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Modelling longevity risks from the primary care data

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Joint work with Nick Steel, Ilyas Bakbergenuly, and AVIVA team

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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.

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Use Of Big Health And Actuarial Data For Understanding Longevity And Morbidity Risks, IFoA 2016-2020

Consortium University of East Anglia: School of Computing Sciences (CMP) and Norwich Medical School (NMS). Aviva Life Plc.

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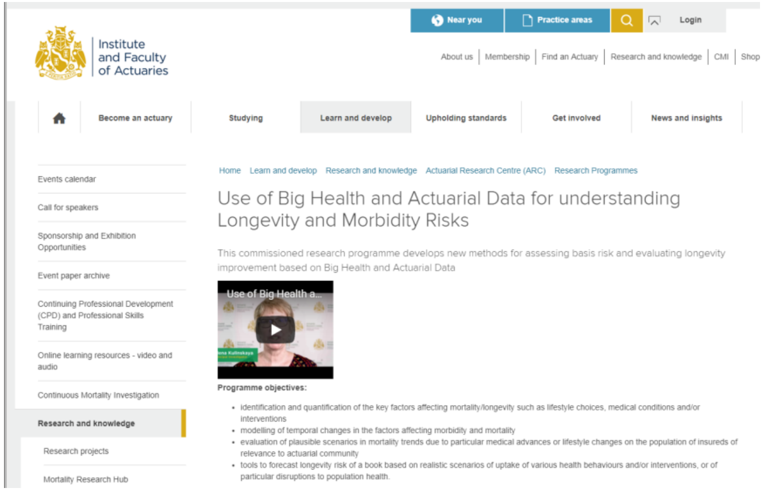
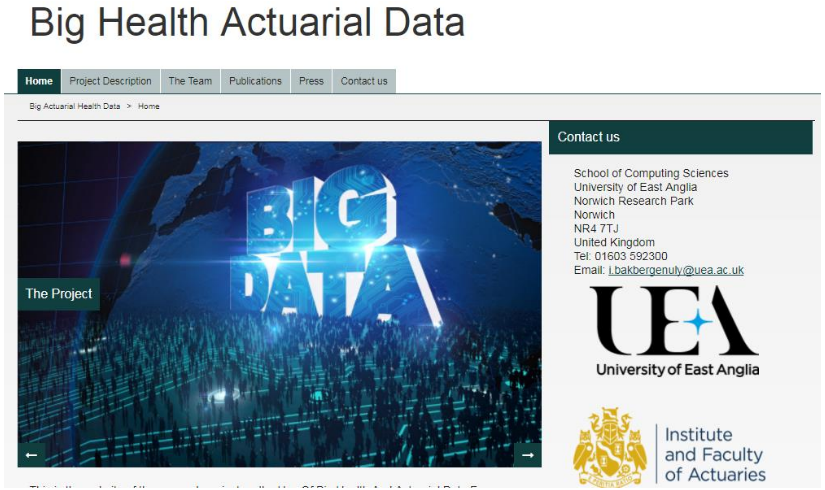
Aviva co-investigators Mr Nigel Wright, Ms Sarah Allen.

Find out more





[bit.ly/arc2173](bit.ly/arc2173)

www.bighealthactuarialdata.ac.uk

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Aims

1. Identification and quantification of the key factors affecting mortality/longevity.
2. Modelling of temporal changes in the factors affecting morbidity and mortality.
3. Evaluation of plausible scenarios in mortality trends due to particular medical advances or lifestyle changes on the population of insureds.
4. Tools to forecast longevity risk of a book.

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Data

- The Health Improvement Network (THIN) data
  - Medical records from primary care
  - Representative of the UK when adjusted for deprivation
- All patients born before 1960 and followed to 01.01.2017, this includes 3.5 million patients
- Added various social economic status variables such as IMD and Mosaic
- Additional Actuarial Data (Club Vita?)

