

Calculation of changes in life expectancy based on proportional hazards model of an intervention

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Abstract

Mortality projections are of great interest to the pension and insurance industry and with an ageing population, the projections need to cover a longer period. A significant question is how to incorporate in mortality projections the longevity risk due to medical advances and uptake of health interventions. We show how hazard ratios obtained from medical studies in combination with the baseline hazards described by Gompertz or Weibull survival distributions, can be translated into changes in individual and population period life expectancy. The impact of medical advances and health interventions can differ among groups of people, such as by sex, age, and deprivation. Changes in life expectancy depend on the composition of the population and these attributes. These calculations are illustrated by a case study on statins, a drug that can significantly improve life expectancy. An R program implementing our methodology is provided in the Appendix.

Keywords Hazard Function; Health Data; Mortality; Population Health; Gompertz distribution; Weibull distribution

JEL codes C18, C13, C46, I13

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1 Introduction

Life expectancy (LE) and changes in life expectancy are of great interest to the pensions and insurance industry, society, and government as they affect among others the old-age dependency ratio, social security and pensions, long-term care, and healthcare systems. A significant question in the actuarial community is how to take into account medical advances and their impact on ageing in forecasting mortality [Purushotham et al., 2011]. National life tables are often used in projecting mortality trends in populations of insured and in pension schemes [Barrieu et al., 2012].

However, these mortality projections are susceptible to heterogeneity in mortality rates and their trends (basis risk) and to significant improvement in longevity (longevity risk).

Longevity-trend projections are used for managing longevity risk in pricing and reserving for insurance and annuity products as well as for costing of public and private pensions. Changes in these projections result in significant consequences. As an example, an upwards update of longevity in the French prospective life tables in 2006 from the previously used tables from 1993 resulted in increase of reserves by French insurers by an average of 8% [Barrieu et al., 2012]. Downward changes in longevity in the recent Continuous Mortality Investigation (CMI) projections is a more recent example in the opposite direction. Cohort life expectancies at age 65 are around 6 months lower in CMI 2018 model than in CMI 2017, and are over a year lower than in CMI 2015, for both males (21.921 using CMI2018 vs. 22.454 using CMI2017) and females (24.200 using CMI2018 vs. 24.709 using CMI2017), Continuous Mortality Investigation [2019]. Related revision to longevity-trend assumptions resulted in considerable mortality reserves releases by UK insurance companies. Legal and General reported mortality release of £433 million in 2018 to align to CMI 2016 tables [Legal&General, 2019]. Similarly, Aviva longevity reserve releases were £780 million in 2018 and £779 million in 2017 [Montague, 2019].

Changes in mortality projections also directly affect annuities costs, especially in the decreasing interest rates environment. Khalaf-Allah et al. [2006] provide a method to estimate an increase in annuity values resulting from the reduction in the forces of mortality, and provide numerical examples for different inception ages and rates of interest.

Basis risk in mortality projections arises because policyholder mortality rates and the pace of their evolution typically differ from that of the national or industry-wide

population, which are used in deriving mortality projections such as the CMI models, due to portfolio-specific selection effects. Portfolio membership is very different to the general population and to any other portfolio in respect in its socio-economic mix, lifestyle and health profile. This translates into different mortality levels, different main causes of mortality and mortality improvement projections. Typically, pension scheme members have seen higher improvements in life expectancy than the general population, more so for more affluent pension scheme members who have been largely resilient to recent negative changes as opposed to less affluent members who have seen life expectancy plateau [O'Reilly, 2019]. Modelling mortality, adjusting for the population's characteristics using individual records instead of aggregated records, can explain a higher percentage of heterogeneity in mortality rates and thereby reduce the basis risk of mortality projections. Not only mortality rates, but also longevity improvements can differ by individual profiles of socio-demographic and health factors. By modelling uptake of treatment and estimating the effect of that treatment on longevity conditional on the individual profile, one could assess portfolio-specific longevity risk.

In medicine, the Cox proportional hazards model is the most popular method of time-to-event analysis or survival analysis. The vast majority of clinical trials and observational studies that analyse survival outcomes use this model. The main objective of this study was to develop a method to incorporate proportional hazards modelling into actuarial tasks, from underwriting individual lives to modelling hypothetical changes in population or group life expectancy due to medical advances and health interventions. To do this successfully, some parametric assumptions about the shapes of survival distributions are necessary. We demonstrate that both Gompertz and Weibull survival distributions in combination with the Cox model can be successfully used for actuarial calculations. We demonstrate our methodology on the important example of survival benefits of statins.

Statin therapy for primary prevention of cardiovascular disease (CVD) has been reported to improve life expectancy [Mihaylova et al., 2012]. In 2014, the National Institute for Health and Clinical Excellence (NICE), a UK national body that provides guidelines on prescription of drugs, widened the eligibility criteria for statin therapy for primary prevention of CVD [NICE, 2016], making an additional 4.5 million UK residents eligible for the therapy [NICE, 2014]. Previous studies reported trends in statin prescription over time and by sex, age, and deprivation in the UK

[Finnikin et al., 2017, O’Keeffe et al., 2015, 2016]. However, it is not yet known what the impact of statin prescription in the general population is on the national life expectancy and how this can be related to mortality projections of populations of insureds and pension schemes.

We estimate the effect of statin prescription on longevity at various cardiac risks at ages 70 and 75, where the cut-off points of cardiac risks were informed by the changing guidelines on primary prevention of CVD. We also calculate the hypothetical changes in national life expectancy if all eligible people were to be prescribed a statin. As the populations of insureds and pension schemes are unlikely to be representative of the national population, this study used a representative primary care database to evaluate the effect of statin prescription on individual and national life expectancy by sex, age, and deprivation, so that the results could be applied to an individual and to populations with other socio-demographic compositions.

2 Cox Proportional Hazards Model

Cox proportional hazards model is the most popular method of modelling survival outcomes. It represents the hazard function or force of mortality as $\mu(y, t) = \mu_0(t) \exp(\beta^T y)$ for a vector of parameters β , and a vector of covariates y . The baseline hazard $\mu_0(t)$ is not specified, and interest generally lies in the hazard ratios $\mu(y_1, t)/\mu(y_2, t) = \exp(\beta^T (y_1 - y_2))$, which do not depend on $\mu_0(t)$ and are constant over time. However, some assumptions about the shape of the baseline hazard are useful if an estimate of a survival function or a life expectancy is required. The three parametric distributions compatible with the proportional hazards assumption are exponential, Weibull and Gompertz distributions. Denote the baseline log-hazard by $\lambda_0(t) = \log \mu_0(t)$. Then $\lambda_0(t) = a$ corresponds to the exponential, $\lambda_0(t) = a + bt$ to Gompertz, and $\lambda_0(t) = a + b \log t$ to Weibull baseline hazards. The respective proportional hazards models are called Cox-exponential, Cox-Gompertz and Cox-Weibull survival models [Bender et al., 2005].

When the proportional hazards assumptions are not satisfied, one way to generalise the Cox model is to consider the hazards $\mu(y, t) = \mu_0(\gamma, t) \exp(\beta^T y)$, where the baseline hazard is known up to a multidimensional parameter γ , and to estimate the latter from the vector of predictors y [Bender et al., 2005, Devarajan and Ebrahimi, 2011, Begun et al., 2019]. Another class of models uses time-dependent coefficients

$\mu(x, t) = \mu_0(t) \exp(\beta^T(t)y)$. These classes of survival models will be addressed in our future research.

3 Individual Life Expectancy

3.1 Effective age

To facilitate understanding of the hazard ratio, the hazards can be presented as the difference between chronological age and “effective age”, which is the average chronological age with the same hazard.

For simplicity, consider a single binary risk factor with the reference value $y = 0$ and, in the presence of a risk in question, $y = 1$. Let $\mu_1(t)$ be the hazard function at risk $y = 1$. On the log scale, the log-hazards are $\lambda_1(t) = \lambda_0(t) + \beta$. This means that the log-hazard lines differ only by an increment β . For a monotone-increasing hazard, find the (unique) time increment $\Delta(t)$ such that $\lambda_1(t) = \lambda_0(t + \Delta(t))$. The value of $t + \Delta(t)$ is, by definition, the *effective age* of the person with risk $y = 1$ at chronological age t . The value of $\Delta(t)$ is the difference in effective age between people with/without the risk factor y at age t . If model includes other variables, the difference is adjusted for them.

