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Use of administrative health databases for modelling longevity improvement

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The **'Use of Big Health and Actuarial Data for understanding Longevity and Morbidity Risks'** research programme is being funded by the Actuarial Research Centre.

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www.actuaries.org.uk/arc

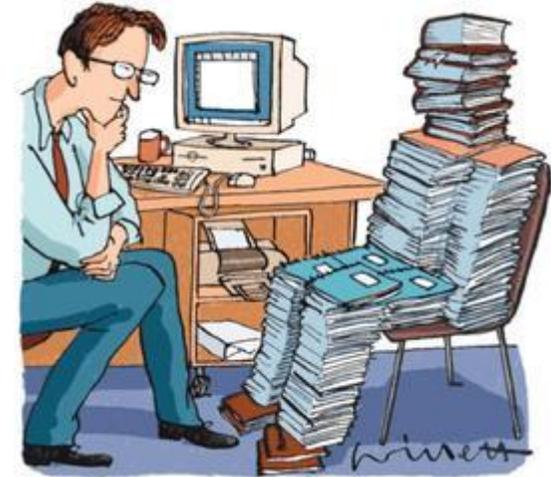
Primary care data

- Our research uses The Health Improvement Network (THIN) primary care data to develop statistical models of longevity/morbidity.
- The advantage of using individual-level medical data is that it is possible to model both the uptake of medical treatment and the effect of that treatment on longevity conditional on the individual sociodemographic and health factors instead of the aggregated profile.
- Survival models, usually the Cox's regression, are fitted to individual level data.
- The conclusions are generalisable to the general population.



The Health Improvement Network (THIN) data

- Anonymised electronic primary care medical records (Vision)
- Data collection began in 2003 using Read codes
- 11 million patients, 3.7 million active patients
- 562 general practices, covering 6.2% of the UK population
- Diagnoses, prescriptions, consultations, postcode deprivation



Subset of THIN selected for our research:

- All patients born before 1960 and followed to 01.01.2017, this includes 3.5 million patients
- Social economic status variables such as Index of Multiple Deprivation (IMD), Townsend and Mosaic
- IMD: income, employment, health, education, crime, housing
- Townsend: employment, car ownership, home ownership, household overcrowding
- Mosaic: consumer classification based on demographics, lifestyles and behaviour of a person



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Target conditions and interventions

The screenshot displays a website interface for 'Big Health Actuarial Data'. At the top, there is a navigation menu with links for 'Home', 'Project Description', 'The Team', 'Publications', 'Press', and 'Contact us'. Below the menu, a breadcrumb trail reads 'Big Actuarial Health Data > Home > Current research'. The main content area features a grid of seven image-based tiles, each representing a specific medical condition or intervention:

- Hypertension**: Image of a doctor examining a patient's blood pressure.
- Myocardial infarction**: Image of a computer monitor displaying a heart rate graph.
- Statins**: Image of several vials in a laboratory rack.
- Hormone replacement therapy**: Image of a doctor in blue gloves holding a syringe.
- Stroke**: Image of a human torso model on a table in a laboratory setting.
- Diabetes**: Image of hands using a glucometer to test a finger.
- Hip replacement**: Image of a doctor showing a hip X-ray on a tablet to another professional.



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Hazard aka “force of mortality” and “mortality intensity”

- The type of regression model typically used in survival analysis in medicine is the Cox’s proportional hazards regression model.
- The Cox’s model estimates the hazard $\mu_i(x)$ for subject i for time x by multiplying the baseline hazard function $\mu_0(x)$ by the subject’s risk score r_i as

$$\mu_i(x, \beta, Z_i) = \mu_0(x) r_i(\beta, Z_i) = \mu_0(x) e^{\beta Z_i}$$

- The risk factors Z have a log-linear contribution to the force of mortality which does not depend on time x .



