University of East Anglia

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How Medical Advances and Health Interventions Will Shape Future Longevity

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Quantifying Longevity Changes

- Medical advances are the major drivers in the longevity increase. But how to quantify this relationship?
- In medicine, Randomized Control Trials (RCTs) are considered to be the gold standard.
- The RCTs estimate the hazards of mortality estimated in a (selective) sample of people and summarised over the observed (limited) time period.
- New health interventions are usually based on these estimated hazards obtained from clinical trials. A lengthy lead time would be needed to observe their effect on population longevity.

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Our approach

- Our research uses The Health Improvement Network (THIN) primary care data, to develop statistical models of longevity.
- 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. Also generalisability to the general population.
- Next, the hazard ratios obtained from the survival models are translated into “effective age” changes in relevant subpopulations, and then aggregated into population life expectancy changes.

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Hazard ratio

- 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* at time *x* as $\mu_i(x, \beta, Z_i) = \mu_0(x)\, r_i(\beta, Z_i) = \mu_0(x) e^{\beta Z_i}$
- Taking a ratio of the hazard functions for two subjects *i* and *j* who differ in one risk factor *z* and not in the other risk factors,

$$\mu(x, \beta, Z) = \frac{\mu_i(x, \beta, Z_i)}{\mu_j(x, \beta, Z_j)} = \frac{\mu_0(x) e^{\beta Z_1}}{\mu_0(x) e^{\beta Z_0}} = \frac{e^{\beta_z z_1}}{e^{\beta_z z_0}} = e^{\beta_z (z_0 - z_1)}$$

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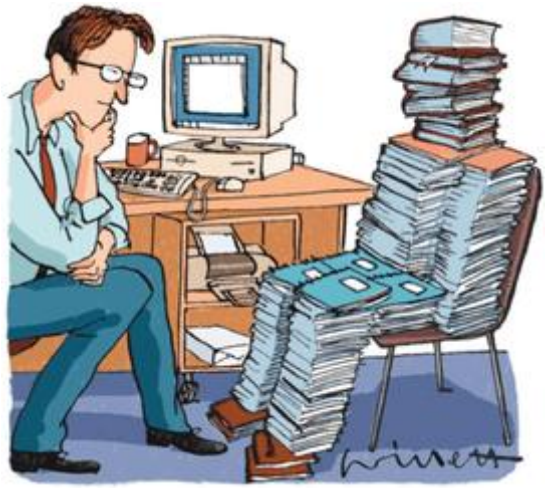
The Health Improvement Network (THIN) data

- 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 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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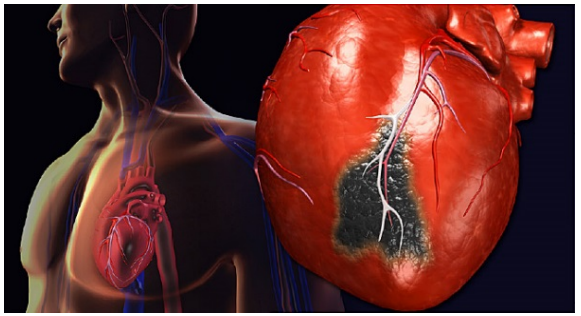
Example: Beta-Blockers after Acute Myocardial Infarction (AMI)

- Myocardial cell death due to prolonged ischaemia, a.k.a. heart attack.
- There are 188,000 hospital episodes attributed to heart attack in the UK each year: that's one around every three minutes.
- In the UK around 7 out of 10 people survive a heart attack.
- An estimated 915,000 people in the UK (640,000 men and 275,000 women) have survived an MI.



(British Heart Foundation, 2016)

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Research question

- What are the survival prospects associated with a history of a single or multiple acute myocardial infarctions in the general population at various ages and how were the survival prospects modified by recommended treatment?
- Gitsels LA, Kulinskaya E, Steel N Survival prospects after acute myocardial infarction in the UK: a matched cohort study 1987–2011. BMJ Open 2017;7:e013570. doi:10.1136/bmjopen-2016-013570.
- University of East Anglia's press release statement: https://www.uea.ac.uk/about/-/beta-blockers-offer-best-chance-of-increased-heart-attack-survival