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Conditions, interventions and lifestyle factors

- We intend to have a target list of between 3-5 conditions or interventions.
- We propose to consider statin prescription, an established longevity-improving intervention as one of the target scenarios. Other conditions will include stroke, atrial fibrillation, type 2 diabetes, and hormone replacement therapy (HRT).
- Health interventions may include an introduction of NICE guidelines on use of particular health sustaining drugs such as statins, or targeted outcomes such as the blood pressure targets.
- Lifestyle factors may include obesity or smoking.
- To be able to ascertain an effect on longevity of a population, we need to model the incidence of a condition or an uptake of an intervention over time in parallel to modelling mortality.

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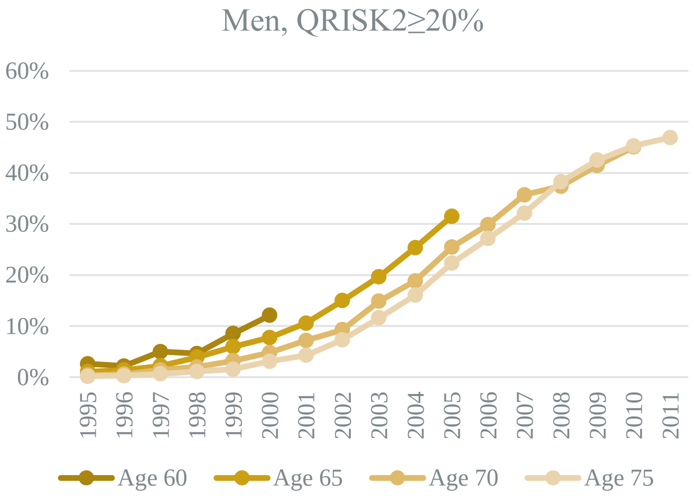
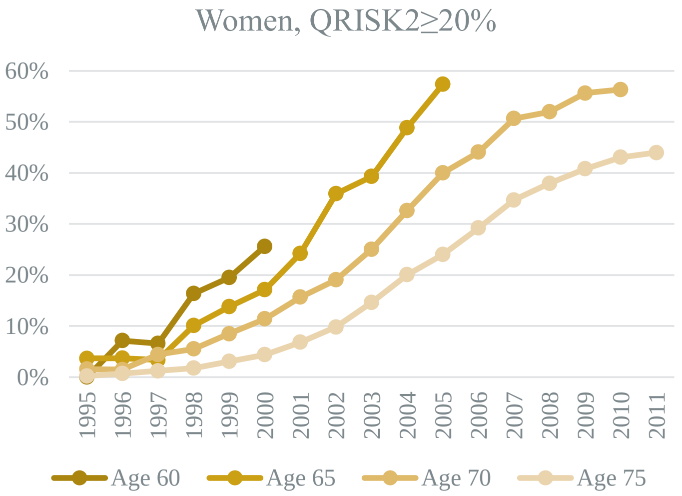
Prevalence of statins prescription for primary prevention of cardiovascular disease over time





