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Modelling longevity risks from the primary care data

Elena Kulinskaya and Lisanne Gitsels

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.

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.

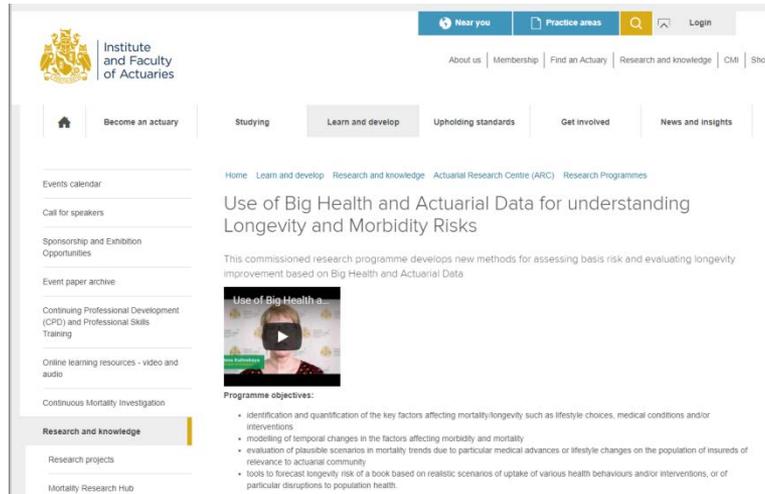
Principal Investigator Prof Elena Kulinskaya, Aviva Chair in Statistics, CMP.

UEA co-investigators Dr Beatriz de la Iglesia (CMP), Mr Ilyas Bakbergenuly (CMP), Dr Lisanne Gitsels (CMP), Prof Ruth Hancock (NMS), Prof Nick Steel (NMS).

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



Find out more



The screenshot shows the website for the Institute and Faculty of Actuaries. The main navigation bar includes 'Near you', 'Practice areas', a search icon, and 'Login'. Below this, there are links for 'About us', 'Membership', 'Find an Actuary', 'Research and knowledge', 'CMI', and 'Shop'. The page is titled 'Use of Big Health and Actuarial Data for understanding Longevity and Morbidity Risks'. It features a video player with the title 'Use of Big Health a...' and a list of programme objectives:

- identification and quantification of the key factors affecting mortality/longevity, such as lifestyle choices, medical conditions and/or interventions
- modeling of temporal changes in the factors affecting morbidity and mortality
- evaluation of plausible scenarios in mortality trends due to particular medical advances or lifestyle changes on the population of insureds of relevance to actuarial community
- tools to forecast longevity risk of a book based on realistic scenarios of uptake of various health behaviours and/or interventions, or of particular disruptions to population health.

Big Health Actuarial Data



The screenshot shows the website for Big Health Actuarial Data. The main navigation bar includes 'Home', 'Project Description', 'The Team', 'Publications', 'Press', and 'Contact us'. The page features a large image with the text 'BIG DATA' and 'The Project'. On the right side, there is a 'Contact us' section with the following information:

School of Computing Sciences
University of East Anglia
Norwich Research Park
Norwich
NR4 7TJ
United Kingdom
Tel: 01603 552300
Email: halkberg@uea.ac.uk

UEA
University of East Anglia

 Institute and Faculty of Actuaries

bit.ly/arc2173

www.bighealthactuarialdata.ac.uk

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.



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?)



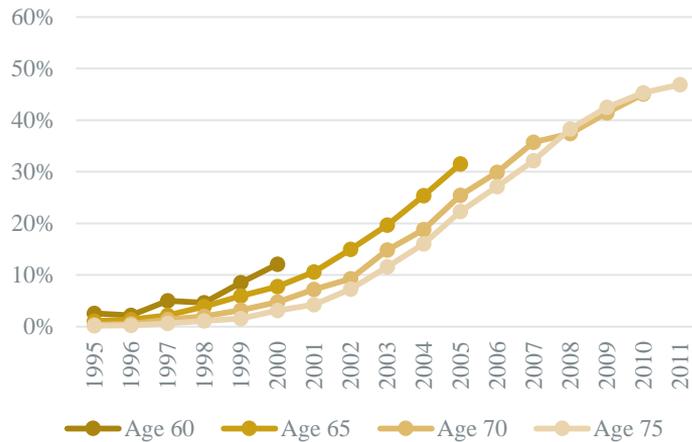
Conditions, interventions and lifestyle factors

- 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.

