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Update on the findings of the research programme so far and future direction

Elena Kulinskaya, Nick Steel, and Lisanne Gitsels

Joint work UEA-Aviva team

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

27 September 2017

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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.

Principal Investigator

Prof Elena Kulinskaya, Aviva Chair in Statistics, CMP

UEA co-investigators

CMP: Dr Beatriz de la Iglesia, Mr Ilyas Bakbergenuly, Dr Lisanne Gitsels

NMS: Prof Ruth Hancock, Prof Nick Steel

Aviva co-investigators

Mr Nigel Wright, actuary; Ms Sarah Allen, Senior Data Analyst, the Life Risk Analytics team.

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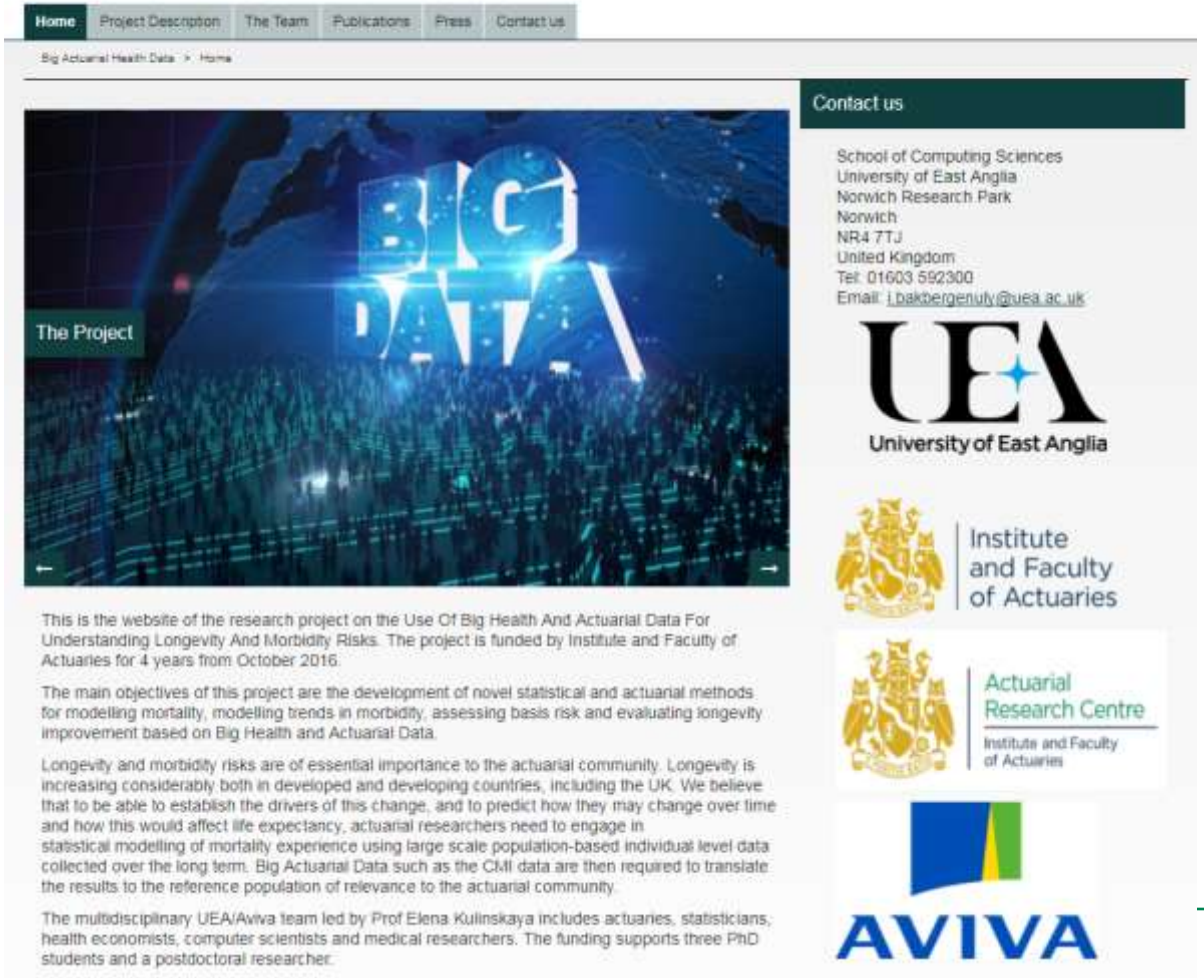
http://www.bighealthactuarialdata.ac.uk/