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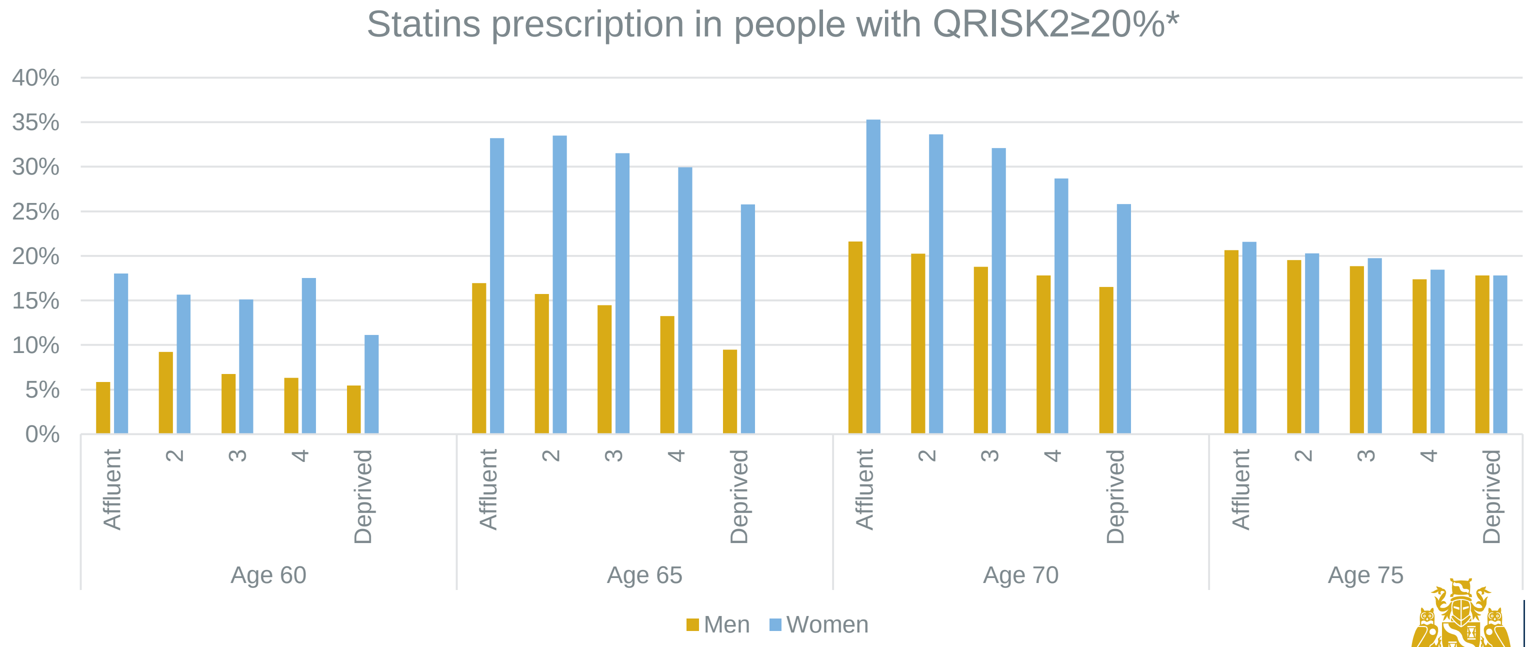
Prevalence of statins prescription for primary prevention of cardiovascular disease by deprivation quintiles (Townsend)



*summarised over 1995-2011

Design and methods

- For each of target conditions we will design a population-based retrospective cohort study using an appropriate extract of the primary care data.
- We intend to use a case-control design with cases matched with several controls from the same GP practice. This provides balanced and comparable cohorts of cases and controls and simplifies the study of comparatively rare conditions without loss of efficiency.
- The full list of relevant confounding variables will be established from medical literature such as systematic reviews, and from expert knowledge within the team. Then, the subset of these variables to be adjusted for, will be found through backward elimination.
- To account for the interdependence of patients from the same GP practice and for missing data, multilevel modelling and multiple imputation will be used.

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Case Study 1

Would intensive systolic blood pressure control increase longevity?

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 (ARO) was one of the main adverse effects, with the odds raised threefold in patients without Chronic Kidney Disease (CKD) at baseline.
- 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

- To replicate the SPRINT design in the primary care setting, we selected patients born between 1920 and 1940 and followed up until January 2011, with a diagnosis of hypertension and prescription of at least one antihypertensive agent from the medication list of SPRINT trial.
- Time interval: 2 weeks to 6 months + new prescription
- Group 1: patients with SBP > 140mmHg which was lowered to less than 120mmHg; 7891 patients from 448 general practices
- Group 2: patients with SBP > 140mmHg which was lowered to 120-140mmHg; 11,276 patients matched to group 1 on age, sex and GP practice