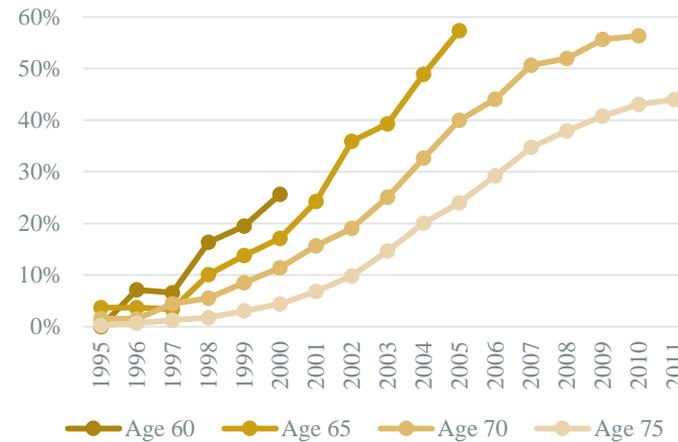


Prevalence of statins prescription for primary prevention of cardiovascular disease over time

Men, QRISK2 \geq 20%

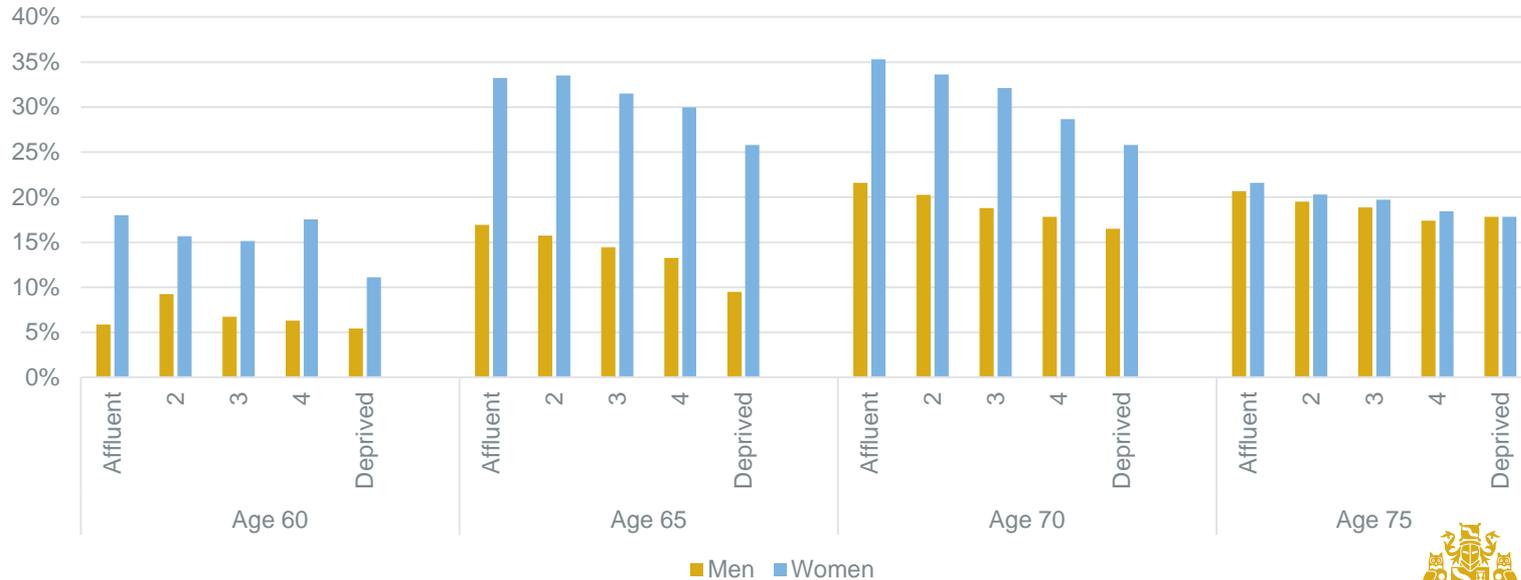


Women, QRISK2 \geq 20%



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

Statins prescription in people with QRISK2 \geq 20%*



*summarised over 1995-2011



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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.