Big Health Actuarial Data



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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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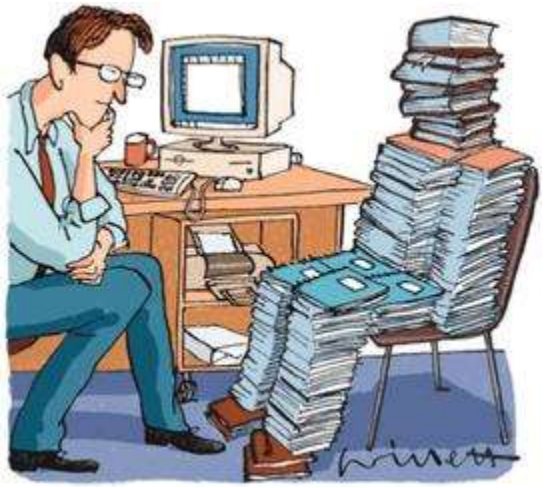
The Health Improvement Network (THIN) data

- 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



Sample selected for this study:

- 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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Conditions, interventions and lifestyle factors

- Conditions
  - Cardiovascular disease, stroke, atrial fibrillation, type 2 diabetes
- Interventions
  - statin prescription for cardiovascular disease
  - hormone replacement therapy (HRT)
  - effective treatment for other conditions (guideline recommended)
- Lifestyle factors and other covariates and potential confounders
  - obesity
  - smoking
  - socio economic deprivation
  - others chosen from systematic reviews and expert knowledge within the team

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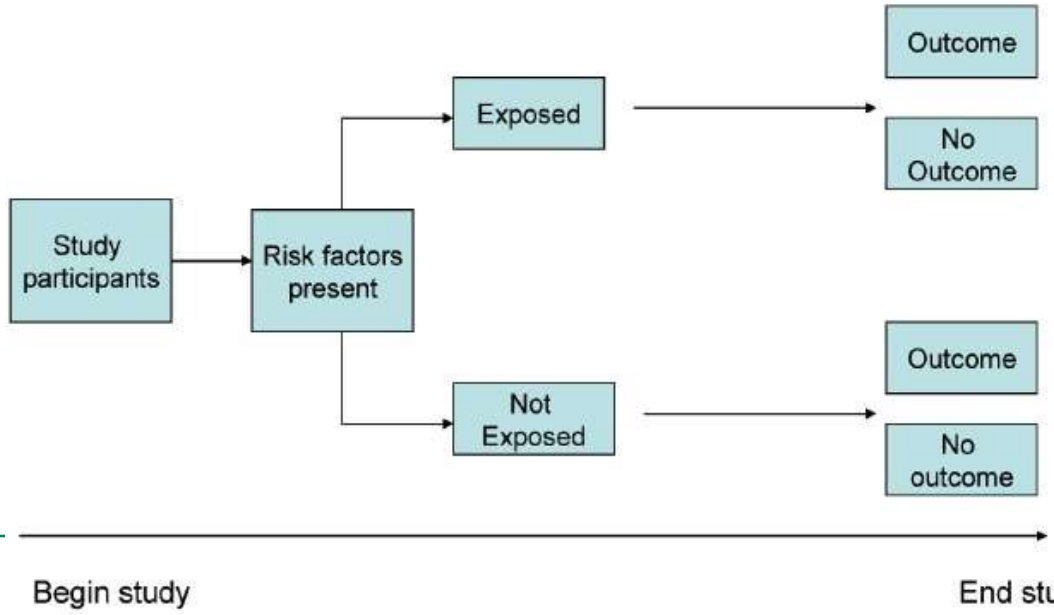
Design and methods