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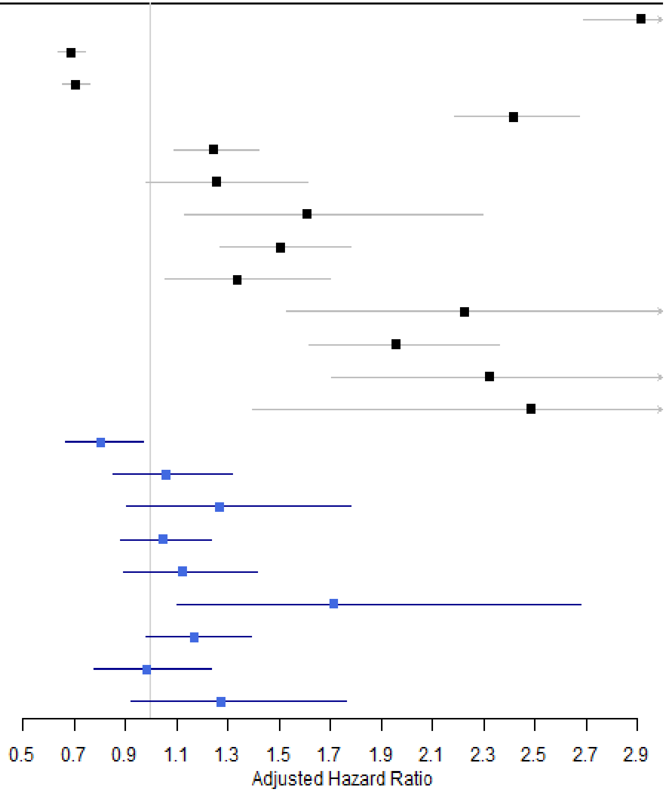
Mortality in THIN: Intensive vs Standard SBP control

Factor	HR (95%CI)
Age>=75	2.91 (2.69-3.15)
Female	0.69 (0.64-0.74)
BMI>25	0.71 (0.66-0.76)
Smoker	2.42 (2.19-2.67)
Increased dose at SBP2	1.24 (1.09-1.42)
I, 0, 2	1.26 (0.98-1.61)
I, 0, 3+	1.61 (1.13-2.30)
I, 1-2, 1	1.50 (1.27-1.78)
I, 1-2, 2	1.34 (1.05-1.70)
I, 1-2, 3+	2.22 (1.53-3.23)
I, 3+, 1	1.96 (1.62-2.36)
I, 3+, 2	2.32 (1.70-3.17)
I, 3+, 3+	2.48 (1.40-4.41)
S, 0, 1	0.80 (0.67-0.97)
S, 0, 2	1.06 (0.85-1.32)
S, 0, 3+	1.27 (0.91-1.78)
S, 1-2, 1	1.04 (0.88-1.24)
S, 1-2, 2	1.12 (0.89-1.42)
S, 1-2, 3+	1.72 (1.10-2.68)
S, 3+, 1	1.17 (0.98-1.39)
S, 3+, 2	0.98 (0.78-1.24)
S, 3+, 3+	1.28 (0.92-1.76)



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

I=intensive treatment, S=standard treatment, the 1st number=number of agents prescribed at SBP1, 2nd number=number of agents prescribed at SBP2.

Mortality: extra prescriptions

- SPRINT: antihypertensive agents reduced the hazard of mortality in comparison to no drugs, but when there were 3+ drugs at baseline, the HR increased to 1.71 with additional prescription.
- THIN: patients prescribed 3+ antihypertensive agents at baseline or who had an increase to 3+ drugs later, had significantly increased hazards of mortality in comparison to those on less drugs, HRs 1.72-2.48.
- Increase in dosage further significantly increased the hazards, HR 1.24.