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.

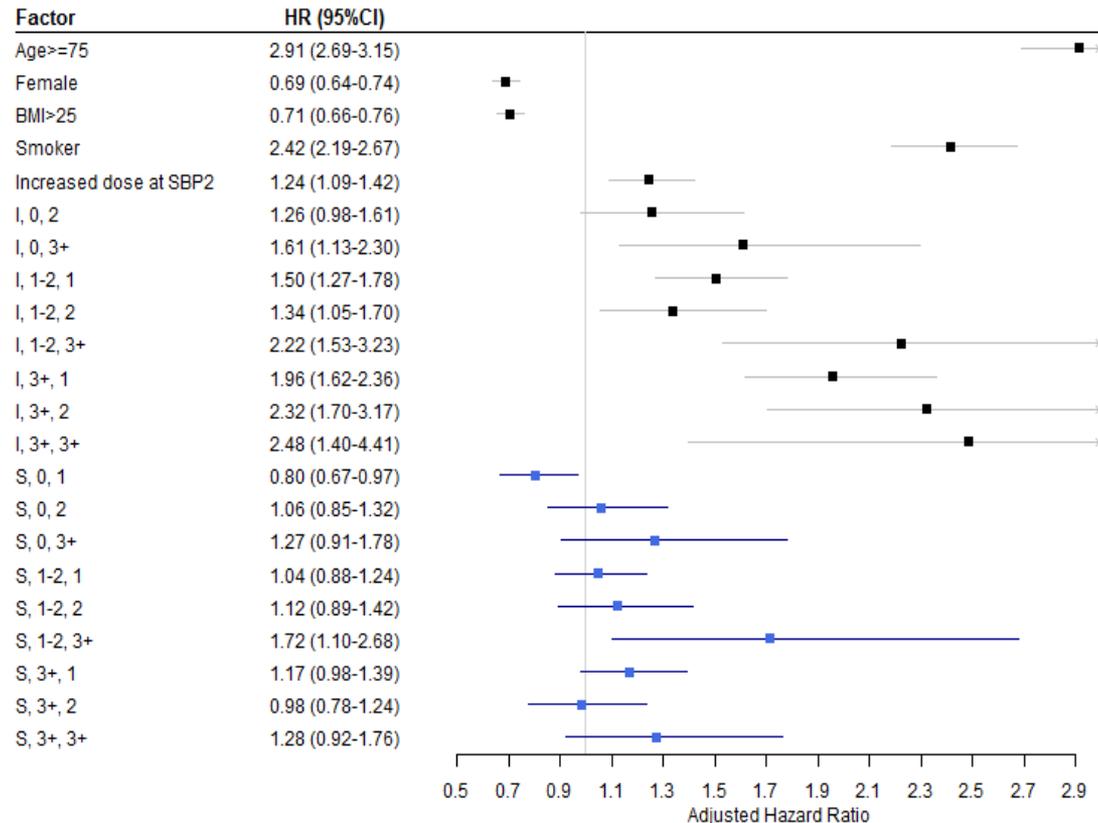


Design

- 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



Mortality in THIN: Intensive vs Standard SBP control



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.