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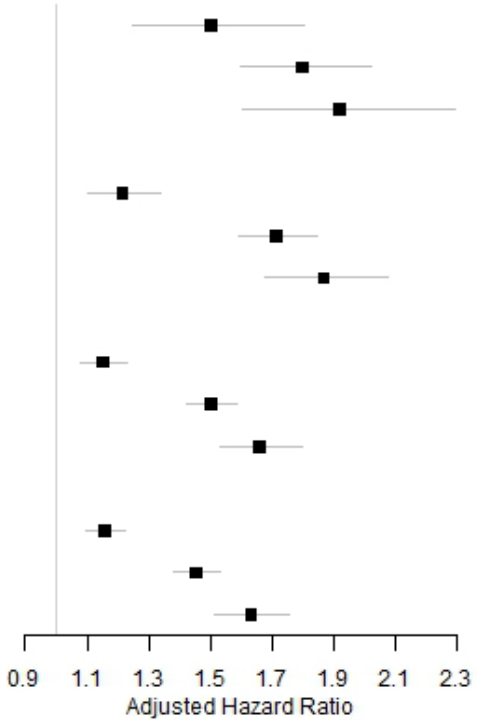
Survival prospects after AMI

Cohort	Ischaemic Heart Disease	Deaths (%per annum)	Adjusted HR (95%CI)
Age 60	No	1,843 (1.28)	
	Angina	165 (2.52)	1.50 (1.25-1.80)
	Single AMI	996 (2.56)	1.80 (1.60-2.02)
	Multiple AMIs	224 (2.89)	1.92 (1.60-2.29)
Age 65	No	5,180 (1.86)	
	Angina	602 (2.83)	1.21 (1.10-1.34)
	Single AMI	2,428 (3.19)	1.71 (1.59-1.84)
	Multiple AMIs	642 (3.81)	1.87 (1.68-2.07)
Age 70	No	9,264 (2.77)	
	Angina	1,293 (3.66)	1.15 (1.08-1.23)
	Single AMI	4,098 (4.38)	1.50 (1.42-1.59)
	Multiple AMIs	1,088 (5.14)	1.66 (1.53-1.80)
Age 75	No	10,686 (3.98)	
	Angina	1,988 (5.28)	1.16 (1.10-1.22)
	Single AMI	4,614 (6.02)	1.45 (1.38-1.53)
	Multiple AMIs	1,281 (7.22)	1.63 (1.51-1.76)



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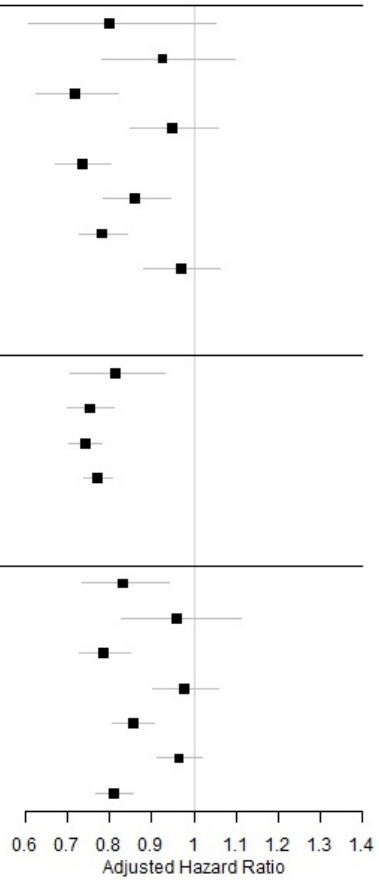
Survival prospects after AMI by treatments

Cohort	Coronary Revascularisation	Adjusted HR (95%CI)
Age 60	Follow-up<5yrs	0.80 (0.61-1.05)
	Follow-up>=5yrs	0.92 (0.78-1.10)
Age 65	Follow-up<5yrs	0.72 (0.63-0.82)
	Follow-up>=5yrs	0.95 (0.85-1.06)
Age 70	Follow-up<5yrs	0.73 (0.67-0.80)
	Follow-up>=5yrs	0.86 (0.78-0.94)
Age 75	Follow-up<5yrs	0.78 (0.73-0.84)
	Follow-up>=5yrs	0.97 (0.88-1.06)
	Statins	
Age 60	Yes	0.81 (0.71-0.93)
Age 65	Yes	0.75 (0.70-0.81)
Age 70	Yes	0.74 (0.70-0.78)
Age 75	Yes	0.77 (0.74-0.81)
	Beta blockers	
Age 60	Yes with AMI	0.83 (0.73-0.94)
	Yes without AMI	0.96 (0.83-1.11)
Age 65	Yes with AMI	0.79 (0.73-0.85)
	Yes without AMI	0.98 (0.90-1.06)
Age 70	Yes with AMI	0.85 (0.81-0.91)
	Yes without AMI	0.96 (0.91-1.02)
Age 75	Yes with AMI	0.81 (0.77-0.86)