Hazard ratio (HR)

- Taking a ratio of the hazard functions for two subjects i and j who differ in one risk factor z (with the values z_0 and z_1 , respectively) but not in the other risk factors,

$$\text{HR}(x, \beta, Z) = \frac{\mu_i(x, \beta, Z_i)}{\mu_j(x, \beta, Z_j)} = \frac{\mu_0(x) e^{\beta Z_i}}{\mu_0(x) e^{\beta Z_j}} = \frac{e^{\beta z z_1}}{e^{\beta z z_0}} = e^{\beta z (z_0 - z_1)}.$$

- This means that the baseline hazard $\mu_0(x)$ does not have to be specified and the hazard ratio $e^{\beta z (z_0 - z_1)}$ is constant with respect to time x .
- Because of this, the Cox's model does not make any assumptions about the shape of the baseline hazard.
- $e^{\beta z (z_0 - z_1)}$ is an adjusted HR, i.e. **all other risks are already accounted for by the model.**



Landmark analysis of the effect of statins

The research objective is to dynamically predict the survival benefits associated with statin therapy over time.

Data: 110,000 patients who turned 60 between 1990 and 2000, were neither diagnosed with cardiovascular disease nor prescribed statins, and were residential in England or Wales and followed up until January 2017.

Analysis: the medical history was updated every half a year. Landmark analyses were carried out by fitting adjusted Cox's proportional hazards regressions of the hazard of all-cause mortality associated with current statin prescription at each landmark from age 60 to 85 (51 time points).

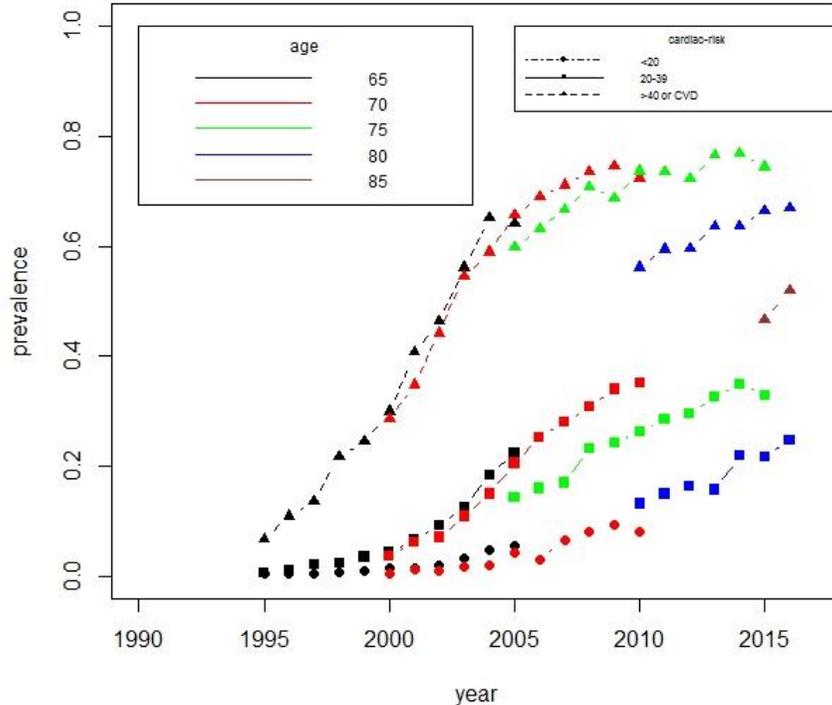


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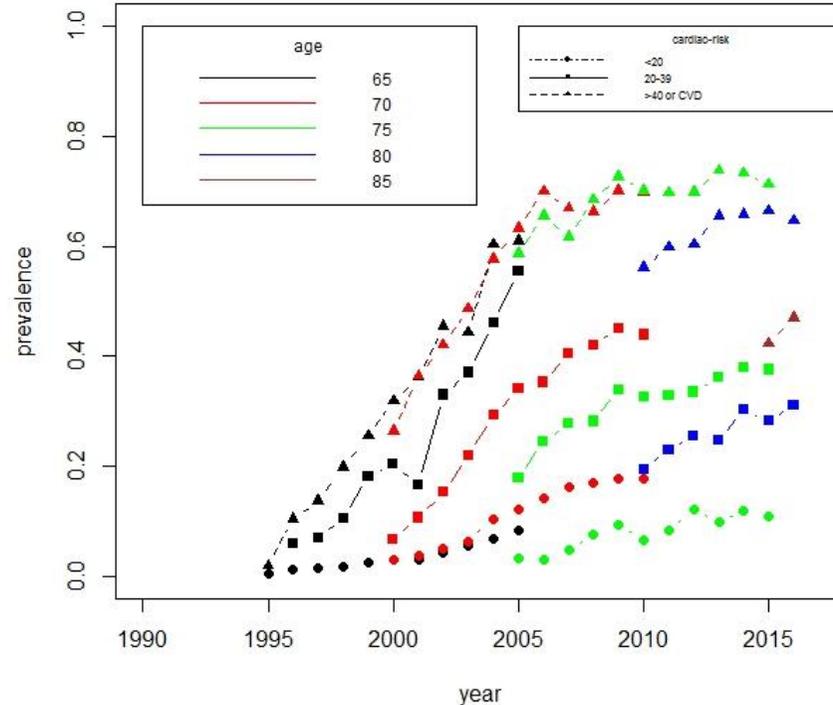
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Prevalence of statin prescription