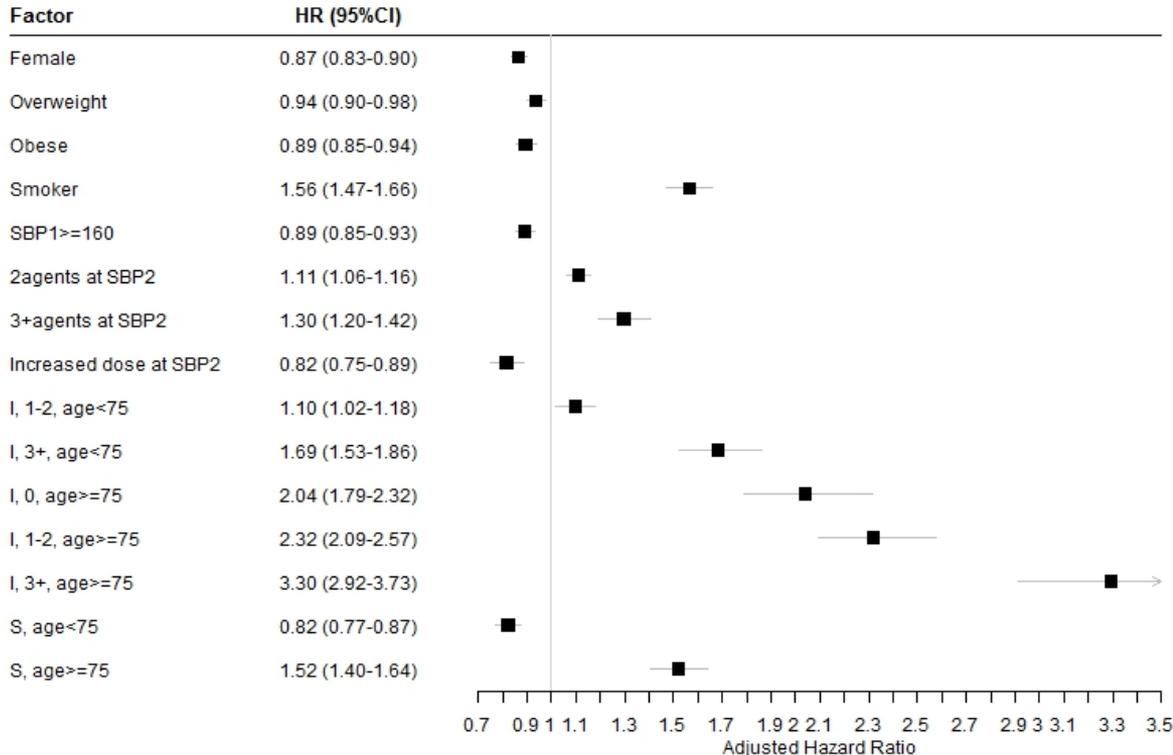


Mortality: extra prescriptions

- 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.



Adverse Renal Outcomes in THIN: Intensive vs Standard SBP control



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.