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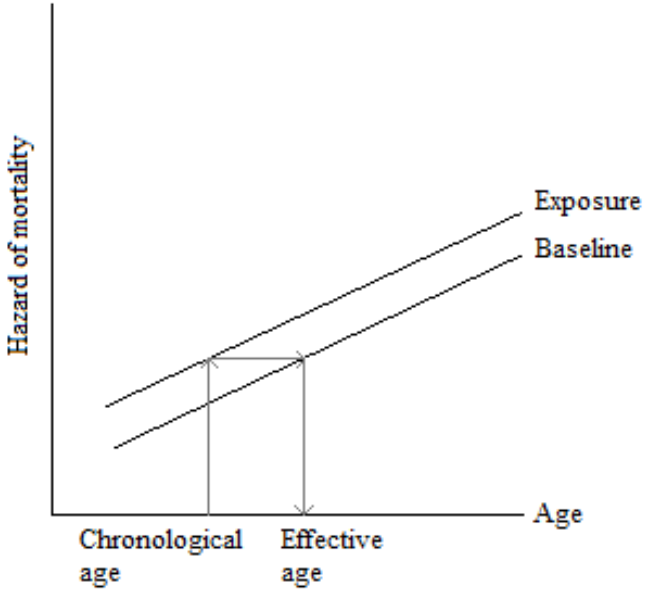
What does HR mean for longevity

- Using Gompertz law, the increase in annual hazard of mortality associated with ageing one year is approximately constant between ages 30 and 95
- For England and Wales in 2010-2012, the increase in the hazard between those ages was approximately 1.1.
- A HR can be translated to the numbers of years gained in effective age as

  log HR/ log (1.1)≈ 10*log(HR).

[Brenner, 1993; Spiegelhalter, 2016]



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How do beta-blockers change effective age

- The hazard of mortality associated with a history of one heart attack by the target ages translated to 3.7 to 5.8 years gain in age for a man and 3.4 to 5.4 years gain in age for a woman.
- The hazard of mortality associated with a prescription of beta blockers to a heart attack survivor translated to 1.6 to 2.3 years decrease in age for a man and 1.5 to 2.2 years decrease in age for a woman.
- Adding up the hazards: a male or female heart attack survivor who is prescribed beta blockers gained 1.6 to 3.9 years in age or 1.5 to 3.7 years in age, respectively

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Translating to population life expectancy

- Take a period life table
- Calculate effective age changes due to a health intervention in relevant subpopulations [risk group, age, sex, deprivation status]
- Take into account uptake rates in these subgroups
- Population LE is the weighted average of the LE in these subgroups

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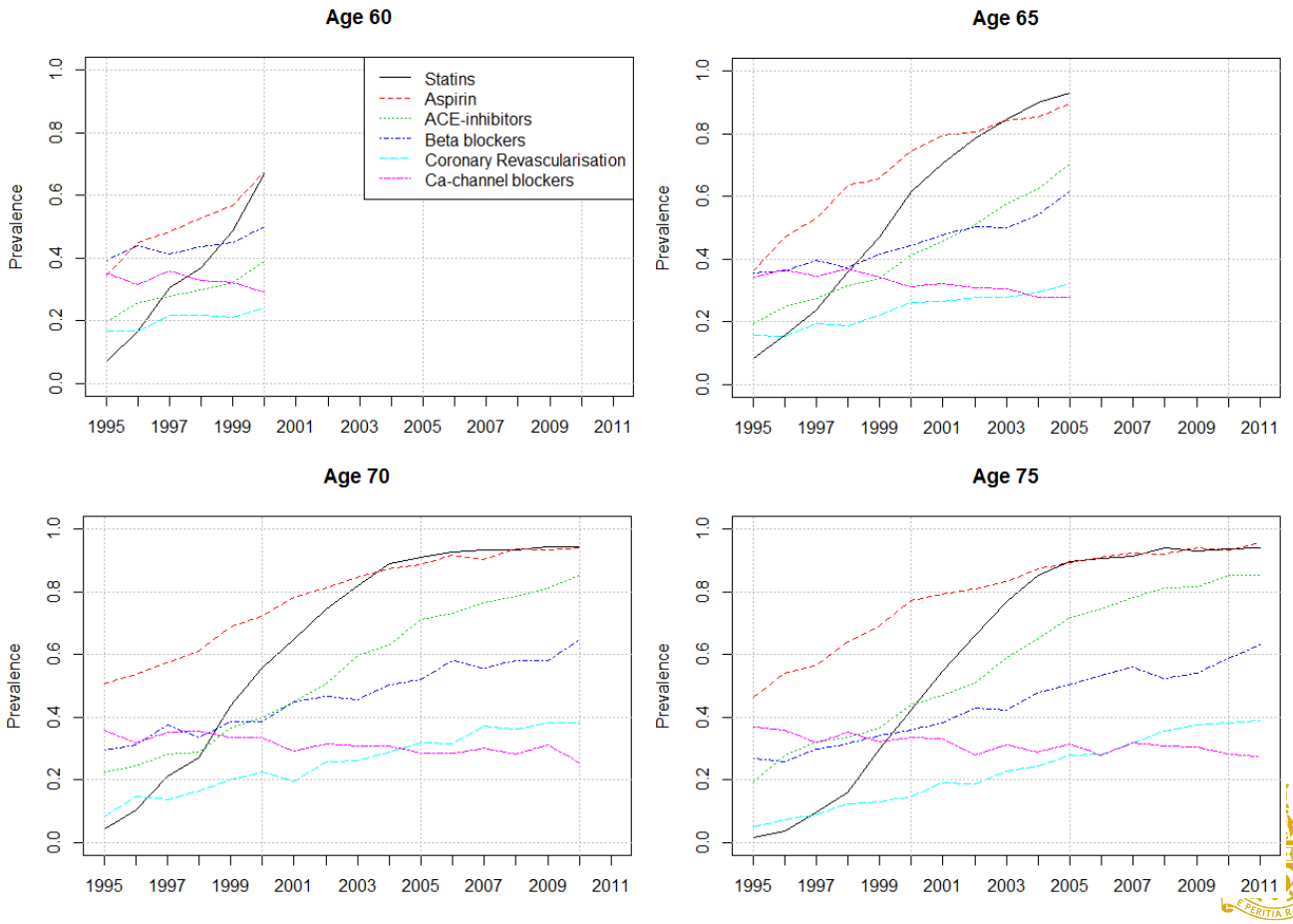
Prevalence of treatment by cohort's age in patients with a history of acute myocardial infarction



