age group	**2000**	a	b*	c*	d*	e*	f*	g*	h*	**1981**
45-54	12620	13921	15052	15031	17925	17650	18192	16393	16517	17779
55-64	24327	27272	29285	28939	33701	33311	39752	38424	43171	46668
65-74	50042	56293	60354	59132	64406	63689	75623	69540	86966	94573
75-84	85689	95654	101873	99707	101539	101208	106332	91487	127182	129434
Total	172679	193140	206563	202809	217571	215857	239899	215843	273836	288454
Difference with previous combination		220462	13423	−3754	14762	−1714	24043	−24056	57993	14617

Table 6.17: Expected number of deaths with smoking 1981 at the start (males).

Age group	**2000**	a	b	c	d	e	f	g	h	i	**1981**
45-54	12620	14486	14121	14101	17343	17232	17724	16059	16188	17844	17779
55-64	24327	28865	27691	27371	32336	32334	37712	36458	41003	47317	46668
65-74	50042	60355	58142	57071	62047	62218	71931	66630	83103	94946	94573
75-84	85689	95748	92311	90452	92050	92656	97211	84482	117564	129897	129434
Total	172679	199454	192265	188996	203775	204440	224577	203627	257858	290003	288454
Difference with previous combination		26775	19586	−3269	14780	665	20137	−20949	54230	32146	−1550

Table 6.18: Expected number of deaths using 1961 initial risk profiles (males).

Age group	**2000**	a	b	c	d	e	f	g	h	i	**1981**
45-54	9255	10153	9864	9842	10322	10316	10090	9161	9223	10042	10658
55-64	17864	19319	18339	18218	20294	20525	22632	20800	23460	25640	23779
65-74	39694	42130	40414	39905	44115	44723	49046	45390	57349	61208	58360
75-84	92212	97699	92804	91204	94252	95386	91859	85421	121264	127060	121281
Total	159025	169302	161422	159168	168983	170949	173627	160772	211296	223949	214078
Difference with previous combination		10277	2397	−2254	9815	1966	2678	−12855	50524	12653	−9871

Table 6.19: Expected number of deaths (females).

Age group	**2000**	a	b*	c*	d*	e*	f*	g*	h*	**1981**
45-54	9255	10153	10815	10790	11319	11310	11040	9974	10042	10658
55-64	17864	19319	19825	19692	21952	22220	24799	22755	25640	23779
65-74	39694	42130	42879	42332	46837	47513	52508	48536	61208	58360
75-84	92212	97699	98297	96597	99899	101129	96626	89674	127060	121281
Total	159025	169302	171816	169412	180007	182173	184973	170939	223949	214078
Difference with previous combination		10277	2514	−2404	10595	2166	2800	−14034	53010	−9871

Table 6.20: Expected number of deaths with smoking 1981 at the start (females).

Age group	**2000**	a	b	c	d	e	f	g	h	i	**1981**
45-54	9255	10471	10202	10180	10672	10666	10436	9488	9570	10601	10658
55-64	17864	19911	18948	18829	20946	21181	23280	21437	24175	23809	23779
65-74	39694	44934	43141	42624	46886	47464	51677	48069	60518	58087	58360
75-84	92212	97496	92475	90900	93930	95038	91572	85136	120811	121932	121281
Total	159025	172812	164766	162533	172434	174348	176964	164129	215074	214429	214078
Difference with previous combination		13787	5741	−2233	9901	1914	2617	−12835	50945	−645	−351

Table 6.21: Expected number of deaths using 1961 initial risk profiles (females).

6.3.8 Discussion

We have calculated the effect of changes in the risk factors intensities on the number of IHD cases, stroke cases and mortality between 1981 and 2000. Among the risk factors, smoking contributes the highest difference in the total number of deaths for males and females if smoking rates in 1981 continue to persist in 2000. In the IMPACT model, changes in risk factors prevalence between 1981 and 2000 have caused 35,944 fewer total deaths from ages 45 to 84 where the biggest contribution comes from smoking. The reduction in smoking has reduced mortality by 48.1% from the total deaths.

In the HW model, there are lower diabetes rates when we use the 1981 diabetes intensities that will lower the total number of deaths for males and females. Therefore, higher diabetes rates in 2000 will increase the number of deaths. This is similar to the result from the IMPACT model where adverse trends in diabetes have increased the IHD deaths in the IMPACT model. An increasing trend can also be seen in the obesity rates where in the IMPACT model, there are additional deaths of 2097. In the HW model, higher obesity rates will reduce the mortality rates as there will be lower lightweight rates. Lightweight has higher mortality rates than obese in the HW model so 1981 BMI intensities have higher number of deaths compared to 2000 model estimated rates.

An additional total of 101157 deaths for males would have occured in 2000 if all the 1981 risk factors intensities including smoking had remained the same in 2000. For females, the number of deaths was reduced by 64,924 due to changes in the risk factors between 1981 and 2000.

To summarize, we have Tables 6.22 and 6.23 that show the total expected number of deaths for males and females from the HW Model and the IMPACT Model. Table 6.22 shows the results from Tables 6.16 and 6.19 taking the combination of risk factors. Results for Table 6.23 are taken from the effect of single risk factors.

The results from the HW Model and the results from the IMPACT Model are not directly comparable. Using the HW Model, we can calculate the effect of changes for one risk factor only and also a combination of risk factors. We assume that the 1981 intensities continue to happen in 2000 and see what would have happened to the number of IHD cases, stroke cases and number of deaths. In the IMPACT Model, the number of deaths prevented or postponed are calculated for each change in each risk

factor between 1981 and 2000.