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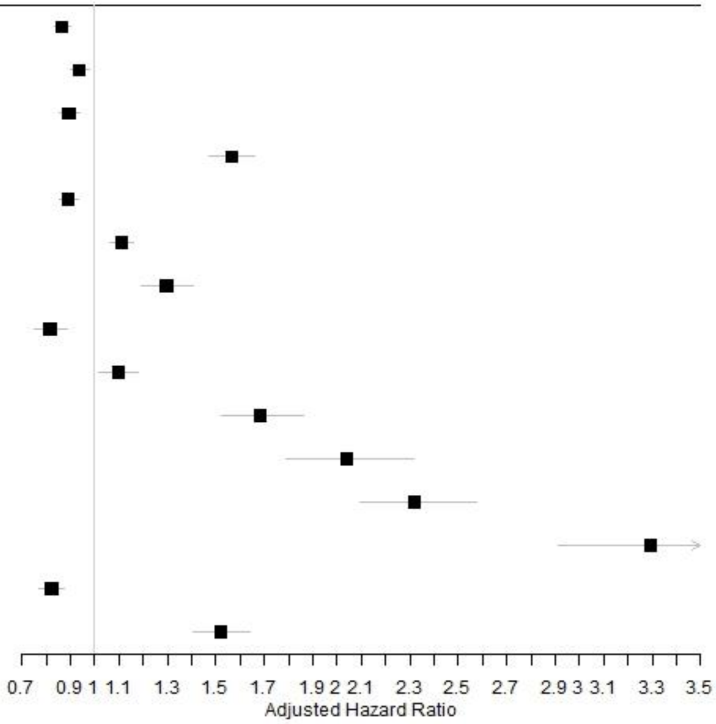
Adverse Renal Outcomes in THIN: Intensive vs Standard SBP control

Factor	HR (95%CI)
Female	0.87 (0.83-0.90)
Overweight	0.94 (0.90-0.98)
Obese	0.89 (0.85-0.94)
Smoker	1.56 (1.47-1.66)
SBP1>=160	0.89 (0.85-0.93)
2agents at SBP2	1.11 (1.06-1.16)
3+agents at SBP2	1.30 (1.20-1.42)
Increased dose at SBP2	0.82 (0.75-0.89)
I, 1-2, age<75	1.10 (1.02-1.18)
I, 3+, age<75	1.69 (1.53-1.86)
I, 0, age>=75	2.04 (1.79-2.32)
I, 1-2, age>=75	2.32 (2.09-2.57)
I, 3+, age>=75	3.30 (2.92-3.73)
S, age<75	0.82 (0.77-0.87)
S, age>=75	1.52 (1.40-1.64)



Standard treatment had a significantly lower HR:
- 0.32 (0.22, 0.46) in SPRINT
- 0.69 (0.66, 0.71) in THIN

I=intensive treatment,
S=standard treatment,
the 1st number=number of agents prescribed at SBP1,
2nd number=number of agents prescribed at SBP2.

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Adverse renal outcomes

- Results were similar in both datasets.
- Standard treatment had a significantly lower HR:
  - 0.32 (0.22, 0.46) in SPRINT
  - 0.69 (0.66, 0.71) in THIN
- The HRs were increased due to higher SBP at baseline, age, obesity, additional medication and by number of agents, especially so for 3+ agents, HR 2.68 (1.36, 5.27) in SPRINT and 1.69 to 3.30 for under/over 75s in THIN.

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Case Study 2

Life expectancy after AMI

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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 mayocardial 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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Data selection

- Outcome: time to death
- Primary exposure: acute myocardial infarction
- Treatments: coronary revascularisation (coronary artery bypass graft and coronary angioplasty), and prescription of ACE inhibitors, aspirin, beta blockers, calcium-channel blockers, and statins
- Confounders: sex, year of birth, socioeconomic status, angina, heart failure, other cardiovascular conditions (valvular heart disease, peripheral vascular disease, and cerebrovascular disease), chronic kidney disease, diabetes, hypertension, hypercholesterolaemia, alcohol consumption, body mass index, and smoking status
- Missing data dealt with by multiple imputation