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Period life expectancies for heart attack survivors

Sex	Period life expectancy	Age 60 (95% CI)	Age 65 (95% CI)	Age 70 (95% CI)	Age 75 (95% CI)
Men	Heart attack [a]	17.43 (17.32-18.32)	14.14 (13.62-14.64)	11.65 (11.28-12.00)	8.83 (8.54-9.11)
	Prescription [b]	18.84 (17.9-19.85)	15.79 (15.27-16.37)	12.69 (12.25-13.01)	10.03 (9.68-10.33)
	No prescription [c]	16.36 (16.89-17.16)	12.71 (12.20-13.16)	10.68 (10.38-11.07)	7.78 (7.54-8.03)
Women	Heart attack [a]	20.33 (19.45-21.23)	16.67 (16.15-17.19)	13.80 (13.41-14.18)	10.56 (10.24-10.85)
	Prescription [b]	21.76 (20.80-22.76)	18.39 (17.85-18.98)	14.91 (14.44-15.24)	11.85 (11.47-12.16)
	No prescription [c]	19.29 (18.47-20.11)	15.35 (14.86-15.84)	12.90 (12.56-13.30)	9.53 (9.26-9.81)

[a] Period life expectancy for heart attack survivors at 2010 prescription level of beta blockers. This is the weighted average of [b] period LE for heart attack survivors with prescription and [c] period LE for heart attack survivors without prescription.

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Example 2: Would intensive systolic blood pressure control increase longevity?

SPRINT trial reported considerable survival benefits of intensive systolic blood pressure (SBP) lowering below 120 mmHg.

Adverse Renal Outcome was one of the main adverse effects, with the odds raised threefold in patients without Chronic Kidney Disease at baseline.

The AHA changed its hypertension guideline on the basis of SPRINT results (Whelton et al. 2017).

The primary objective of our study was to investigate the survival benefits of intensive SBP lowering in UK primary care and to compare them to SPRINT results.

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Design

The sample included 54,683 patients (50-90 yo) who were treated for hypertension between 2005 and 2013 and followed-up to 2017.

Group 1: patients with SBP > 140 mmHg (SBP1) which was lowered to less than 120; 19,756 (36%) patients.

Group 2: SBP> 140 mmHg lowered to 120-140 mmHg; 34,927 (64%) patients.

Time interval: 2 weeks to 6 months + new prescription.

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Results

SPRINT: the standard treatment has a hazard ratio (HR) of 1.42 (1.06, 1.90) compared to intensive treatment:

a decrease in effective age of 3.4 to 3.6 years.

AHA Guidelines: boost to the life expectancy in the US?

THIN: the intensive group had significantly increased HR of 1.35 (1.14, 1.27):

an increase in effective age of 1.7 to 1.8 years.

In both studies, more than 2 BP lowering drugs, and increase in dosage (THIN) further significantly increased the hazards of mortality and the hazard of adverse renal outcomes.

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Summary

- Estimating longevity risk and evaluating associated uncertainty is one of the main topics of concern to actuarial community.
- Clinical trials deal with a selective population of patients, and usually are of short duration.
- To establish the drivers of changes in longevity, and to predict how they may change over time, we need to use individual level health data found in large health databases, and to use sophisticated tools for modelling the mortality experience of participating populations.
- The results can be translated into individual and population level life expectancy changes.

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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 ARC.