- Population-based retrospective cohort study for each of target conditions
- Cases matched with several controls from the same GP practice. Controls will be matched on sex, age, and time period of diagnosis/intervention.
- Regression analysis to quantify effect of diagnoses and interventions on survival
- 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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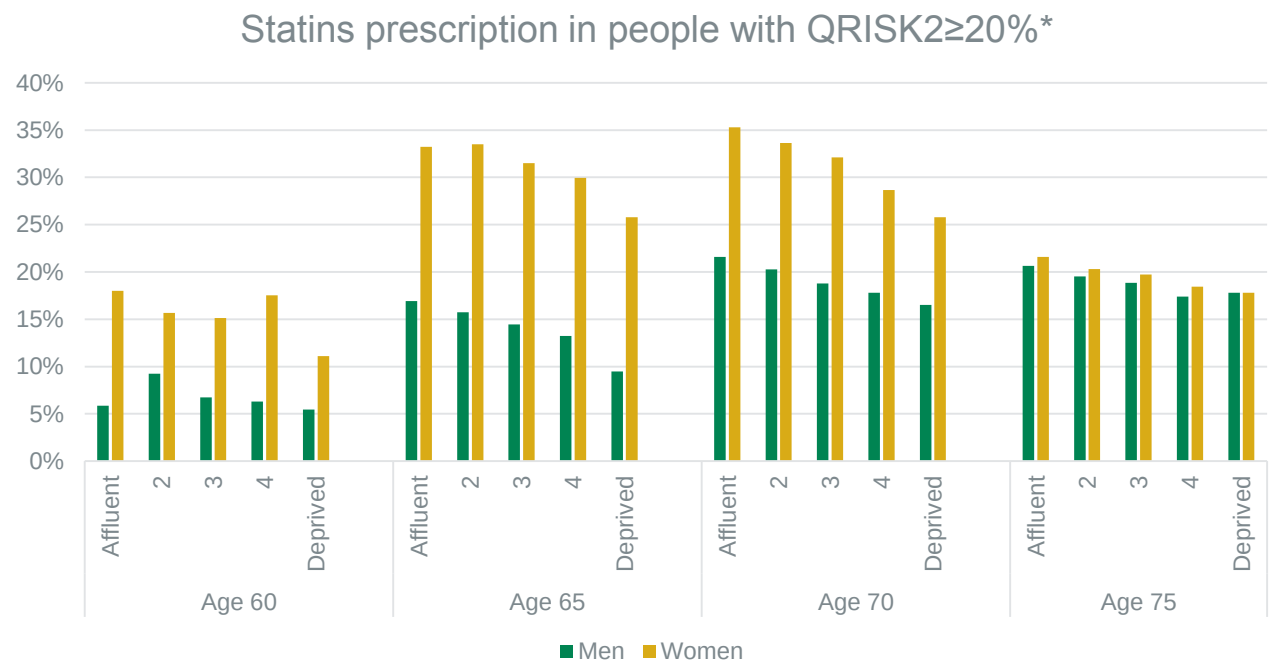
Prevalence of statins prescription for primary prevention of cardiovascular disease by deprivation quintiles (Townsend)



*summarised over 1995-2011

	Cohort size →	QRISK2≥20% →	Statins
Age 60	120,000	4,000	300
Age 65	200,000	35,000	5,000
Age 70	250,000	125,000	25,000
Age 75	200,000	175,000	35,000

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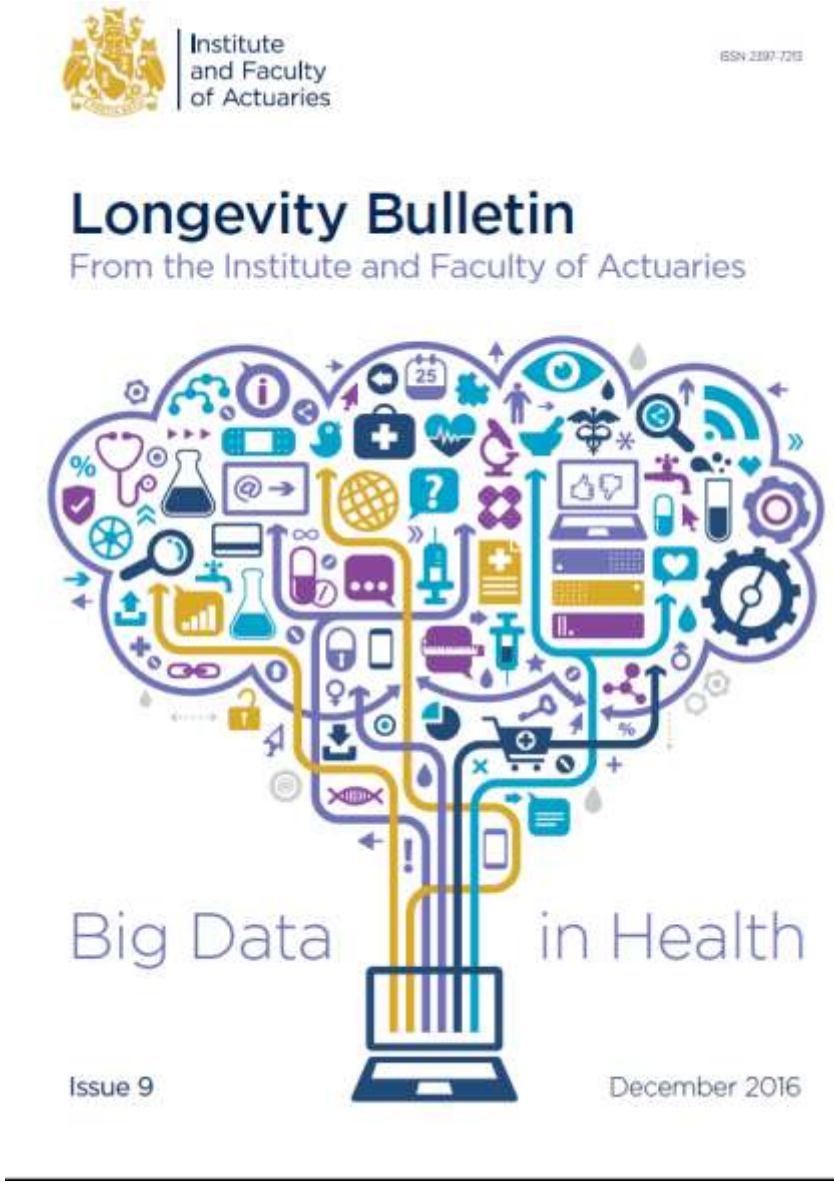