3.2 Effective age under Cox-Gompertz model

Under the Gompertz model applied to numerous populations over time, the increase in annual hazard of mortality associated with ageing one year is approximately constant between ages 50 and 95 [Brenner et al., 1993, Spiegelhalter, 2016, Vaupel, 2010]. For England and Wales in 2010, this increase was 1.103 for men and 1.111 for women.

Theorem on effective age (Spiegelhalter (2016)) Consider a hazard function $\mu(t)$ under the proportional hazards assumption, i.e. let $\mu(y, t) = \mu_0(t) \exp(\beta y)$ for a binary factor $y = 0$ or $y = 1$. Let $\mu_0(t) = \exp(a + bt)$ (Gompertz baseline hazard), and denote the hazard function for $y = 1$ by $\mu_1(t)$. Then, $\mu_1(t) = \mu_0(t + \Delta)$, where Δ does not depend on t . The time difference between the chronological and effective age, $\Delta = \beta/b$.

Corollary Consider an intervention at time T . Assume that the hazard function is $\mu(y, t) = \exp(a + bt + \beta y)$. Denote the survival functions at age t without/with intervention by $S_0(t)$ and $S_1(t)$, respectively. Then

1. For $t \geq T$,

$$S_1(t) = S_0(T)S_0(t + \Delta)S_0^{-1}(T + \Delta).$$

2. For age $z \geq T$, life expectancy

$$e_1(z) = e_0(z + \Delta). \quad (1)$$

Proof The hazards are $\mu_0(t)$ for $t \leq T$ and $\mu_0(t + \Delta)$ for $t > T$. Cumulative hazards are $M_0(t)$ for $t \leq T$ and $M_0(T) + \int_T^t \mu_0(t + \Delta)dt = M_0(T) - M_0(T + \Delta) + M_0(t + \Delta)$ for $t > T$. Thus, $S_1(t) = S_0(T)S_0^{-1}(T + \Delta)S_0(t + \Delta)$. Given that $S_0(T) = S_1(T)$, (1) follows.

By definition, the life expectancy at age z ,

$$e_1(z) = \frac{\int_z^\infty S_1(t)dt}{S_1(z)} = \frac{\int_z^\infty S_0(T)S_0(t + \Delta)S_0^{-1}(T + \Delta)dt}{S_0(T)S_0(z + \Delta)S_0^{-1}(T + \Delta)} = \frac{\int_z^\infty S_0(t + \Delta)dt}{S_0(z + \Delta)} = e^{(z+\Delta)}.$$

Missov and Lenart [2013] give the expressions of life expectancy for Gompertz and Gompertz-Makeham distributions.

3.3 Effective age under Cox-Weibull model

The Weibull distribution is also well suited to describe disease- and ageing-related outcomes. Matsushita et al. [1992] use it to describe Japanese survival rates over time, and Li and Zhang [2015] describe Weibull modelling of cancer progression and death rates. Juckett and Rosenberg [1993] argue that the Gompertz distribution is better suited to describe all-cause mortality, whereas the Weibull distribution is a better descriptor of single causes-of-death.

The Weibull hazard function with scale σ and shape k is given by

$$\mu_0(t) = \frac{k}{\sigma} \left(\frac{t}{\sigma}\right)^{k-1}.$$

The log-hazard function can be written as $\lambda_0(t) = a + (k - 1) \log(t)$ for $a = \log(k) - k \log(\sigma)$. Under the assumption of proportional hazards, $\lambda_1(t) = \lambda_0(t) + \beta y$. The calculation to obtain the effective age includes the log-hazards $\lambda_1(t_1) = \lambda_0(t)$, or $(k - 1) \log(t_1) = (k - 1) \log(t_0) + \beta$. This results in $t_1 = t_0 \exp(\beta/(k - 1))$, so we can communicate constant percentage increase or decrease in effective age or, rather, accelerated aging due to risk y . The use of Cox-Weibull model for actuarial applications will be further explored in our future research.

4 Period Life Expectancy

For a population, the period life table supposes 100,000 live births and shows the number l_x surviving to exact age x . The survival function at age x is $S(x) = l_x/100000$. There are typically separate life tables for males and females but otherwise this survival function is a weighted average of the survival functions of the people with different risk profiles at age x within the population. Suppose that the population consists of multiple risk groups $j = 1, \dots, J$. The treatment of interest ($i = 0; 1$) is prevalent in each risk group from age T , but its effect may vary. Let $S_{ij}(x)$ be the survival function of group j with treatment i at age x ; let f_j be the prevalence of risk group j at age T ($\sum_j f_j = 1$), and let $p_{j,i}$ be the prevalence of the treatment of interest in group j at age T , $i = 0, 1$.

Then the value of the overall population survival function $S(x)$, at age $x = T$ is the weighted mean of the survival functions in the individual risk groups with/without the treatment:

$$S(T) = \left[\sum_j f_j p_{j,1} S_{1j}(T) + \sum_j f_j (1 - p_{j,1}) S_{0j}(T) \right] / \sum_j f_j. \quad (2)$$

The sum of weights in the above equation is 1, but we kept the denominator as, in real data, the estimated prevalences f_j are subject to rounding and perhaps other errors.

Assume that the proportional hazards assumption holds, so that the force of mortality (hazard) at age x , $\mu_{ij}(x, Y) = \mu_0(x)\mu_{ij}(Y)$, where $\mu_0(x)$ is the baseline hazard at age x and the age-independent component (which depends also on other factors Y) can be modelled by

$$\log(\mu_{ij}(Y)) = a_{ij} = a_0(T) + \alpha_i + \beta_j + \gamma_{ij} + \beta^T Y, \quad (3)$$

where $a_0(T)$ is the baseline value which may depend on the time of intervention T ; α_i , β_j , and γ_{ij} are main effects and interaction of risk group j and treatment i , centered at the baseline (i.e. $\alpha_0 = \gamma_{0j} = 0$), and the covariates Y have no interactions with the treatment or the risk of interest.

4.1 Survival function under Cox-Gompertz model

Assuming the Gompertz baseline hazard, the log-hazards for treatment i in risk group j is $a_{ij} + bx$, so the log-hazards in various subgroups differ by intercept but have the

same slope. The survival functions are $S_{ij}(x) = \exp(-e^{a_{ij}}b^{-1}(e^{bx} - 1))$. Substituting a_{ij} from (3), the survival functions at age $x \geq T$, where T is the intervention age, are

$$S_{ij}(x|Y, T) = \exp(-e^{a_0(T)+\alpha_i+\beta_j+\gamma_{ij}+\beta^TY}b^{-1}(1 - e^{bx})). \quad (4)$$

Assuming that at age T , the prevalence of the risk groups and treatments within the groups, does not depend on Y , then Y can be integrated out (incorporating the result into the $a_0(T)$ term) to obtain

$$\begin{aligned} S(x|T) &= \sum_j f_j p_{j,1} \exp(-e^{a_0(T)+\alpha_1+\beta_j+\gamma_{1j}}b^{-1}(1 - e^{bx})) \\ &+ \sum_j f_j (1 - p_{j,1}) \exp(-e^{a_0(T)+\beta_j}b^{-1}(1 - e^{bx})). \end{aligned} \quad (5)$$

This is a non-linear equation with one unknown, a_0 . The left-hand side is given by the period life-table, and the slope b should be determined for a particular population of interest. As $S(x)$ is a decreasing function of a_0 , equation (5) has a unique solution.

After solving equation (5) for $a_0(T)$, we can find component survival functions $S_{ij}(x)$ for any set of prevalences $\{f_j\}$ and $\{p_{j,1}\}$.