statin prescription in male patients



statin prescription in female patients



The median age of the statin prescription was at 70 (IQR 66-74).
The prevalence of current statin prescription differed by cardiac risk, sex, age and study population.



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The survival effect of statins was adjusted for:

- Cardiac risk at three levels: low (QRISK2 < 20%), medium (QRISK2 of 20-39%), and high (QRISK2 \geq 40% or CVD diagnosis).
- sex, year of birth, Townsend deprivation quintile, chronic kidney disease, diabetes, treated hypertension, hypercholesterolaemia, aspirin, BMI, alcohol consumer status, smoking status and general practice.



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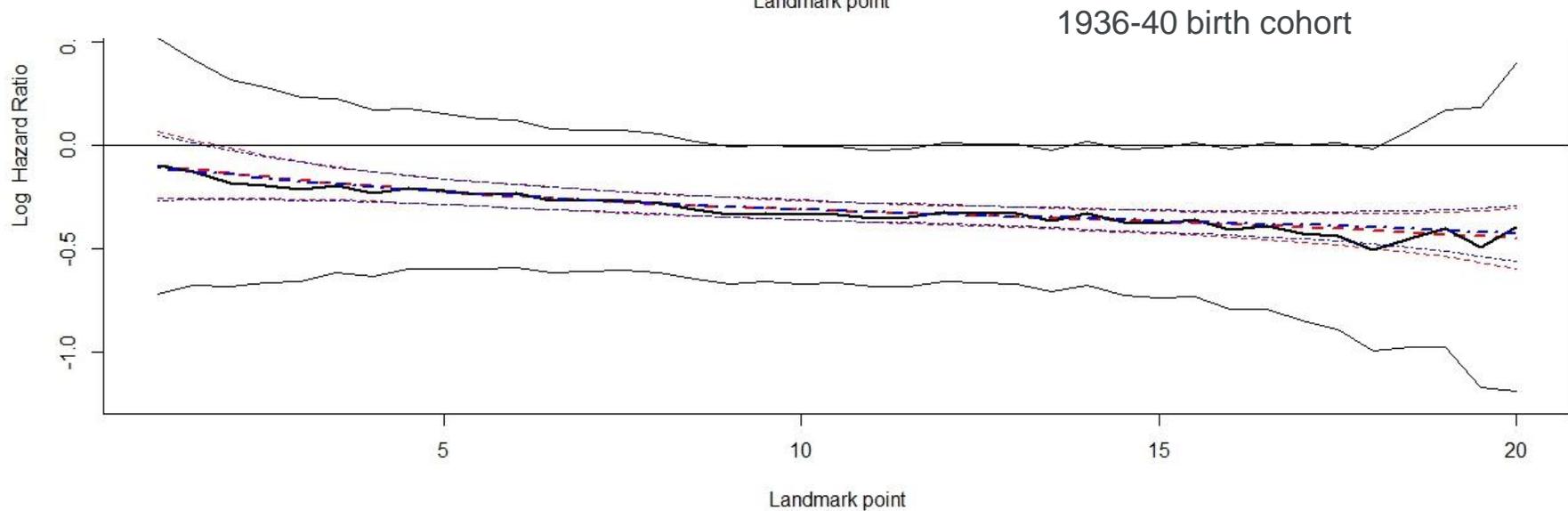
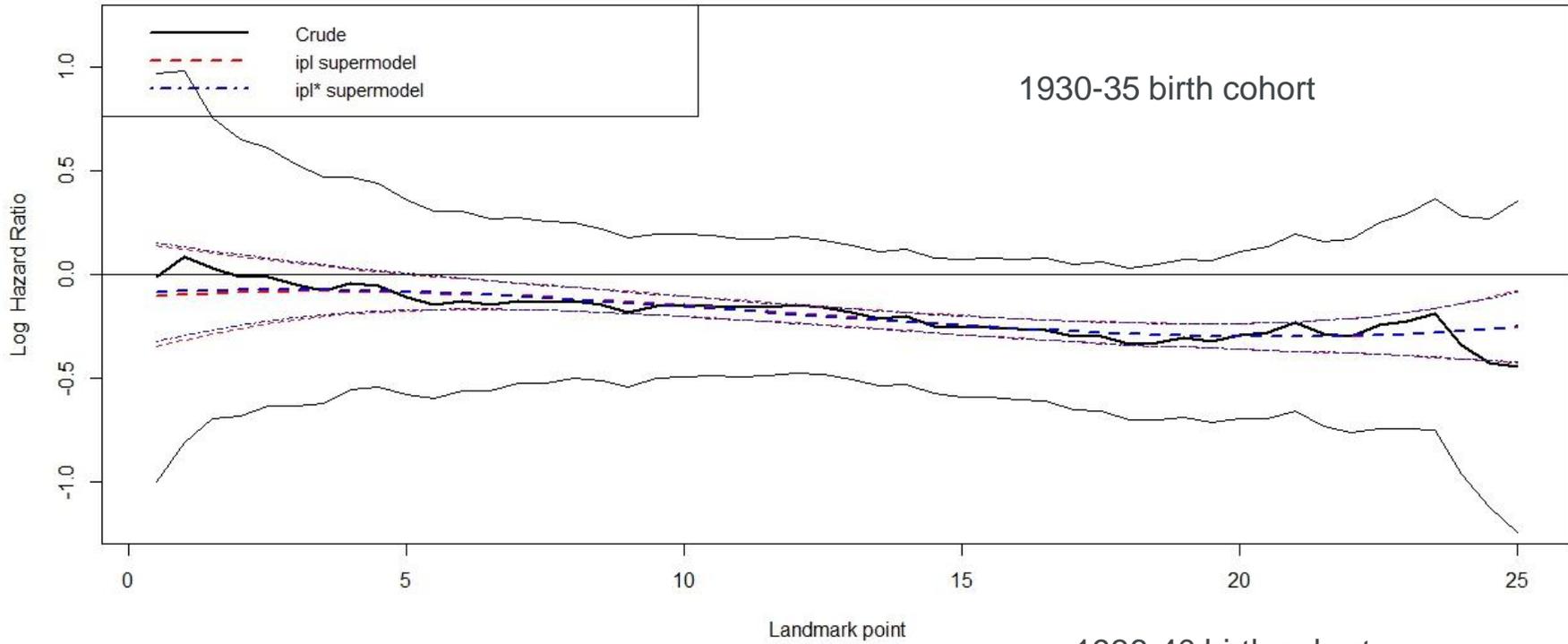
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The four stages of the modelling process

- A Cox's model was fitted on complete cases at baseline age to inform the imputation model. Both models included all medical history if prevalent.
- Cox's models were fitted on the imputed datasets at ages 65, 70, 75, 80 and 85 to inform the final landmark model. These models included all medical history and tested for interactions of statin prescription with sex, year of birth and cardiac risk and the interactions of the previous stage.
- The final, fully adjusted, Cox's landmark models were fitted at 10 imputed datasets. The landmarking was smoothed with an integrated partial log-likelihood (IPL).
- Ten landmark models pooled using Rubin's rules.



Adjusted hazard of all-cause mortality associated with current statin prescription.