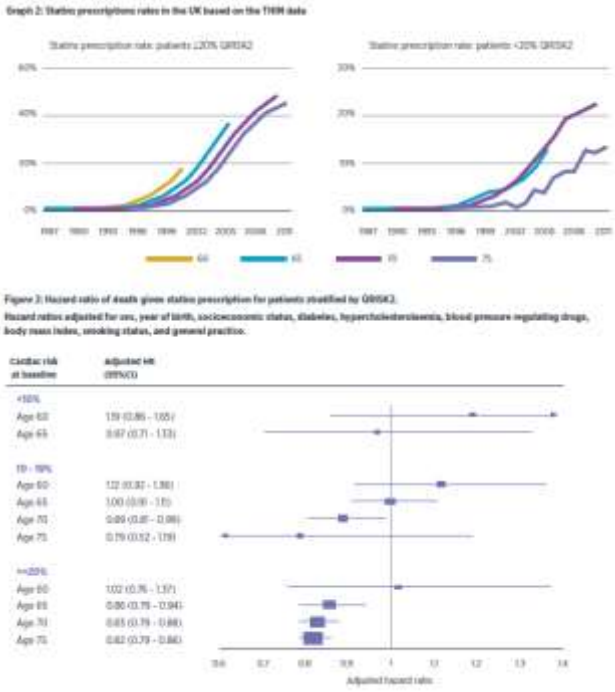
6. Use of big health and actuarial data for understanding longevity and morbidity risk

Professor Elena Kulinskaya and Lisanne Gitsels, PhD candidate, University of East Anglia

Introduction

Estimating longevity risk and evaluating associa
is one of the main topics of concern to actuaria
It is well known that longevity is increasing con
in developed and developing countries, includir
Kingdom. We believe that to be able to establi
of this change, and to predict how they may ch
and how this would affect life expectancy, resea
to harvest Big Health Data (Hemmingway, 2014
large health databases, and to use sophisticate
modelling the mortality experience of participa
using individual level health data. Big Actuarial
the Continuous Mortality Investigation (CMI) da
utmost importance in translating the results to
population of relevance to the actuarial commu

Contemporary evidence-based underwriting ne
account for a large number of important and tir
determinants of health and longevity, such as d
factors (gender, social class), lifestyle factors (s
alcohol usage) and medical advances, and their
Many public health interventions are aimed at i
health of populations. These vary from offering
to encouraging lifestyle changes to managemer
medical conditions. However, actuarial and mec
often aim at somewhat differing objectives. Wh
is of primary interest to an actuary, exacerbatio
conditions is often the interest of a medical res
instance, not death but a cardiac event may be
endpoint in many medical studies of heart dise
Additionally, clinical trials while of the gold star
studying medical interventions, deal with a sele
of patients, and usually are of short duration.