4.2 Estimating changes in life expectancy

The remaining life expectancy (LE) at age x for the Gompertz distribution $G(a, b)$ can be written as $\int_z^\infty G_{(a,b)}(x)dx = b^{-1} \exp(b^{-1}e^a)E_1(b^{-1}e^{a+bx})$, where $E_1(z) = \int_z^\infty t^{-1} \exp(-t)dt$ denotes the exponential integral, Missov and Lenart [2013]. However, this expression should be divided by the survival $S(z)$, to provide a proper LE at z . Thus, the life expectancy at age z for a Gompertz distribution is obtained as

$$e_{G(a,b)}(z) = \frac{b^{-1} \exp(b^{-1}e^a)E_1(b^{-1}e^{a+bz})}{\exp(-e^a b^{-1}(e^{bz} - 1))}. \quad (6)$$

The component life expectancies $e_{ij}(z)$ are obtained for each component distribution $G(a_{ij}, b)$.

To calculate the population life expectancy, consider the survival function of the overall population, which is a finite mixture of subpopulations, $S(x) = \sum w_k S_k(x)$, $\sum w_k = 1$. The index k here stands for a pair $\{j, i\}$. Then the life expectancy at age z is

$$e(z) = \frac{\int_z^\infty S(x)dx}{S(z)} = \frac{\sum_k w_k S_k(z) \int_z^\infty S_k(x)dx / S_k(z)}{\sum_k w_k S_k(z)} = \frac{\sum_k w_k S_k(z) e_k(z)}{\sum_k w_k S_k(z)}. \quad (7)$$

Taking all $p_{j,1} = 0$, we obtain a hypothetical life expectancy $e_0(z)$ if there were no intervention of interest, and, for all $p_{j,1} = 1$, a hypothetical life expectancy $e_1(z)$ with full uptake of the intervention.

An R program implementing our methodology to evaluate changes in period life expectancy due to an intervention, assuming an underlying Gompertz distribution, is provided in the Appendix. It requires a q_x vector of hazards across an age range of interest, the data on the prevalences $\{p\}$ and $\{f\}$, and the hazard ratios of the risk groups and the intervention in each risk group on mortality. The program fits a Gompertz distribution to q_x over the age range, finds the value of $a_0(T)$ from equation (5), and calculates component survival functions $S_{ij}(x)$ and life expectancies $e_{ij}(x)$ (with/without intervention) for a requisite age $x \geq T$. It also calculates hypothetical period LEs without/with intervention. The program uses the R package *expint* to evaluate the exponential integral $E_1(z)$.

4.3 General case of an intervention effect under proportional hazards

So far we have considered the Cox-Gompertz model. However, our method of calculating survival function and life expectancy does not depend on assuming a Gompertz distribution. In general, given proportional hazards, $\mu(t) = a\mu_0(t)$, the cumulative hazard $M_a(x) = \int_0^x a\mu_0(t)dt = aM_0(x)$. And the survival function $S_a(x) = \exp(-aM_0(x))$. So, instead of equation (4), we obtain

$$S_{ij}(x|Y) = \exp(-\exp(a_0(T) + \alpha_i + \beta_j + \gamma_{ij} + \beta^T Y)M_0(x)). \quad (8)$$

Substituting (8) into (2) yields

$$S(T) = \sum_j f_j p_{j,1} \exp(-e^{a_0(T) + \alpha_1 + \beta_j + \gamma_{1j}} M_0(T)) + \sum_j f_j (1 - p_{j,1}) \exp(-e^{a_0(T) + \beta_j} M_0(T)). \quad (9)$$

For a given cumulative baseline hazard $M_0(T)$, we then solve for a_0 .

5 Case study: survival benefits of statins

5.1 Modelling of effects of statins on survival

Statins are a class of lipid-lowering drugs that are prescribed to prevent cardiovascular disease (CVD). Statins have been publicly available since 1987, but the drugs started to become popular from 2000 onward. NICE's recommendations on statin therapy for CVD have changed over time, mostly widening the eligibility criteria. For primary prevention, the eligibility criterium in the UK is based on the 10-year risk of a first cardiac event calculated using QRISK2, which incorporates information on multiple demographic, medical, and lifestyle factors (<https://www.qrisk.org/>). The most significant changes in statins eligibility criteria were in 2006, when the threshold of cardiac risk at which to prescribe statins was lowered to a QRISK2 $\geq 20\%$ (previously $\geq 40\%$) [Hippisley-Cox et al., 2008]; in 2007, when statins became first line treatment for CVD survivors [NICE, 2013]; and in 2014, when the cardiac risk threshold was further lowered to a QRISK2 score $\geq 10\%$ [NICE, 2016]. With the latest change, an additional 4.5 million UK patients became eligible.

In this section, we evaluate survival benefits of statins for an individual and their effect on the period life expectancy in England and Wales. We also quantify the potential impact of the NICE 2014 guideline on life expectancy. This work builds on our previous research [Gitsels et al., 2016, 2017], where we estimated the hazard ratios associated with statin prescription for primary and secondary prevention of CVD in patients at retirement age. We make use of the oldest two cohorts consisting of people born between 1920-40 and who reached the baseline age of 70 or 75 during the study period of 1987-2011. The age cohorts were selected from The Health Improvement Network (THIN) primary care database. When adjusted for sex, age and deprivation, THIN patients are representative of the UK population [Blak et al., 2011, Hall, 2009].

At the end of study period in 2010, statins were prescribed in 20% of patients with a QRISK2 score of $< 20\%$, in 45% of patients with a QRISK2 score of $\geq 20\%$, and in 90% of patients with CVD. QRISK2 score increases with age and by age 70, there were practically no patients with a QRISK2 score of $< 10\%$ and by age 75, there were no male patients with a QRISK2 score of $< 20\%$. Given cardiac risk group, statins were prescribed more in women, in younger patients, and in patients from less deprived areas, although these differences decreased over time, see Tables A.1

and A.2 for details.

In our previous work [Gitsels et al., 2016], we developed 12 Cox proportional hazards models to estimate the effect of statin prescription on all-cause mortality for three QRISK2 groups ($< 10\%$, $10 - 19\%$ and $\geq 20\%$) by 4 key ages (60, 65, 70 and 75 years old). However, the models from [Gitsels et al., 2016] did not include the effects of QRISK2 groups, denoted by β_j in Equation (3), required for derivation of changes in life expectancy due to statins. Therefore, we pooled the data for QRISK2 groups $10 - 19\%$ and $\geq 20\%$ at ages 70 and 75 from Gitsels et al. [2016], and fitted the same Cox models after adding the QRISK2 group to the predictors. The final models adjusted for sex, year of birth, socioeconomic status measured by Townsend score (TS) [Townsend, 1987], diabetes, hypercholesterolaemia, blood pressure regulating drugs, body mass index, and smoking status. The models included a random effect on general practice to take into account the interdependence of patients from the same practice. Interactions between statins, QRISK2 groups and the other risk factors were tested, but none was significant.

For this case study, we use the adjusted hazard ratios (HRs) of QRISK2 groups and of statin prescription on all-cause mortality obtained from the analysis. Additionally, we use the adjusted HRs for all-cause mortality of heart attack survivors, from Gitsels et al. [2017], as a substitute for HRs for CVD sufferers. These HRs are given in Table 1. The proportional hazards assumption was checked by Grambsch and Therneau’s test [Therneau and Grambsch, 2000] and was found valid.

5.2 Fitting Gompertz distributions to the period life table data

In this Subsection we demonstrate that the Gompertz distribution provides an adequate model for all-cause mortality, for the England and Wales population. We use the period life table by Townsend score (TS) quintiles centered at 2010 provided by Office of National Statistics [2017] (ONS). Log-hazard ratios and fitted regression lines for males and females between the ages 60 – 90 by TS quintiles are depicted in Figure 1. The linearity of the log-hazard increase by age is evidence of good approximation by a Gompertz distribution. We used the robust regression program *rlm* from R package *MASS*.