In the IMPACT Model, a reduction of 34% in smoking between 1981 and 2000 has prevented 29715 deaths. From our model, if smoking rates in 1981 continue to persist in 2000, there will be 30738 more deaths. From Table 6.23, an obvious difference in the expected deaths is from BMI. With IMPACT, there is a negative number of deaths prevented or postponed which means the negative changes in obesity have increased the number of deaths prevented or postponed by 2097. However in the HW Model, if 1981 BMI intensities continue to happen in 2000, there will be higher expected deaths, as despite the obesity rates in 1981 being lower, lightweight has higher mortality than obese in our model.

Risk factor	HW Model			IMPACT Model
	Male	Female	Total	Total
Smoking	20461	10277	30738	29715
Hypertension	13069	9815	22884	5868
Hypercholesterolaemia	−1567	1966	399	7900
BMI	12374	2397	14771	−2097
Diabetes	−3437	−2254	−5691	−2888

Table 6.22: Results from effect of combination of risk factors.

Risk factor	HW Model			IMPACT Model
	Male	Female	Total	Total
Smoking	20461	10277	30738	29715
Hypertension	12530	9497	22027	5868
Hypercholesterolaemia	−1388	1877	489	7900
BMI	12374	2397	14771	−2097
Diabetes	−3677	−2408	−6085	−2888

Table 6.23: Results from effect of single risk factor.

Chapter 7

Conclusions

7.1 Conclusions

The adjusted HW model can be used to calculate the effect of changes in the risk factors prevalence rates on IHD, stroke and mortality between 1981 and 2000. The major risk factors associated with these conditions are age, sex, smoking, BMI, diabetes, hypertension and hypercholesterolaemia.

Among these risk factors, smoking is found to be the highest contributor affecting the number of IHD, stroke and mortality. Almost 31,000 deaths for males and females will happen if the smoking rates in 1981 continued to happen in 2000. This shows that the reduction in smoking has saved these lives. It also suggests that the smoking ban and promotion towards no smoking has shown a successful effect. The age range that we have considered in our model has higher mortality rates for smokers with IHD that the prevalence of IHD has decreased in 2000 especially for males.

Adverse effect is shown in diabetes as there would be 6,085 fewer deaths for males and females if 1981 diabetes intensities continued to happen in 2000. More prevention strategies need to be implemented to control the diabetes prevalence rates to keep the prevalence rates from increasing over time. It is also important to lower the prevalence of diabetes as it has a direct effect on IHD and mortality.

Hypertension has a direct effect on IHD, stroke and mortality, whereas hypercholesterolaemia has a direct effect on IHD but not on stroke and a mixed effect on mortality (Chatterjee *et al.*, 2008(a), Tables 9 and 10). Hence, increasing the levels of hypertension to 1981 levels will tend to increase the prevalence of IHD, stroke and

number of deaths. 1981 hypercholesterolaemia levels increase the prevalence of IHD, particularly for females, but have little effect on the prevalence of stroke or the number of deaths. Increasing the IHD levels to 1981 levels have different effects for males and females as the trends over time are different for both males and females and the numbers of deaths are affected by the adjustments for sudden deaths following MI and stroke that are included in the adjusted HW model.

The HW model can be used to calculate the effect of changes in one single risk factor and also a combinations of factors. The IMPACT model does not deal with the changes in any combination of factors. Looking at the effect of changes in a combination of factors can allow us to see the relation between these risk factors to the changes in the numbers of IHD cases, stroke cases and deaths. The HW model can be used to forecast the future prevalence rates for the risk factors in the UK as it is adjusted to match the UK observed prevalence rates where as the IMPACT model uses the β coefficient from various countries that might not represent the trend in the UK over time. As for the time period, the HW model is more flexible as we can choose any time period that we want.

Our model can be be applied to other countries by adjusting the intensities to match the observed prevalence rates from that country or by calculating new parameterisations if data are available.

7.2 Limitations

Our model only includes people from ages 45 to 84. This is because we have to run the model for 19 years (from 1981 to 2000) and to find the model estimated prevalence rates for those aged 45 or below in 2000, we need to start at age 26 and below which is not applicable to the HW model. The chosen age range is also used because there are more cases of IHD and stroke in these age groups. We limit our upper age to 84 to follow the IMPACT Model.

Cancer is a major cause of deaths in the UK and other countries. At present, cancer deaths are included in the mortality transition rates but cannot be differentiated in the same way as IHD and stroke. The model could be extended to include cancer in the future. Another limitation is that our model is not fully dynamic. We have two static parameterisations of the model which, when applied to appropriate initial risk

profiles, produce model estimated prevalence rates for 1981 and 2000.

7.3 Further research

We can consider future changes in our model by answering this question: what will happen if the intensity of some factor changes in the future? This will be based on research findings and medical advances for the prevention of the risk factors. For example, the introduction of statins in the 1990s to lower cholesterol level could be considered and we could explore how it affects the prevalence of hypercholesterolaemia. A study on the polypill by Wald and Law (2003) stated that the polypill can prevent the risk of IHD and stroke in middle–aged and older people and we could use the model to see what happens in the future if these intensities change due to this medical advance and the impact it has on the event rates. New law enforcements such as the regulation of smoking, can also affect the future rates.

We can include other causes of death in our model to explain more about the mortality rates in England and Wales such as cancer. We could also extend the upper age limit by including those aged above 84 as longevity is increasing. We could also make the model fully dynamic by making some or all of the transition intensities to depend on calendar year. In the future, we could use the model to apply it to other countries and this would depend on what data were available.

Chapter 8

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