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Case Study 1

Treatments of Acute Myocardial Infarction and Life Expectancy

27 September 2017

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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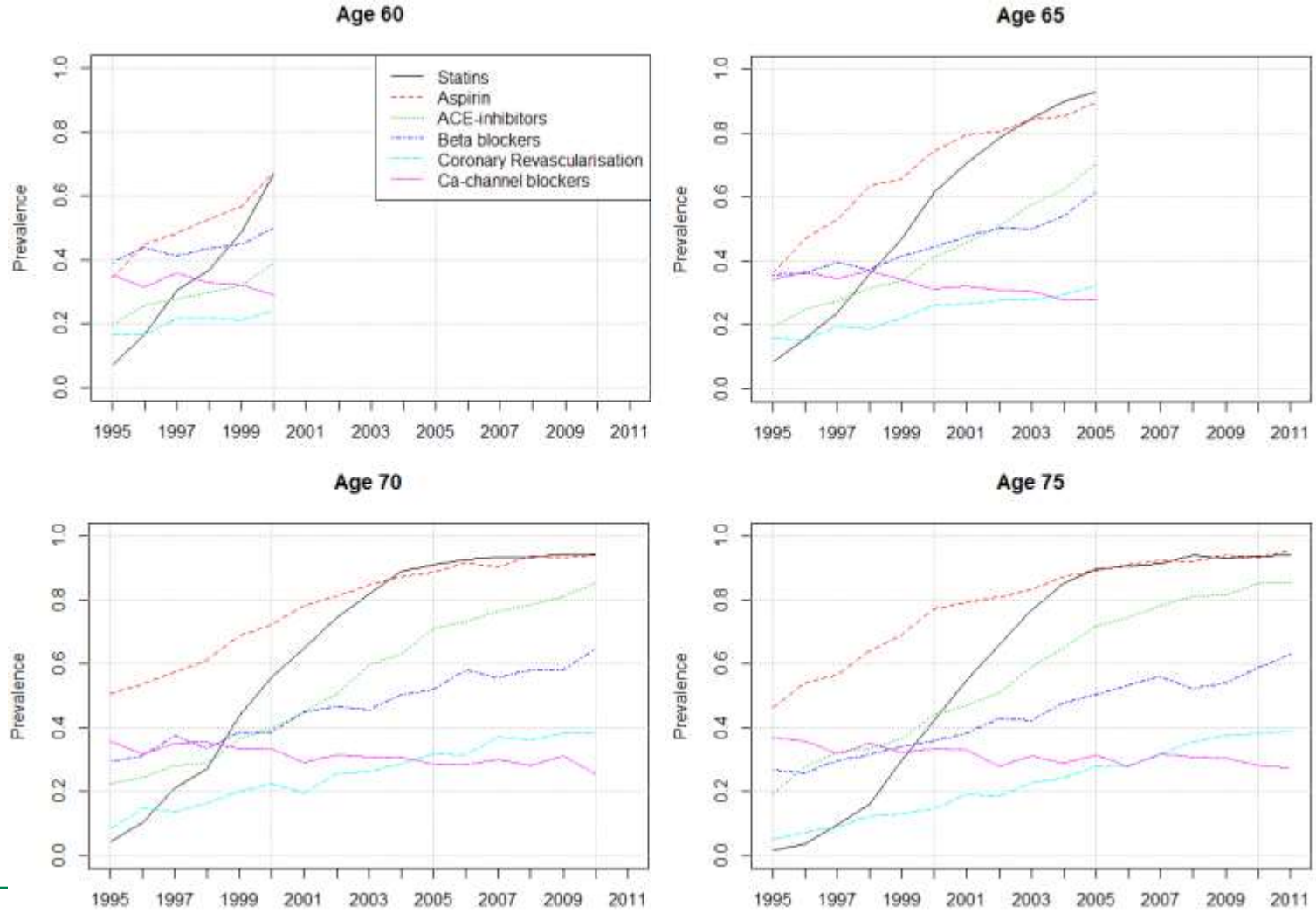
Data selection