The hazards clearly differ among the TS quintiles, from the highest at TS quintile 5 (most deprived) to the lowest at TS quintile 1 (least deprived), and by gender

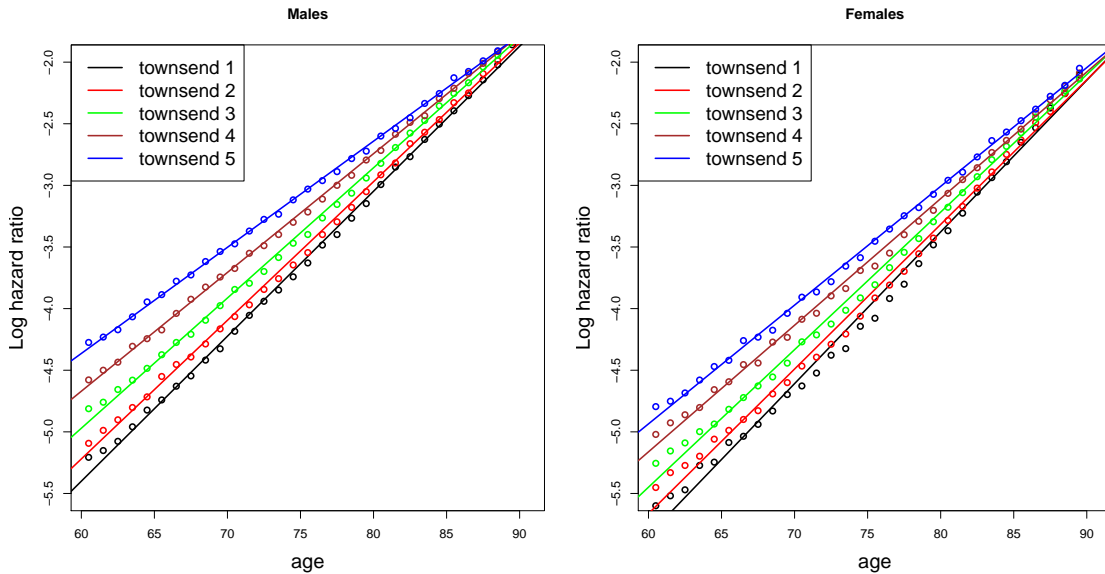


Figure 1: Log-hazard ratios between the ages 70 – 90 from the ONS period life table centered at 2010 (circles) and fitted regression lines by Townsend score quintiles and sex.

(higher for males), resulting in corresponding differences in life expectancy.

Using the Gompertz distributions with the estimated regressions coefficients (a, b) , we calculated the LEs from Equation (6) and compared them with the LEs from the ONS life table at ages 70 and 75. The differences were at most 0.3 year. Since the deaths are assumed to have occurred in the middle of each interval in the life tables, we added a correction $c \leq 0.5$ to age x when estimating the coefficients (a, b) . The optimum corrections (from 0.2 to 0.5) differ somewhat by sex and TS quintile, and result in an absolute difference of at most 0.1 year between the calculated LE and the ONS LE at ages 70 and 75, see columns 4 and 5 in Table 2. These age corrections had no visible effect on the estimated differences in LE with/without statins. Table A.3 lists the parameters of the fitted distributions.

5.3 Verifying the Gompertz assumption for the data on statins

To evaluate the fit of the Gompertz distribution to the survival distribution in the statins study, we first obtain the predicted baseline survival function $\hat{S}_0(t)$ from the Cox regression with the baseline values of all predictors, using *survfit* function from *survival* package in R. The estimated cumulative baseline hazard $\hat{M}_0(t) = -\log(S_0(t))$. This results in a step function with steps at the event times. The top

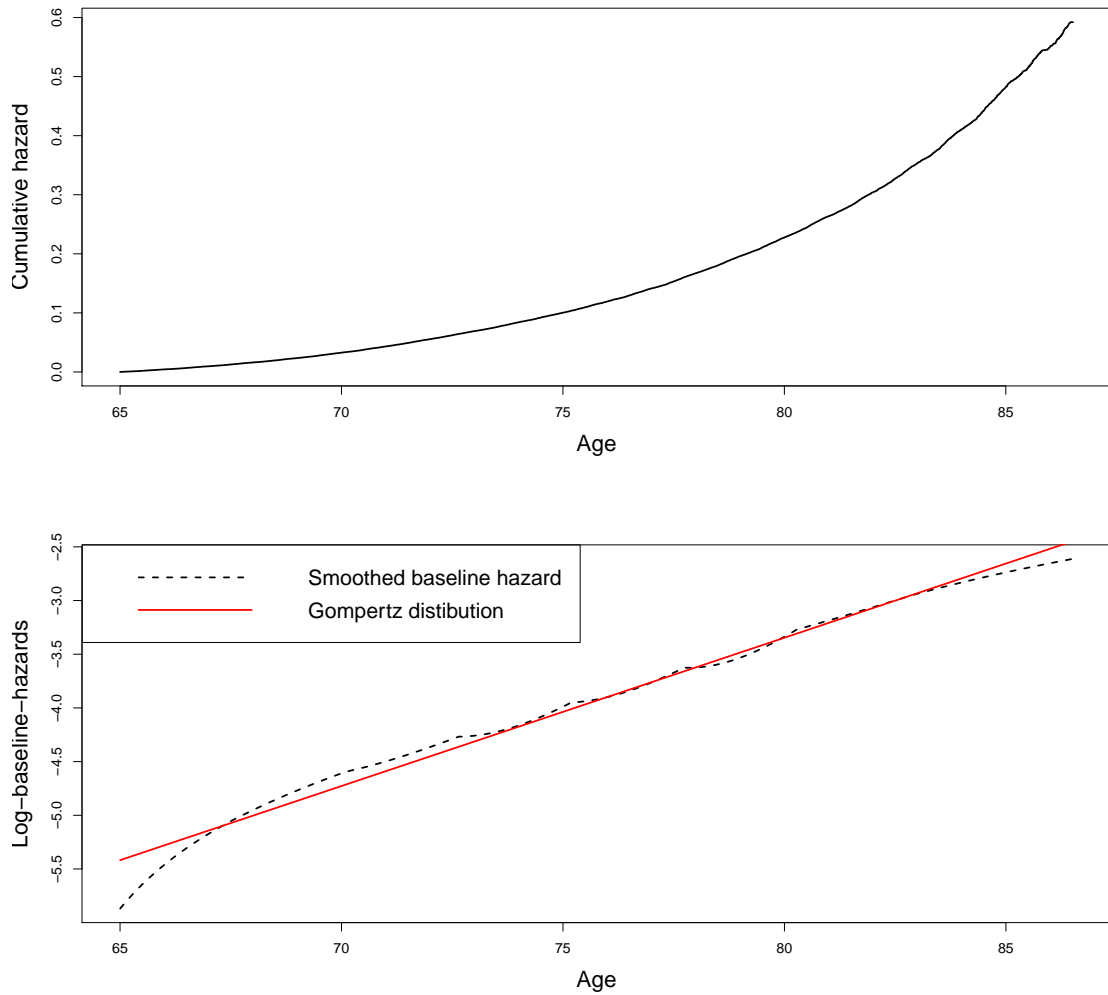


Figure 2: Top: estimated baseline cumulative hazard function $\hat{M}_0(t)$. Bottom: smoothed baseline hazard $\hat{\mu}_0(t)$ (black) and fitted linear regression line (red) for the statins survival study. Time is age in years.

panel of Figure 2 depicts this function for baseline age 65. The baseline hazard $\mu_0(t)$ is the derivative of $M_0(t)$, but the estimated cumulative hazard $\hat{M}_0(t)$ needs to be smoothed prior to numerical differentiation. We used the LOESS (locally estimated scatterplot smoothing) method implemented in the program *loess* from R package *stats*, with span 0.65. The derivative was calculated as the slope of the smoothed cumulative hazard function between consecutive event times. The logarithm of this derivative (i.e. the log of the estimated baseline hazard function) is plotted in the bottom panel of Figure 2 (black line). The solid red line is the fitted linear regression line for ages 65-85. Overall, the log baseline hazard is very well approximated by a straight line, so the Gompertz distribution is a suitable assumption.

5.4 Changes in effective age due to statins

For England and Wales in 2009-11, the increase b in the Gompertz annual hazard of mortality between ages 70-90 was approximately 0.1034 for men and 0.1108 for women (calculated from the ONS period life table centered at 2010.). As the Gompertz and proportional hazards assumptions hold, we used the theorem on effective age in Section 3.2 to calculate the number of years lost or gained in effective age for cardiac risk group j by sex g as:

$$\Delta t_j \approx \log(\text{HR}_j) / \log(b_g), \quad (10)$$

where $\log(\text{HR}_j) = \alpha_1 + \gamma_{1j}$ is the log hazard ratio of statin prescription on all-cause mortality for a patient in risk group j , cf (3), and b_g is the increase in the annual hazard of mortality for sex g . The HR_j values for statins are given in Table 1.