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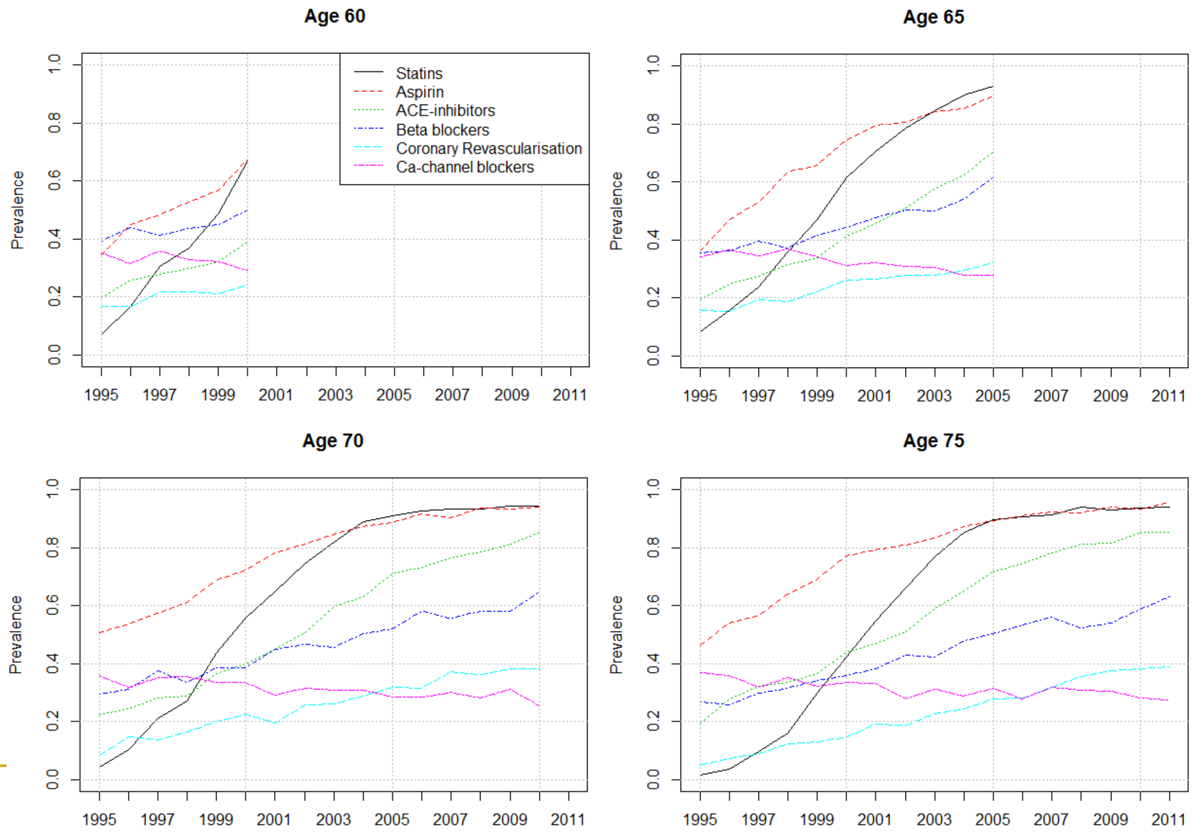
Prevalence of treatment by cohort's age in patients with a history of acute myocardial infarction