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



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>

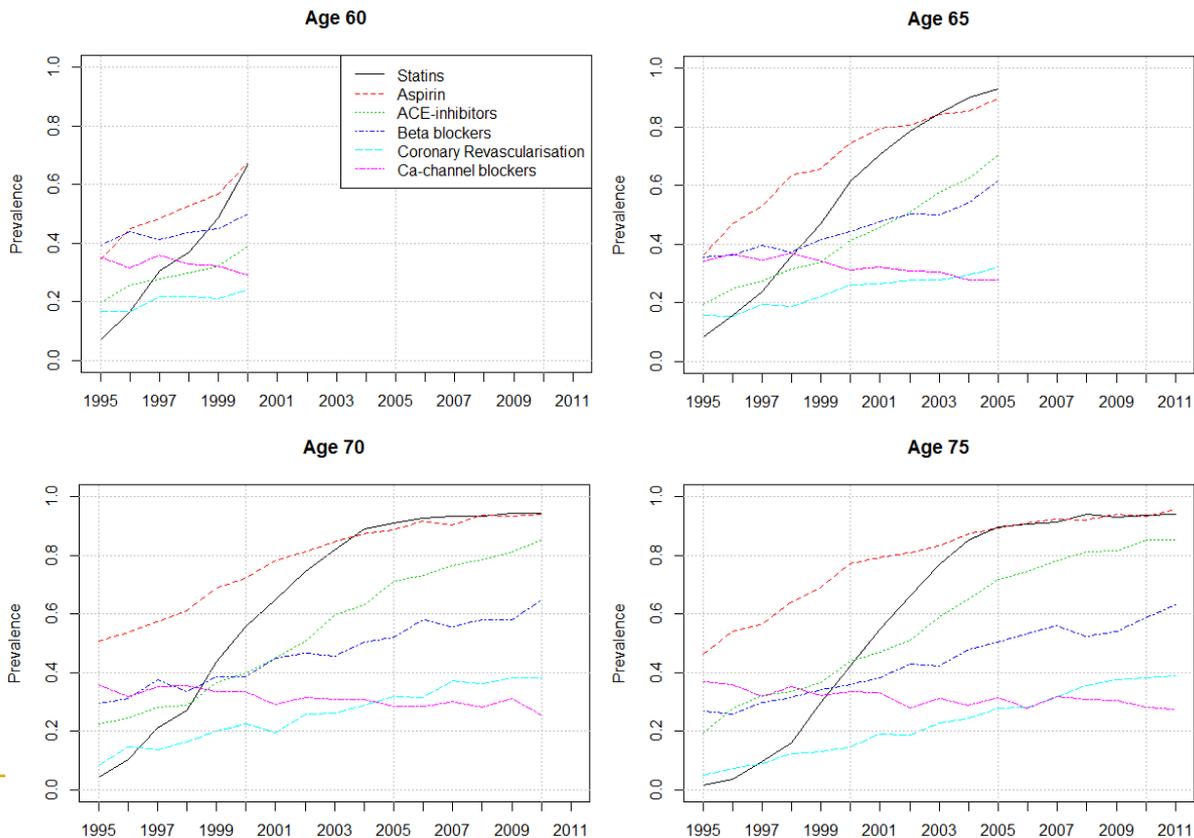


Data selection

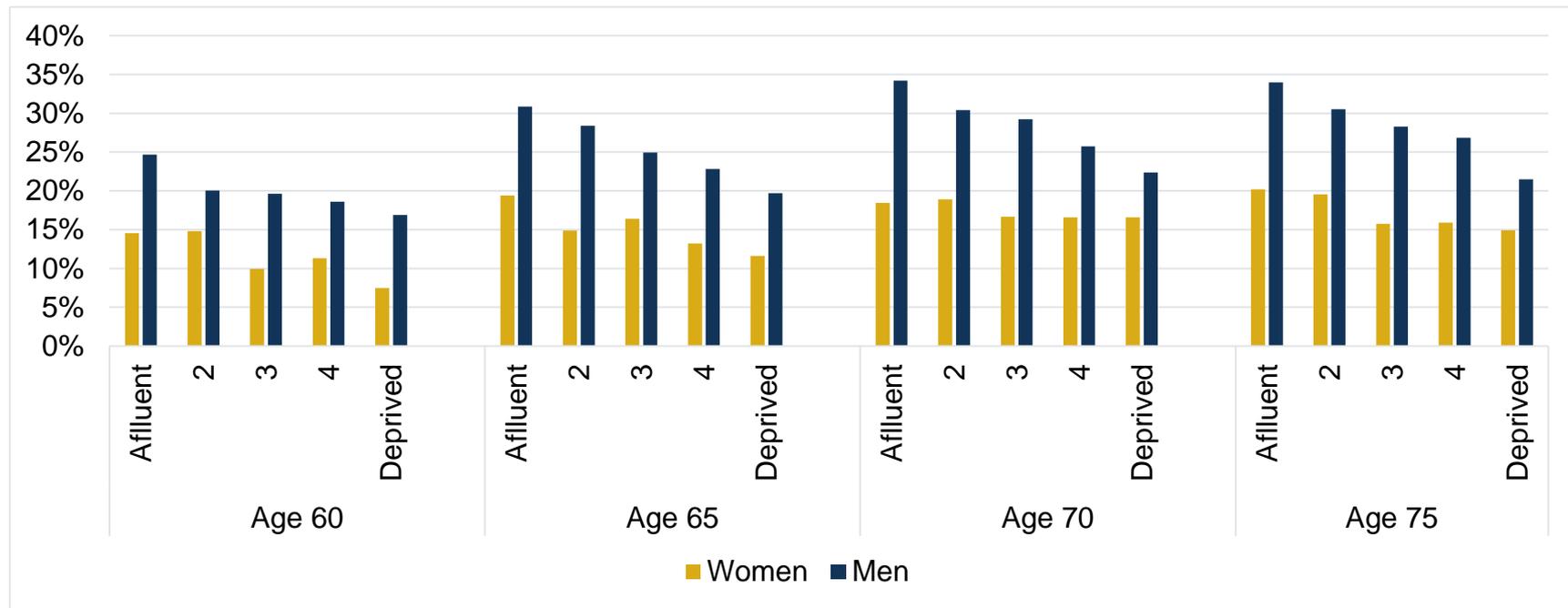
- Outcome: time to death
- Primary exposure: acute myocardial infarction
- Treatments: coronary revascularisation (coronary artery bypass graft and coronary angioplasty), and prescription of ACE inhibitors, aspirin, beta blockers, calcium-channel blockers, and statins
- Confounders: sex, year of birth, 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