The longevity improvement associated with statin prescription translates to a reduction in effective age of up to three years. The reduction is largest for 70-year old male heart attack survivors (2.91 years). Overall, statins result in larger changes in effective age at higher ages and for higher cardiac risk groups. They appear to result in greater changes in effective age in males than in females. This is solely due to different rates of increase b in the annual hazards of mortality for males and females as the HR of statins was exactly the same for both sexes (there were no interactions between statins effects and sex in our analysis).

5.5 Changes in life expectancy due to statins at ages 70 and 75

Since the mortality rates, the cardiac risk distribution and the statin prescription rates differ by gender and by socio-economic status (measured by Townsend score quintiles), we analysed the life tables separately for each TS quintile-by-gender combination.

For each life table, we substitute the LE at age 70 or 75, denoted by $e_{G(a,b)}$ in Table 2 (obtained from Equation (6) using the fitted Gompertz distribution $G(a,b)$ with parameters from Table A.3), into the left-hand side of the Equation (5), and solve for the value of $a_0(T)$. The requisite prevalences of the three cardiac risk groups (denoted by f_j for $j = 1, 2, 3$) and the prevalences of statin prescription in these groups in 2010 (the $p_{j,i}$ values) required for the right-hand side of (5) are given in Tables A.1 and A.2, and the HRs of statins and of the cardiac risk groups themselves

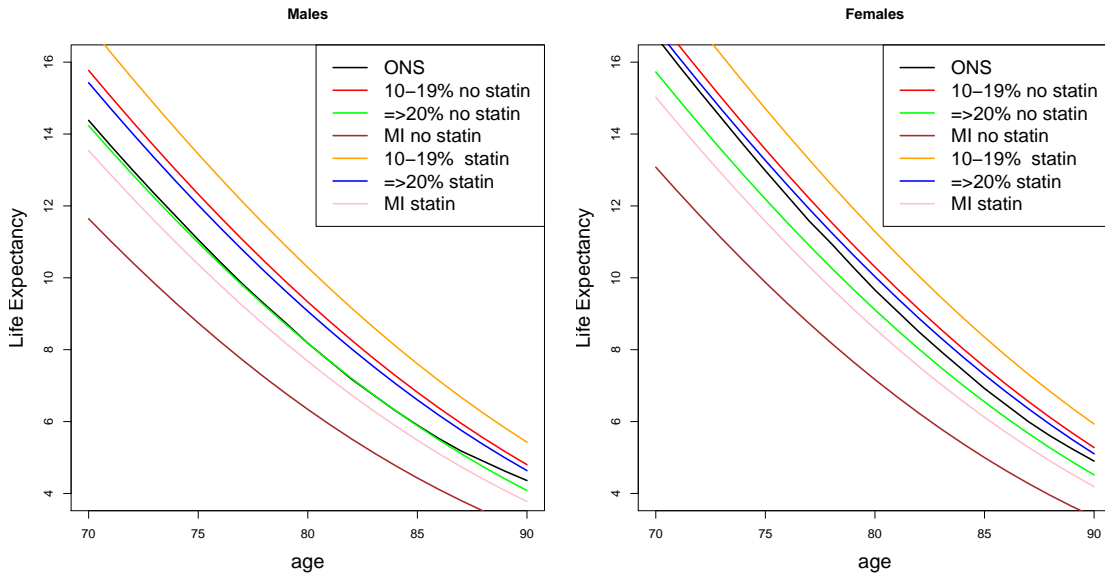


Figure 3: Life expectancy by cardiac risk group with and without statins for ages 70 – 90 based on the ONS period life table centered at 2010 (black line) for males and females.

are given in Table 1.

The resulting $a_0(T)$ values for each sex-by-TS quintile combination are also provided in Table A.3. These values were used to calculate period life tables for component cardiac risk by statin prescription subpopulations for each (i, j) combination. The resulting component LE values at ages 70 and 75, denoted by e_{ij} , and their 95% confidence intervals are provided in Table 2, and the differences due to statins within each risk group in Table A.4.

Increase in individual LE due to statins depends on cardiac risk, and is highest for heart attack survivors (1.41 – 2.02 years), and is lower in the two QRISK2 groups (1.14 – 1.35 years across ages 70 and 75). The effect of statins increases with deprivation, which could be explained by the composition of cardiac risk, where more can be gained in terms of LE in the higher cardiac risk groups.

We also calculated the period LE and its increase due to statins in each cardiac risk group for the total England and Wales population by averaging the LE across all TS quintiles, as in Equation (7), and plotted the results in Figure 3. For men, the ONS period LE almost coincides with the LE in QRISK2 $\geq 20\%$ group without statins, probably because this is the most populated group. For women, the ONS LE is between the LE for the same cardiac risk group with and without statins, probably due to higher prevalence of statin prescription in women.

We also calculated national life expectancy with and without statins, by averaging

the LE across cardiac risk groups, taking $p = 0$ (for no statins) and $p = 1$ (for statins) in Equation (5). These values are denoted by e_0 and e_1 , respectively, in Table 2, and the differences $e_1 - e_0$, $e_{ONS} - e_0$, and $e_1 - e_{ONS}$ are provided in Table A.4.

The national life expectancy for women aged 70 or 75 would be increased by up to 0.91 or 0.79 years, respectively ($e_1 - e_{ONS}$ values), if all eligible women under the current guideline of primary and secondary prevention of CVD were prescribed statins. Similarly, the national life expectancy for men aged 70 or 75 would be increased by up to 0.79 or 0.63 years (Table A.4). The most improvement would come from the areas of medium deprivation. We discuss the reliability of these findings in more detail in the Discussion Section.

6 Discussion

The main objective of this study was to develop a method to evaluate the potential impact of recent medical advances and/or public health decisions on issues of actuarial interest. We demonstrated how to incorporate hazard ratios, obtained in medical studies by the use of the Cox proportional hazards model, into underwriting individual lives, or into pricing or reserving methodology based on the population life expectancy. Both Gompertz and Weibull survival distributions, in combination with the Cox model, can be successfully used for actuarial calculations. The Cox-Gompertz model appears to be especially suitable for modelling potential changes in human life expectancy.

We demonstrated our methodology in detail on the important example of survival benefits of statins. In total, 11.8 million people in the UK (almost all men over 60 and all women over 75) are currently eligible for statins, Ueda et al. [2017], making new guidelines on statin eligibility [NICE, 2014] a health intervention on a truly massive scale. Our results show that life expectancy at ages 70-75 in the newly eligible group of patients with QRISK2 score of 10 – 20% may increase by 1.18 to 1.35 years (95% confidence interval 0.86 – 1.71 years). However, it is unlikely that there will ever be a 100% statin prescription rate in all eligible patients as it is up to the patient to decide whether to take statins [Ueda et al., 2017]. Furthermore, statins initiation does not mean compliance; about half of the patients discontinue statins of which about 75% restart again [Vinogradova et al., 2016].

Our methodology based on the Cox-Gompertz model has two components: cal-

ulation of change in effective age for an individual, and calculation of change in LE for a subpopulation, homogeneous on risk. The change in effective age depends both on the hazard ratio of mortality due to an intervention, and on the yearly increase in annual hazard of mortality. However, change in LE can vary substantially with sex, cardiac risk, and deprivation. This may make the information on changes in effective age misleading, as seemingly large changes in effective age may correspond to very modest increases in life expectancy.

Secondly, we developed a method of using the period life table data to obtain separate survival functions and the LEs for the component subpopulations. This method uses the proportional hazards assumption of the Cox model to approximate the Gompertz distribution $G(a, b)$ fitted to the period life table data, by a weighted sum of component Gompertz distributions $G(a_{ij}, b)$, with the same slope b , but with intercepts a_{ij} that depend on the hazard ratios from the Cox model. To facilitate the use of our methods in actuarial practice, we provide an R program in the Appendix.