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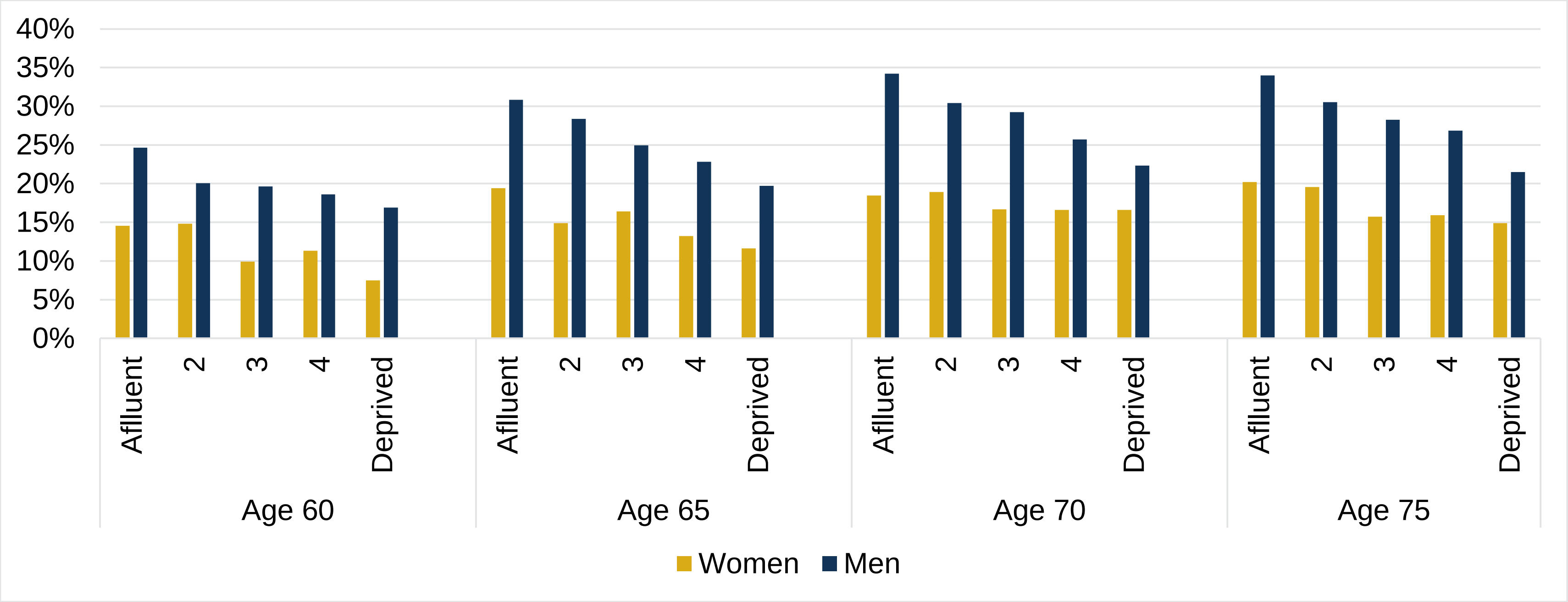
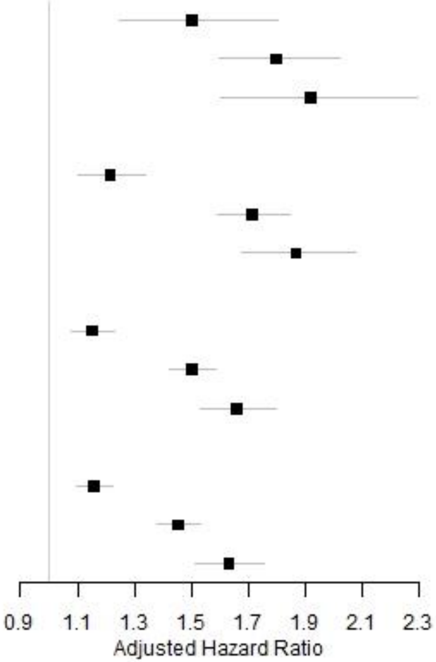
Prevalence coronary revascularisation given ischaemic heart disease