More efficient drugs?

www.pulsetoday.co.uk/gps-set-for-mass-drug-switch-to-atorvastatin-after-analysis-shows-price-could-fall-by-95/13482969.article

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PULSE At the heart of general practice since 1960

OPINION 'After about 20 patients, there is not an iota of empathy left'

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GPs set for mass drug switch to atorvastatin after analysis shows price could fall by 95%

22 February 2012

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f SHARE ON FACEBOOK Exclusive GPs are set to be enrolled in schemes to switch patients en masse to atorvastatin in the wake of an analysis for the Government's

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Reduction in low-density lipoprotein cholesterol

Statins are grouped by NICE into three different intensity categories according to the percentage reduction in LDL cholesterol

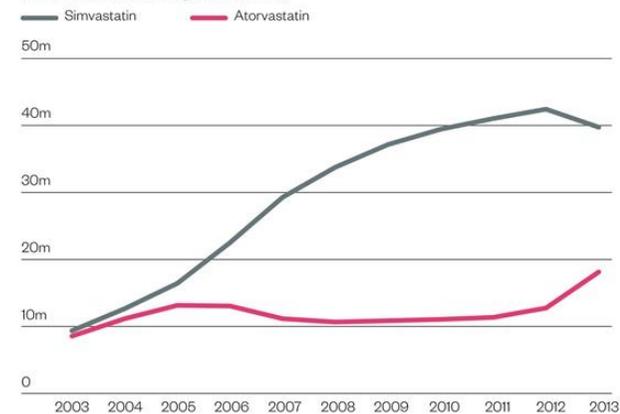
- 20% to 30%: low-intensity statin
- 31%-40%: medium-intensity statin
- Above 40%: high-intensity statin

	5mg	10mg	20mg	40mg	80mg
Fluvastatin	—	—	●	●	●
Pravastatin	—	●	●	●	—
Simvastatin	—	●	●	●	●
Atorvastatin	—	●	●	●	●
Rosuvastatin	●	●	●	●	—

Source: National Institute for Health and Care Excellence

Atorvastatin vs simvastatin

Items dispensed in England (millions)



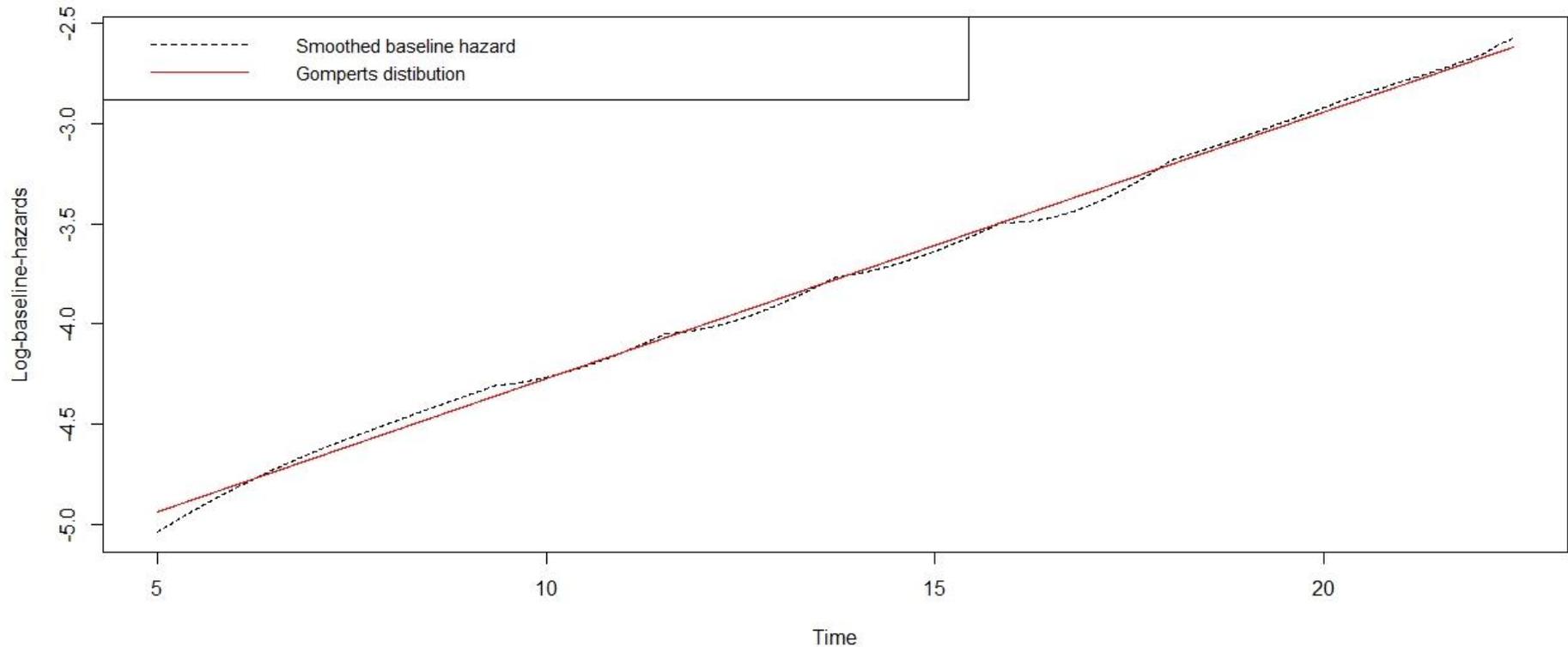
Source: Health and Social Care Information Centre