Our methodology for calculating component LEs appears to be reliable when the proportional hazards assumption holds. However, these calculations are considerably less reliable when pooling these components into a combined life expectancy, say for all patients on statins. This is because the calculations in question assume constant weights. In the statins example, this assumption requires a constant cardiac risk distribution starting from ages 70 or 75. However, cardiac risk clearly increases with age.

To explore this issue further, Figure 4 compares the ONS period LE, the combined LE reconstructed (using fixed weights) from the component LEs and survival functions estimated at age 70, and the combined estimated LEs with/without statins.

The true LE from the ONS and the combined LE are close at age 70, but they diverge at later ages, and the estimated combined LE is noticeably higher because it assumes a favorable cardiac risk across older ages. Even though these differences are not huge (the maximum for men is 0.29 year at age 82, and for women it is 0.41 year at age 85), it would make more sense to use time-dependent weights, and perhaps time-dependent hazards, in this calculation. We intend to address this more general setting in our future research.

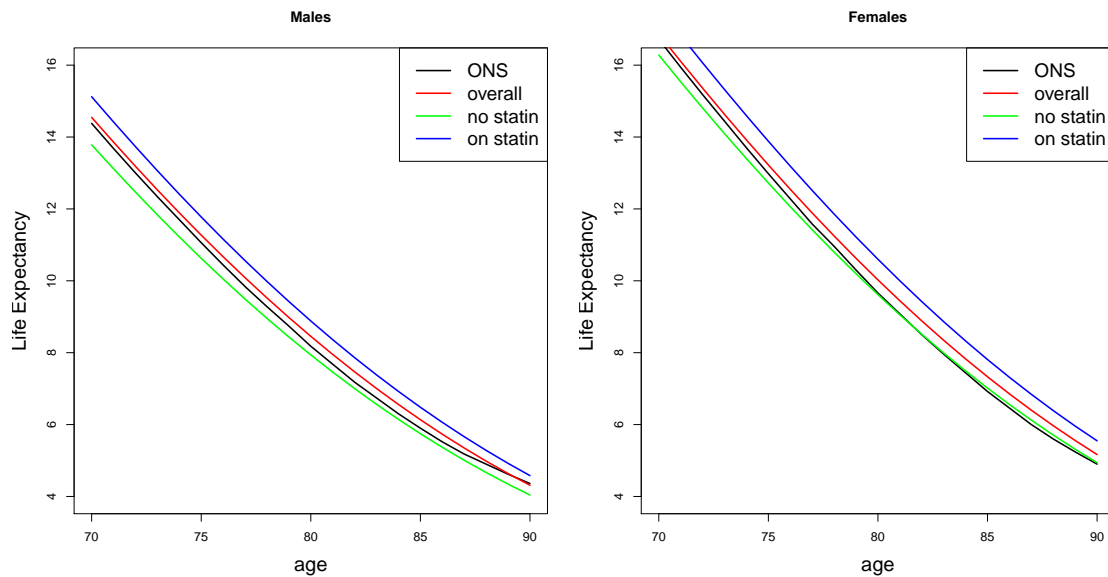


Figure 4: Life expectancy from the ONS period life table centered at 2010 (black line), estimated LEs with/without statins (blue and green lines, respectively), and the combined as in Equation (7) overall population life expectancy (red line) for males and females. (Gompertz parameters were fitted at age 70.)

7 Conclusions

Robust projections of life expectancy are essential for sound financing of private-sector annuities, pensions, and life and long-term care insurance; and for a range of publicly-funded programmes including state pensions, disability benefits, and state-financed long-term care. Improvements in longevity increase the number of beneficiaries of such programmes and for tax-financed public schemes, they can also affect the funding base through increases in the old-age dependency ratio. This paper has shown that a change in national guidelines for drug prescribing, and the consequent change in prescription rates, can result in a step change in life expectancy. This suggests that, where there is a discrete change in national guidance or prescribing practice, the likely effect on life expectancy needs to be estimated and taken into account. The analysis in this paper indicates that for projections of future longevity of people aged over 70 and at increased risk of CVD, statin prescription patterns should be incorporated as they have a significant effect on mortality. The increase in life expectancy in this group of up to two years should be incorporated in the pricing of annuities and life insurance products for them. The increase in the population life expectancy, which depends on the composition of the population, should be incor-

porated in reserving of annuities or funding of pension benefits. Our methods and results could also help with quantifying impact on life expectancy from future drug development scenarios.

Cardiac risk group	Age	HR Statins (95% CI)	Changes in effective age (Men) Δ (95% CI) (years)	Changes in effective age (Women) Δ (95% CI) (years)
No heart attack	70	0.84 (0.80-0.88)	-1.69 (-2.16, -1.24)	-1.57 (-2.01, -1.15)
	75	0.82 (0.79-0.86)	-1.92 (-3.18, -1.46)	-1.79 (-2.97, -1.36)
	70	0.74 (0.70-0.78)	-2.91 (-3.45, -2.40)	-2.72 (-3.22, -2.24)
	75	0.77 (0.74-0.81)	-2.53 (-2.91, -2.04)	-2.36 (-2.72, -1.90)
Cardiac risk group	Age	HR cardiac risk (95% CI)	Changes in effective age (Men) Δ (95% CI) (years)	Changes in effective age (Women) Δ (95% CI) (years)
QRISK2 10 – 19%	70	0.80 (0.77 - 0.83)	-2.16 (-2.53, -1.80)	-2.01 (-2.36, -1.68)
	75	0.87 (0.80 - 0.94)	-1.35 (-2.16, -0.60)	-1.26 (-2.01, -0.56)
QRISK2 \geq 20%	70	1	0	0
	75	1	0	0
Heart attack	70	1.50 (1.42 - 1.59)	3.92 (3.39, 4.48)	3.66 (3.17, 4.19)
	75	1.45 (1.38 - 1.53)	3.59 (3.11, 4.11)	3.35 (2.91, 3.84)

Table 1: Hazard ratios (HR) of statins and of cardiac risk groups on mortality, and the resulting changes in effective age for men and women obtained by fitting the Gompertz $G(a, b)$ distribution to the ONS period life table centered at 2010. The b parameters are 0.1034 for men and 0.1108 for women.