- 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



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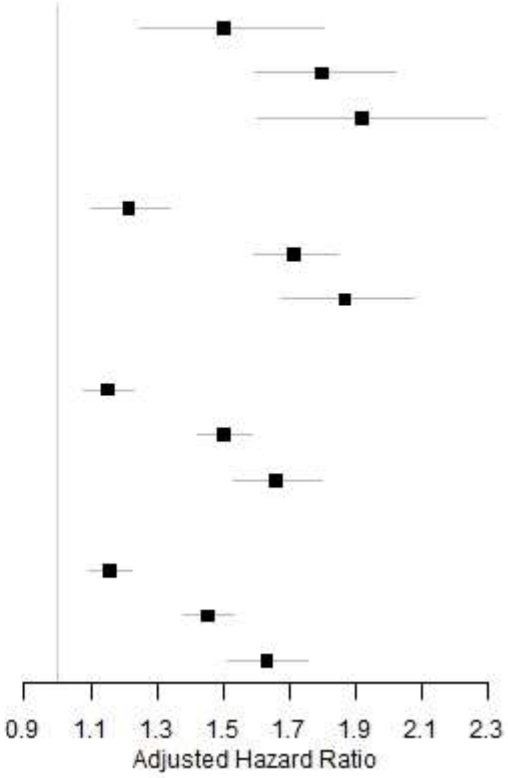
Survival prospects after AMI

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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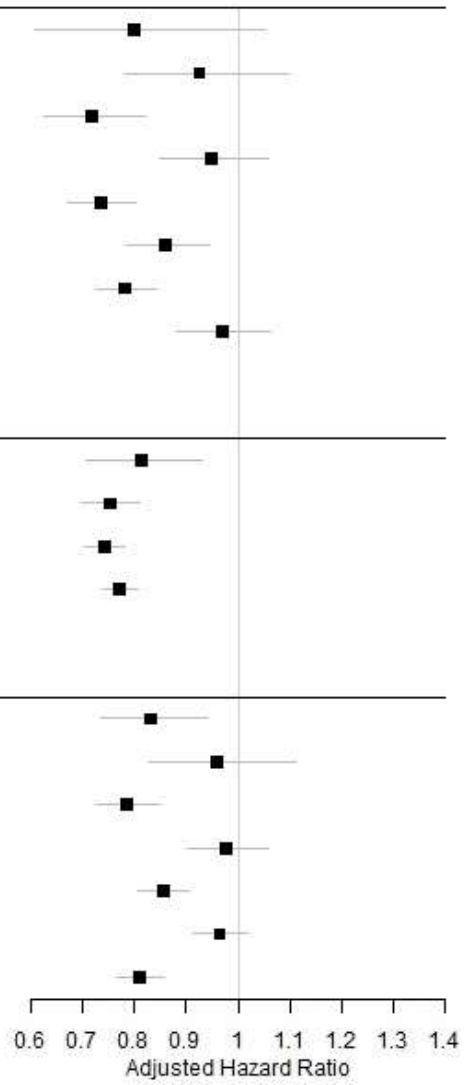
Survival prospects by treatments

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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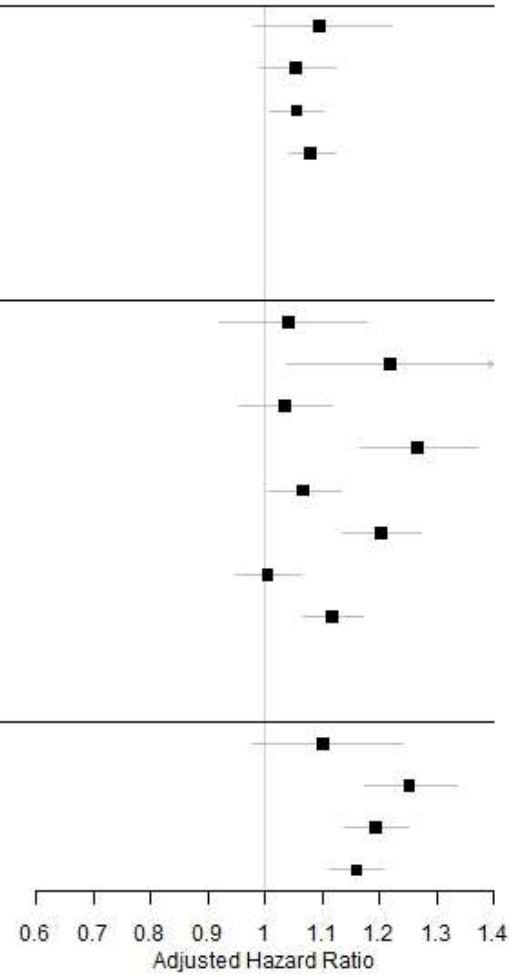
Survival prospects by treatments (cont.)