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Baseline hazard in the landmark model

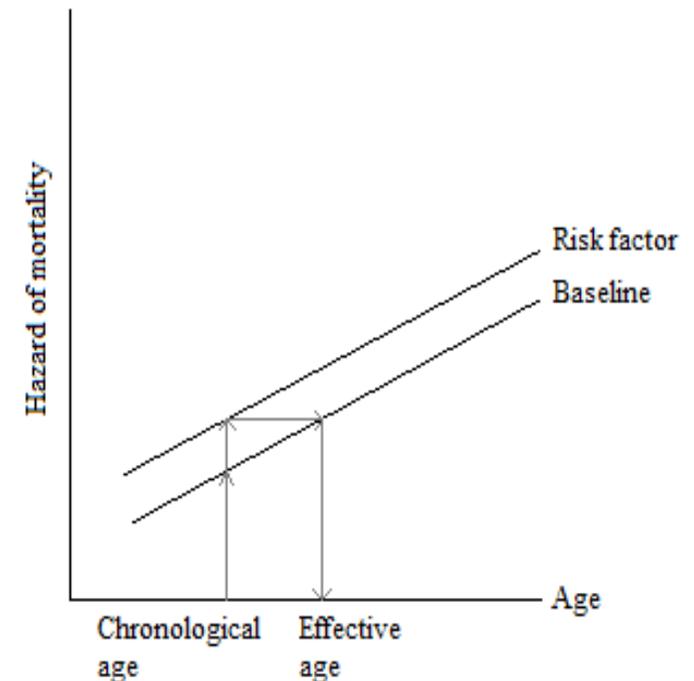


What does HR mean for an individual

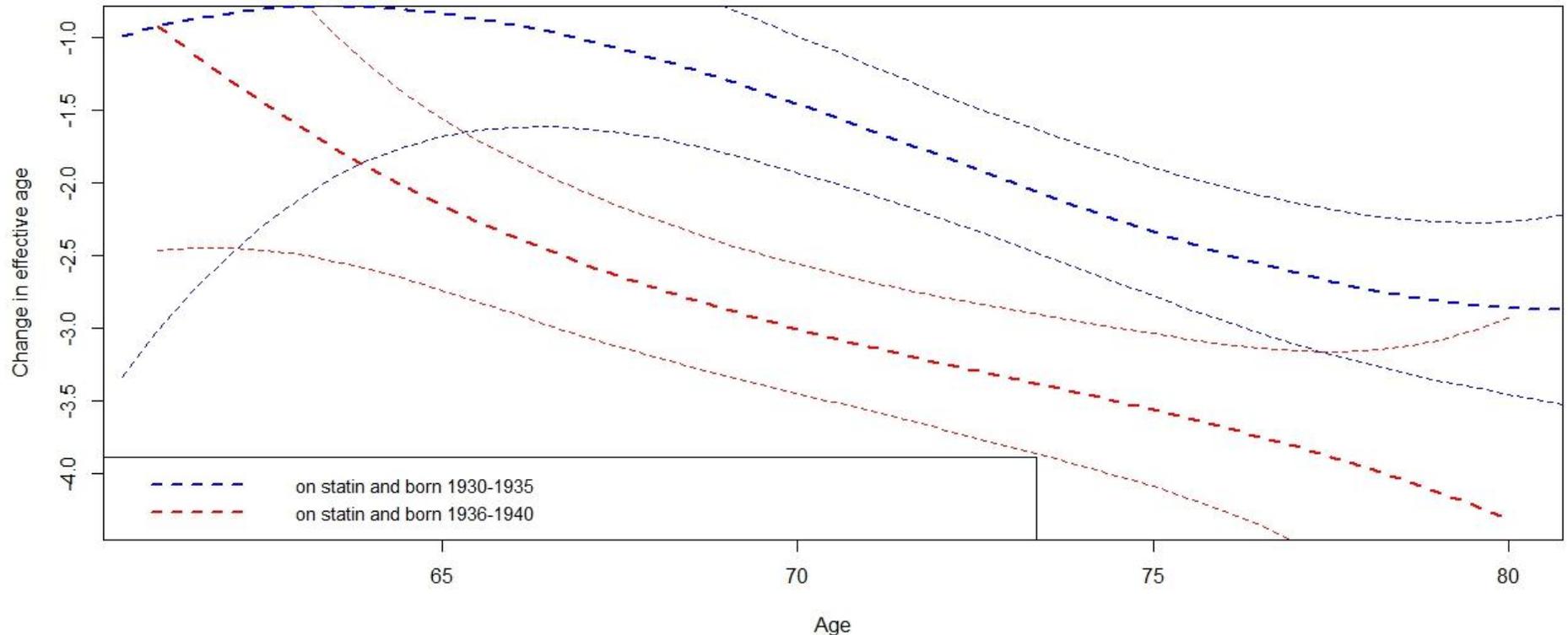
- Using Gompertz law, the increase in annual hazard of mortality associated with ageing one year is approximately constant between ages 50 and 90.
- For England and Wales in 2010-2012, the increase in the hazard between those ages was approximately 1.1 per year.
- A HR can be translated to the numbers of years gained in effective age as

$$\log \text{HR} / \log (1.1) \approx 10 * \log(\text{HR}).$$

[Brenner, 1993; Spiegelhalter, 2016]



Uptake of statins and changes in effective age



The log HRs and, therefore, effective age lines are cubic polynomials of age with estimated coefficients.



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Changes in population life expectancy due to medical interventions

- Period life expectancy e_x at age x is a weighted average of component LEs, of people with different risk profiles, with the weights defined by the prevalence p of the risk factor of interest and/or the uptake of relevant intervention.
- Splitting the overall LE into these components allows to estimate hypothetical changes in life expectancy at the population level at different scenarios.



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Statins and increase in period life expectancy

In our previous study [Gitsels et al.(2016)] for YOB 1920-1940 followed up to 2010:

- Increase in individual LE due to statins was 1.12-1.24 years at ages 70 and 75;
- Statins contributed to 0.4-0.7 years increase in LE at ages 70-75 so far, with the largest improvements in 75 yo men from the most deprived areas;
- At 100% uptake, LE of women aged 70 or 75 would be increased by up to 0.8 or 0.7 years; and LE for men aged 70 or 75 would be increased by up to 0.6 or 0.7 years, most improvement possible in affluent areas.
- These results are about what we would expect from our older cohort (1930-1935). The younger cohort should have larger impact of statins on LE.
- Current prescription rate at age 85 is about 30% lower than in the younger ages.
- Given our landmark analysis results, we now believe that large changes in LE at older ages are possible if the elderly embrace statins.



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A gateway to global actuarial research

The Actuarial Research Centre (ARC) is the Institute and Faculty of Actuaries' (IFoA) network of actuarial researchers around the world.

The ARC seeks to deliver cutting-edge research programmes that address some of the significant, global challenges in actuarial science, through a partnership of the actuarial profession, the academic community and practitioners.

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Questions

Comments

The views expressed in this presentation are those of the presenter.



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