sex	TS	age	LE_{ONS}	LE_G	e_{01}	e_{02}	e_{03}	e_{11}	e_{12}	e_{13}
F	1	70	17.7	17.67	17.92(17.8,18.04)	16.45(16.33,16.56)	13.90(13.79,14.00)	19.10(18.90,19.32)	17.59(17.40,17.80)	15.77(15.55,16.02)
F	2	70	17.4	17.39	17.72(17.6,17.85)	16.21(16.09,16.33)	13.61(13.50,13.72)	18.94(18.74,19.15)	17.39(17.19,17.60)	15.52(15.30,15.77)
F	3	70	16.8	16.82	17.30(17.16,17.43)	15.76(15.63,15.89)	13.12(13.00,13.24)	18.54(18.35,18.76)	16.96(16.77,17.16)	15.06(14.84,15.30)
F	4	70	16.2	16.21	16.89(16.72,17.05)	15.29(15.13,15.45)	12.58(12.44,12.72)	18.18(18.00,18.38)	16.53(16.36,16.72)	14.57(14.36,14.80)
F	5	70	15.5	15.59	16.56(16.36,16.76)	14.93(14.73,15.12)	12.17(12.00,12.34)	17.89(17.74,18.06)	16.20(16.05,16.36)	14.19(14.01,14.39)
M	1	70	15.6	15.67	16.75(16.59,16.92)	15.28(15.12,15.44)	12.75(12.60,12.90)	17.94(17.79,18.11)	16.43(16.28,16.59)	14.61(14.43,14.80)
M	2	70	15.2	15.21	16.40(16.23,16.57)	14.91(14.74,15.07)	12.35(12.20,12.50)	17.62(17.46,17.78)	16.07(15.92,16.23)	14.23(14.05,14.42)
M	3	70	14.4	14.51	15.83(15.64,16.01)	14.30(14.12,14.47)	11.72(11.56,11.88)	17.07(16.92,17.22)	15.49(15.34,15.64)	13.61(13.44,13.80)
M	4	70	13.7	13.78	15.21(15.00,15.41)	13.64(13.44,13.83)	11.02(10.85,11.20)	16.49(16.35,16.64)	14.86(14.73,15.00)	12.94(12.78,13.11)
M	5	70	13.0	13.09	14.65(14.44,14.86)	13.04(12.84,13.23)	10.37(10.20,10.54)	15.99(15.84,16.15)	14.29(14.15,14.44)	12.32(12.14,12.50)
F	1	75	13.7	13.61	14.13(14.04,14.26)	13.29(13.20,13.41)	11.17(11.08,11.28)	15.37(15.19,15.50)	14.50(14.33,14.63)	12.64(12.47,12.79)
F	2	75	13.4	13.43	14.00(13.90,14.13)	13.14(13.04,13.27)	10.98(10.89,11.10)	15.26(15.09,15.40)	14.37(14.20,14.50)	12.48(12.30,12.62)
F	3	75	13.0	13.00	13.58(13.46,13.73)	12.71(12.60,12.86)	10.54(10.44,10.67)	14.86(14.70,14.98)	13.95(13.80,14.08)	12.04(11.88,12.17)
F	4	75	12.6	12.59	13.26(13.13,13.42)	12.37(12.25,12.52)	10.15(10.04,10.29)	14.58(14.43,14.71)	13.65(13.50,13.77)	11.68(11.53,11.81)
F	5	75	12.2	12.15	12.83(12.68,13.02)	11.93(11.79,12.11)	9.70(9.57,9.86)	14.18(14.04,14.28)	13.22(13.09,13.33)	11.24(11.10,11.35)
M	1	75	12.0	11.96		11.87(11.75,12.03)	9.83(9.72,9.97)		13.04(12.92,13.14)	11.24(11.11,11.35)
M	2	75	11.6	11.62		11.53(11.40,11.70)	9.48(9.36,9.64)		12.71(12.60,12.80)	10.90(10.78,11.00)
M	3	75	11.1	11.12		11.07(10.94,11.24)	9.01(8.90,9.17)		12.26(12.15,12.35)	10.43(10.31,10.53)
M	4	75	10.5	10.51		10.51(10.38,10.68)	8.45(8.34,8.60)		11.72(11.60,11.82)	9.87(9.75,9.97)
M	5	75	10.1	10.11		10.08(9.92,10.28)	8.00(7.86,8.17)		11.32(11.23,11.39)	9.43(9.33,9.51)

Table 2: Life expectancies at ages 70 and 75 and their 95% confidence intervals by sex and Townsend (TS) deprivation score quintile (1 = least and 5 = most) for people with and without statins, for three cardiac risk groups (1 : 10 – 19%, 2 : $\geq 20\%$, 3 : CVD). e_{ij} denotes life expectancy in cardiac risk group j without/with statins ($i = 0$ or 1, respectively). For instance, e_{01} is the calculated life expectancy for people without statin ($i = 0$) in cardiac risk group 1 (QRISK2 10 – 19%).

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Appendix

A.1 Supplementary tables

		Age 70			Age 75		
Sex	Townsend deprivation quintile	QRISK2 10 – 19%	QRISK2 ≥ 20%	CVD	QRISK2 10 – 19%	QRISK2 ≥ 20%	CVD
Women	1st (least)	72%	18%	9%	13%	73%	14%
	2nd	68%	22%	10%	10%	74%	15%
	3rd	60%	28%	12%	8%	74%	18%
	4th	50%	34%	16%	4%	75%	21%
	5th (most)	35%	42%	23%	2%	73%	25%
	Total	62%	25%	12%	9%	74%	17%
Men	1st (least)	16%	65%	19%	0%	72%	28%
	2nd	12%	68%	21%	0%	69%	31%
	3rd	9%	66%	25%	0%	67%	33%
	4th	5%	66%	29%	0%	65%	35%
	5th (most)	1%	69%	29%	0%	60%	40%
	Total	11%	66%	23%	0%	68%	32%

Table A.1: Distribution of cardiac risk by sex, age, and deprivation in 2010, from Gitsels et al. [2016].

		Age 70			Age 75		
Sex	Townsend deprivation quintile	QRISK2 10 – 19%	QRISK2 ≥ 20%	CVD	QRISK2 10 – 19%	QRISK2 ≥ 20%	CVD
Women	1st (least)	25%	57%	82%	13%	41%	84%
	2nd	23%	56%	87%	13%	41%	84%
	3rd	22%	54%	88%	15%	45%	88%
	4th	24%	56%	86%	9%	45%	86%
	5th (most)	25%	59%	88%	6%	50%	90%
	Total	23%	56%	86%	13%	43%	86%
Men	1st (least)	19%	46%	91%	NA	42%	90%
	2nd	12%	46%	89%	NA	48%	90%
	3rd	18%	44%	90%	NA	45%	90%
	4th	30%	44%	92%	NA	42%	89%
	5th (most)	27%	43%	88%	NA	53%	91%
	Total	18%	45%	90%	NA	45%	90%

Table A.2: Rate of statin prescription by sex, age, deprivation, and cardiac risk in 2010, from Gitsels et al. [2016].

sex	TS	age	c	a	b	a_0	a_L	a_U	e_{ONS}	$e_{G(a,b)}$
F	1	70	0.4	-13.21	0.12	-13.03	-13.01	-13.05	17.7	17.67
F	2	70	0.4	-12.69	0.12	-12.52	-12.50	-12.54	17.4	17.39
F	3	70	0.4	-12.14	0.11	-11.98	-11.96	-12.00	16.8	16.82
F	4	70	0.4	-11.32	0.10	-11.19	-11.16	-11.21	16.2	16.21
F	5	70	0.4	-10.71	0.10	-10.62	-10.59	-10.64	15.5	15.59
M	1	70	0.5	-12.46	0.12	-12.40	-12.37	-12.42	15.6	15.67
M	2	70	0.5	-11.97	0.11	-11.92	-11.90	-11.95	15.2	15.21
M	3	70	0.5	-11.31	0.11	-11.28	-11.25	-11.31	14.4	14.51
M	4	70	0.5	-10.45	0.10	-10.43	-10.40	-10.46	13.7	13.78
M	5	70	0.5	-9.53	0.09	-9.52	-9.50	-9.55	13.0	13.09
F	1	75	0.2	-13.19	0.12	-13.14	-13.12	-13.16	13.7	13.61
F	2	75	0.2	-12.67	0.12	-12.62	-12.61	-12.64	13.4	13.43
F	3	75	0.2	-12.11	0.11	-12.07	-12.05	-12.09	13.0	13.00
F	4	75	0.2	-11.30	0.10	-11.26	-11.24	-11.29	12.6	12.59
F	5	75	0.2	-10.69	0.10	-10.65	-10.63	-10.68	12.2	12.15
M	1	75	0.4	-12.45	0.12	-12.43	-12.41	-12.46	12.0	11.96
M	2	75	0.4	-11.96	0.11	-11.94	-11.92	-11.97	11.6	11.62
M	3	75	0.4	-11.30	0.11	-11.29	-11.27	-11.32	11.1	11.12
M	4	75	0.2	-10.42	0.10	-10.42	-10.40	-10.45	10.5	10.51
M	5	75	0.2	-9.51	0.09	-9.50	-9.48	-9.53	10.1	10.11

Table A.3: TS, Townsend deprivation quintile with 1 =least and 5 =most. Parameters a and b and the age correction c for the Gompertz distributions $G(a, b)$ fitted to ONS period life tables centered at 2010, and the resulting life expectancy values $e_{G(a,b)}$ compared with the ONS life expectancy e_{ONS} . Also the a_0 values and their 95% confidence limits (a_L and a_U) obtained by solving Equation (2).