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:

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

(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	-1.1	0.8	0.9
65	-2.7	2.2	2.3	-1.3	1.0	1.1
70	-3.0	2.2	2.4	-0.9	0.7	0.8
75	-2.6	1.6	1.9	-0.9	0.6	0.7

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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Case Study 2

Intensive Blood Pressure Control and Life Expectancy

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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 > 140 mmHg (SBP1) which was lowered to less than 120; 7891 patients from 448 general practices
- Group 2: SBP lowered to 120-140 mmHg; 11276 patients matched to group 1 on age, sex and GP practice

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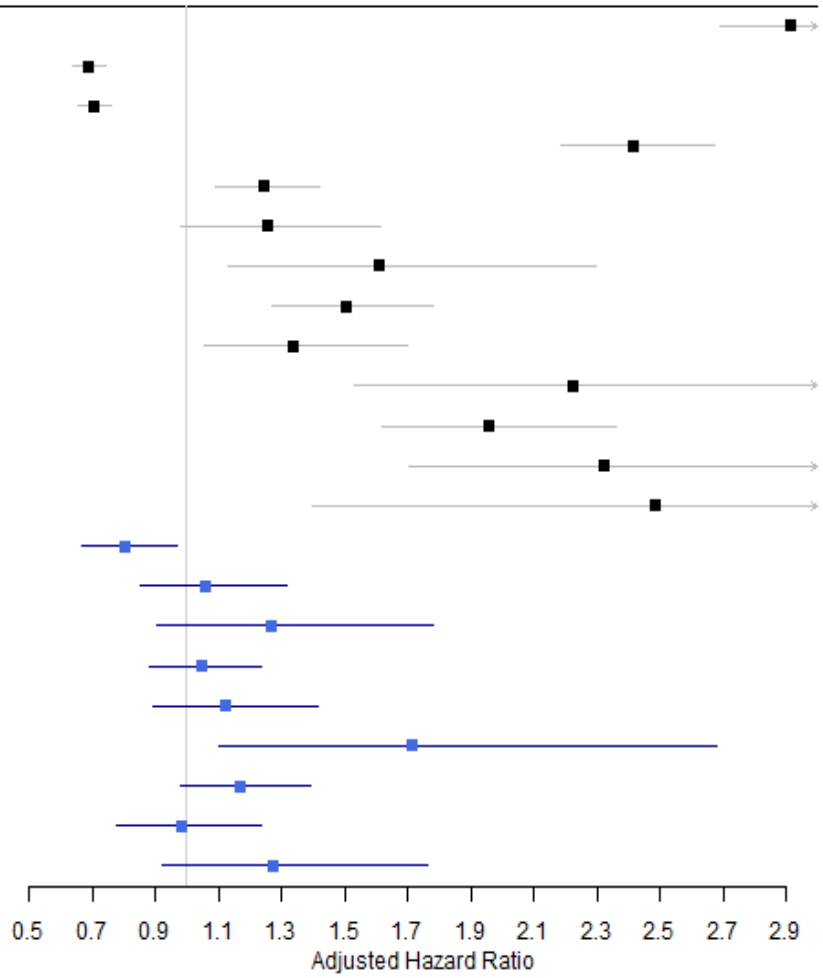
Mortality in THIN: Intensive vs Standard SBP control

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.