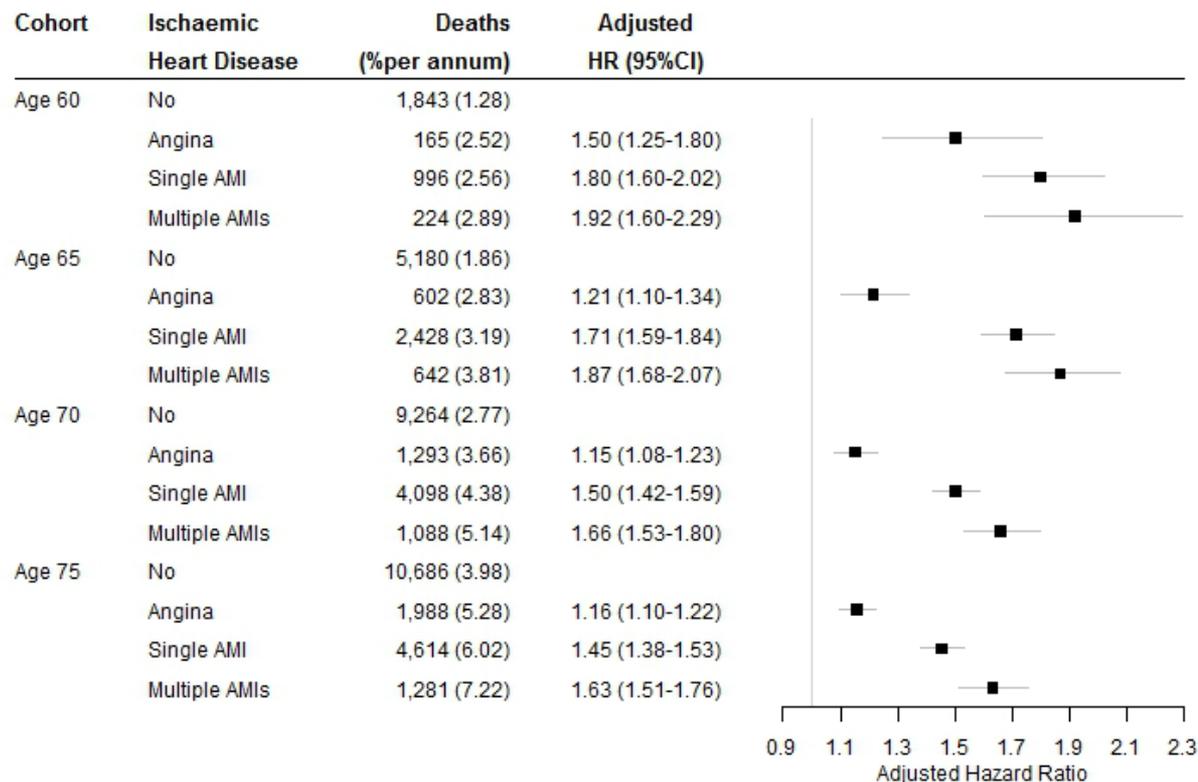
Prevalence of treatment by cohort's age in patients with a history of acute myocardial infarction



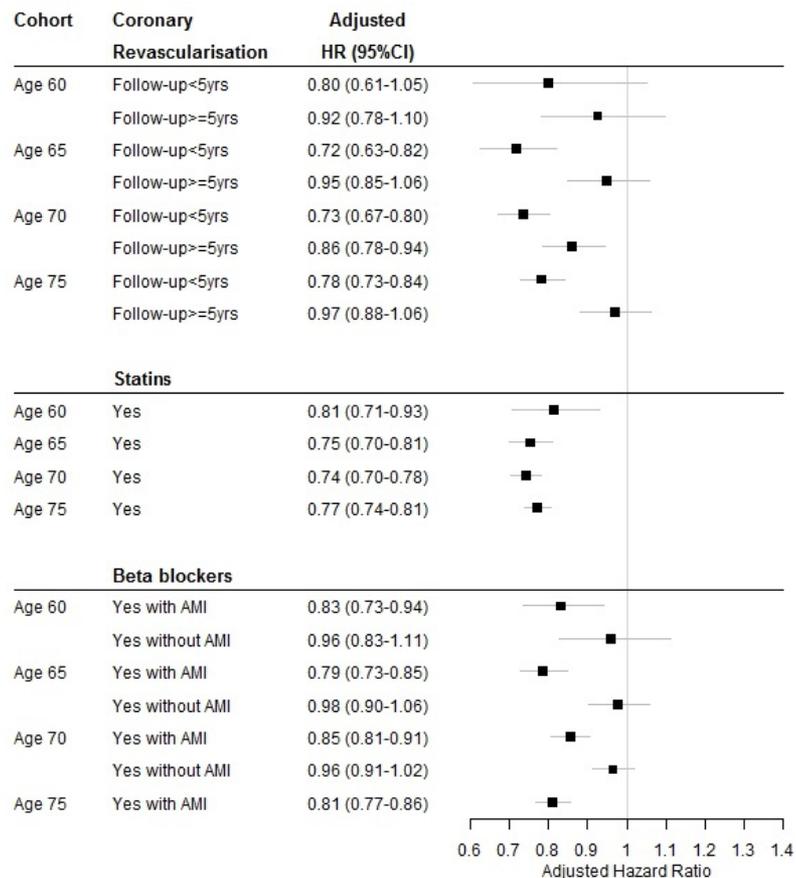
Prevalence coronary revascularisation given ischaemic heart disease