sex	T5	age	$e_{11} - e_{01}$	$e_{12} - e_{02}$	$e_{13} - e_{03}$	$e_1 - e_0$	$e_1 - e_{ONS}$	$e_{ONS} - e_0$
F	1	70	1.18(0.86,1.52)	1.14(0.84,1.47)	1.87(1.55,2.23)	1.23(0.92,1.56)	0.84(0.64,1.06)	0.39(0.28,0.50)
F	2	70	1.22(0.89,1.55)	1.18(0.86,1.51)	1.91(1.58,2.27)	1.26(0.94,1.60)	0.87(0.67,1.09)	0.39(0.27,0.51)
F	3	70	1.24(0.92,1.60)	1.20(0.88,1.53)	1.94(1.60,2.30)	1.30(0.97,1.64)	0.91(0.71,1.12)	0.39(0.26,0.52)
F	4	70	1.29(0.95,1.66)	1.24(0.91,1.59)	1.99(1.64,2.36)	1.36(1.02,1.72)	0.88(0.70,1.08)	0.48(0.32,0.64)
F	5	70	1.33(0.98,1.70)	1.27(0.93,1.63)	2.02(1.67,2.39)	1.42(1.08,1.78)	0.88(0.72,1.04)	0.54(0.36,0.74)
M	1	70	1.19(0.87,1.52)	1.15(0.84,1.47)	1.86(1.53,2.20)	1.27(0.96,1.60)	0.74(0.59,0.91)	0.53(0.37,0.69)
M	2	70	1.22(0.89,1.55)	1.16(0.85,1.49)	1.88(1.55,2.22)	1.30(0.99,1.63)	0.69(0.54,0.86)	0.61(0.45,0.77)
M	3	70	1.24(0.91,1.58)	1.19(0.87,1.52)	1.89(1.56,2.24)	1.34(1.02,1.68)	0.79(0.64,0.95)	0.55(0.38,0.73)
M	4	70	1.28(0.94,1.64)	1.22(0.90,1.56)	1.92(1.58,2.26)	1.38(1.06,1.72)	0.72(0.58,0.87)	0.66(0.48,0.85)
M	5	70	1.34(0.98,1.71)	1.25(0.92,1.60)	1.95(1.60,2.30)	1.40(1.07,1.75)	0.77(0.62,0.93)	0.63(0.45,0.82)
F	1	75	1.24(0.93,1.46)	1.21(0.92,1.43)	1.47(1.19,1.71)	1.23(0.94,1.46)	0.66(0.49,0.80)	0.57(0.45,0.66)
F	2	75	1.26(0.96,1.50)	1.23(0.93,1.46)	1.50(1.20,1.73)	1.26(0.97,1.49)	0.79(0.62,0.92)	0.47(0.35,0.57)
F	3	75	1.28(0.97,1.52)	1.24(0.94,1.48)	1.50(1.21,1.73)	1.28(0.98,1.52)	0.70(0.55,0.83)	0.58(0.43,0.69)
F	4	75	1.32(1.01,1.58)	1.28(0.98,1.52)	1.53(1.24,1.77)	1.32(1.01,1.55)	0.70(0.55,0.82)	0.62(0.46,0.73)
F	5	75	1.35(1.02,1.60)	1.29(0.98,1.54)	1.54(1.24,1.78)	1.33(1.03,1.57)	0.58(0.45,0.69)	0.75(0.58,0.88)
M	1	75		1.17(0.89,1.39)	1.41(1.14,1.63)	1.22(0.95,1.43)	0.56(0.44,0.66)	0.66(0.51,0.77)
M	2	75		1.18(0.90,1.40)	1.42(1.14,1.64)	1.23(0.96,1.45)	0.58(0.47,0.67)	0.65(0.49,0.78)
M	3	75		1.19(0.91,1.41)	1.42(1.14,1.63)	1.24(0.96,1.46)	0.60(0.48,0.69)	0.64(0.48,0.77)
M	4	75		1.21(0.92,1.44)	1.42(1.15,1.63)	1.25(0.97,1.46)	0.63(0.51,0.72)	0.62(0.46,0.74)
M	5	75		1.24(0.95,1.47)	1.43(1.16,1.65)	1.26(0.98,1.49)	0.53(0.44,0.61)	0.73(0.54,0.88)

Table A.4: T5, Townsend deprivation quintile with 1 =least and 5 =most. Difference in life expectancy at ages 70 and 75 for people with and without statins, for three cardiac risk groups (1 : 10 – 19%, 2 : \geq 20%, 3 : *CVD*.) e_{ij} denotes life expectancy in cardiac risk group j without/with statins ($i = 0$ or 1, respectively.)

A.2 R procedure to implement life expectancy calculations for the Cox-Gompertz model

```
#####description #####
#required packages in R: MASS, expint
# qx- probabilities that someone aged x will die before
      age (x+1) (a vector of length L+1)
# age_range-range of ages in the format x:x+L for fitting
      a Gompertz distribution with estimated parameters a
      and b to qx values.
# age_correction - continuity correction for discrete age
      intervals, the default value is 0.5.
# age - the age of interest for life expectancy
      calculation
# alpha1 - hazard ratios of treatment on mortality in
      each of J risk group (a vector of length J)
# beta - the hazard ratios of J risk groups on mortality
      (a vector of length J)
# p - prevalences of treatment prescription at age of
      interest (a vector of length J)
# f - risk groups prevalences at the age of interest (a
      vector of length J)
# OUTPUT:
# LE0 and LE1 - vectors of length J of life expectancies
      without/with treatment for each risk group.

life_expectancy<-
function(qx, age_range, age, alpha1, beta, p, f, age_correction
      =0.5){
  suppressWarnings(require(MASS))
```



```

age_range<-age_range+age_correction
rlm_model = rlm(log(qx)~age_range)
a<-rlm_model$coefficients [[1]]
b<-rlm_model$coefficients [[2]]
#
#####

component_survival_function<-function(mu,b,a,age,p,f,
  alpha1,beta)
{
exp(-exp(a)/b*(exp(b*age)-1))-
sum(f*(1-p)*exp(-exp(mu+beta)/b*(exp(b*age)-1))+
f*p*exp(-exp(mu+alpha1+beta)/b*(exp(b*age)-1)))/sum(f)
}
#
#####

ll=-1000
uu=0
mu<-uniroot(component_survival_function,
c(ll,uu),tol=0.0000001,
b=b,a=a,age=age,
p=p,f=f,
alpha1=alpha1,
beta=beta) [[1]]
#
#####

a0<-mu+beta
a1<-mu+alpha1+beta
#
#####

```

```

LE<-function(a,b,age){
  suppressWarnings(require(expint))
  LE<-(1/b)*exp(exp(a)/b)*expint_E1(b^(-1)*exp(a+b*age))/
  exp(-exp(a)*(exp(b*age)-1)/b)
  return(LE)
}
#calculation of life expectancies using Gompertz
  distribution
LE0<-LE(a0,b,age)
LE1<-LE(a1,b,age)
#
#####

column_names<-rep(NA, times=length(p))
for(i in 1:length(p)){
  column_names[i]=paste("_Risk_group",i,sep = "")
}
output<-rbind(rep(age, times=length(p)),LE0)
output<-rbind(output,LE1)
colnames(output)<-column_names
rownames(output) <- c("age","LE0","LE1")
return(output)
}
#
#####

##Example##
##Data from ONS for year 2010, Townsend score quintile 1,
#Females, age = 70
qx<-c(0.00370, 0.00401, 0.00421, 0.00513, 0.00527,
      0.00618,

```

```

0.00650, 0.00716, 0.00798,
  0.00912,0.00978,0.01086,0.01255,
0.01324,0.01587,0.01694,0.01988,0.02233,0.02638, 0.03073,
0.03446, 0.03974, 0.04714,0.05304, 0.06033, 0.07061,
0.07943, 0.09330, 0.10489, 0.12199, 1.00000)
age_range<-60:90
f<-c(0.72,0.18,0.09) # three cardiac risk groups
p<-c(0.25,0.57,0.82) # statin prescription rates
alpha1<-log(c(0.84,0.84,0.74))
beta<-log(c(0.8,1,1.50))
age=70
age_correction=0.5
res<-life_expectancy(qx,age_range,age,alpha1,beta,p,f,age
  _correction)
#      Risk group1 Risk group2 Risk group3
#age      70.00000    70.00000    70.00000
#LE0      18.00376    16.52738    13.9726
#LE1      19.18810    17.67704    15.8533

```