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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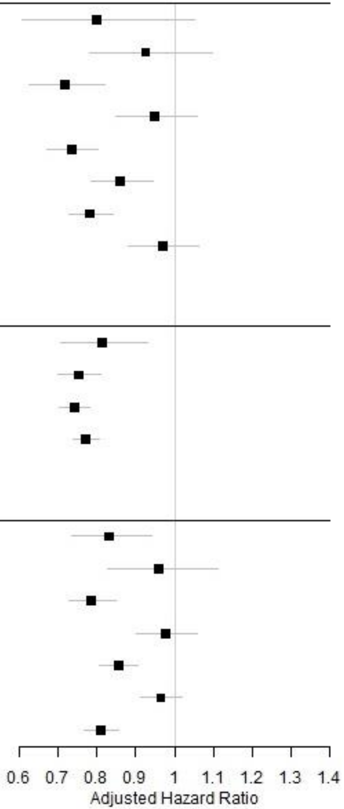
Survival prospects by treatments

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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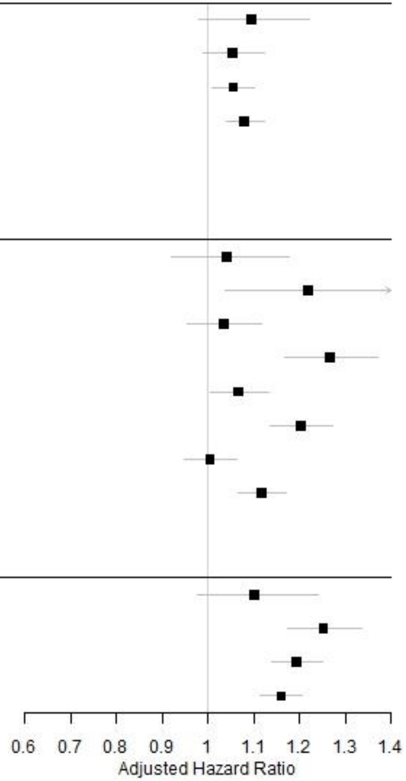
Survival prospects by treatments (cont.)

Cohort	Aspirin	Adjusted HR (95%CI)
Age 60	Yes	1.10 (0.98-1.22)
Age 65	Yes	1.05 (0.99-1.12)
Age 70	Yes	1.05 (1.01-1.10)
Age 75	Yes	1.08 (1.04-1.12)
	Ca-channel blocker	
Age 60	Yes with AMI	1.04 (0.92-1.18)
	Yes without AMI	1.22 (1.04-1.43)
Age 65	Yes with AMI	1.03 (0.96-1.12)
	Yes without AMI	1.27 (1.17-1.37)
Age 70	Yes with AMI	1.07 (1.00-1.13)
	Yes without AMI	1.20 (1.14-1.27)
Age 75	Yes with AMI	1.00 (0.95-1.06)
	Yes without AMI	1.12 (1.06-1.17)
	ACE-inhibitor	
Age 60	Yes	1.10 (0.98-1.24)
Age 65	Yes	1.25 (1.17-1.34)
Age 70	Yes	1.19 (1.14-1.25)
Age 75	Yes	1.16 (1.11-1.21)



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What does this 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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Potential longevity increase in AMI patients

	Statins			Beta blockers		
		Men	Women		Men	Women
Age	Effective age reduction	Longevity increase (years)		Effective age reduction	Longevity increase (years)	
60	-2.1	1.7	1.8	-1.9	1.6	1.7
65	-2.7	2.2	2.3	-2.4	1.9	2.0
70	-3.0	2.2	2.4	-1.6	1.2	1.3
75	-2.6	1.6	1.9	-2.1	1.4	1.6

NB1: Change in effective age and period life expectancy based on the UK life tables of 2013-15 (ONS, 2016).
NB2: Assumption that the increase in annual hazard of mortality associated with ageing one year in AMI patients is the same as in the general population.

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Conclusions and recommendations

- Heart attack survivors are to a lesser extent worse off than previously estimated
- Survival benefits associated with coronary revascularisation and prescription of statins and beta blockers → more prescriptions
- Survival harms associated with prescription of aspirin and ACE inhibitors → further research
- Advocating equality in treatment

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Overall 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.
- This does require some time lag to be able to obtain sufficient population-based data.

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Questions

Comments

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