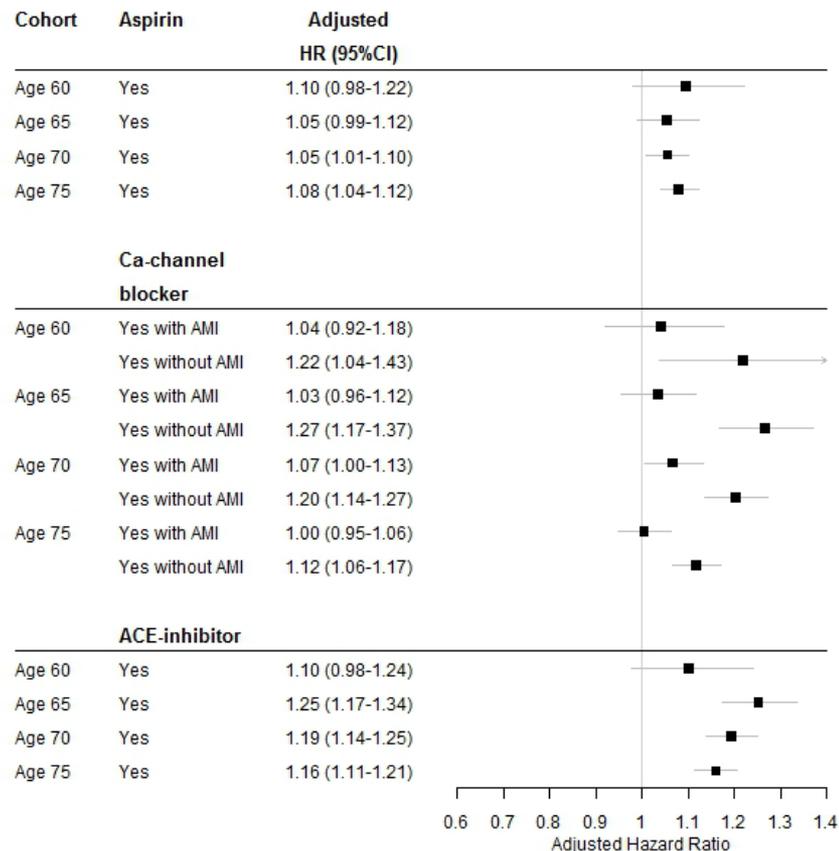
Survival prospects after AMI



Survival prospects by treatments



Survival prospects by treatments (cont.)



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

(Brenner, 1993; Spiegelhalter, 2016)



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.



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



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.



References

- Brenner H, Gefeller O, Greenland S. (1993) Risk and rate advancement periods as measures of exposure impact on the occurrence of chronic diseases. *Epidemiol Camb Mass.* 4(3):229–36.
- 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.
- Spiegelhalter (2016) How old are you, really? Communicating chronic risk through ‘effective age’ of your body and organs. *BMC Medical Informatics and Decision Making*, 16:104
- The SPRINT Research Group. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. *New England Journal of Medicine*, 2015 373:2103-2116, DOI: [10.1056/NEJMoa1511939](https://doi.org/10.1056/NEJMoa1511939)



Questions

Comments

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