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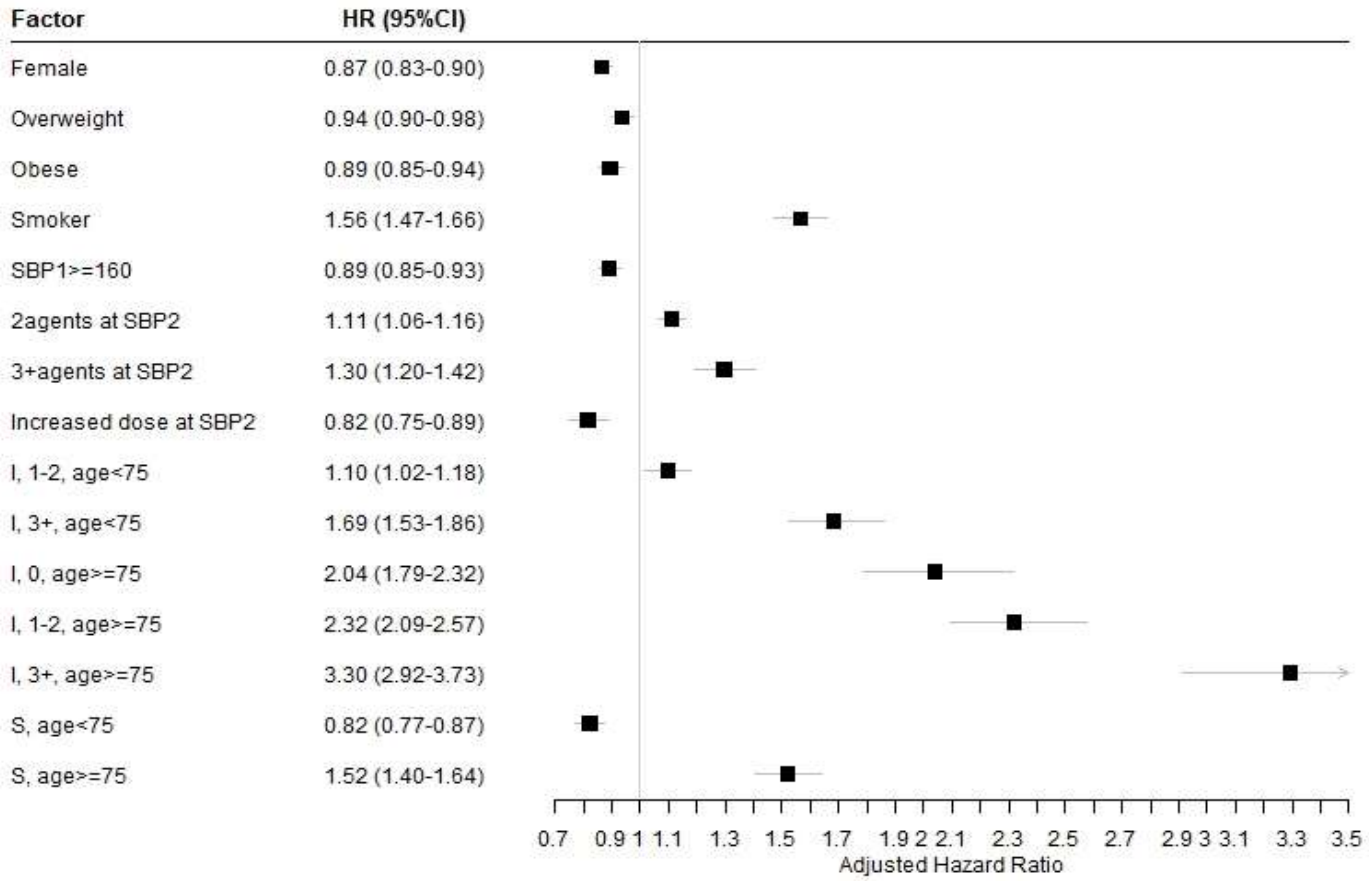
Mortality: extra prescriptions

- 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.

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

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Impact

Medicine and public health

- Inform guidelines on treatment/management of cholesterol, blood pressure, and cardiovascular disease
- Clinicians discuss risks and benefits of treatment initiation with their patients

NICE guidelines

PLOS ONE

RESEARCH ARTICLE

Survival Benefits of Statins for Primary Prevention: A Cohort Study

Lisanne A. Gitsels[1]*, Elena Kulinskaya[1], Nicholas Steel[2]

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OPEN ACCESS

Citation: Gitsels LA, Kulinskaya E, Steel N (2016) Survival Benefits of Statins for Primary Prevention: A Cohort Study. PLoS ONE 11(11): e0166847. doi:10.1371/journal.pone.0166847

Abstract

Objectives

Estimate the effect of statin prescription on mortality in the population of England and Wales with no previous history of cardiovascular disease.

Methods

Primary care records from The Health Improvement Network 1987–2011 were used. Four cohorts of participants aged 60, 65, 70, or 75 years at baseline included 118,700, 199,574, 247,149, and 194,085 participants; and 1.4, 1.9, 1.8, and 1.1 million person-years of data,

- NICE recommend that GPs ‘offer atorvastatin 20 mg for the primary prevention of CVD to people who have a 10% or greater 10-year risk of CVD’
- Four out of five men over 50, and most women over 60 in the UK

- ‘There was no reduction in all-cause mortality for statin prescription initiated in participants with a QRISK2 score <10% at any baseline age, or in participants aged 60 at baseline in any risk group. Mortality was lower in participants with a QRISK2 score 20%’

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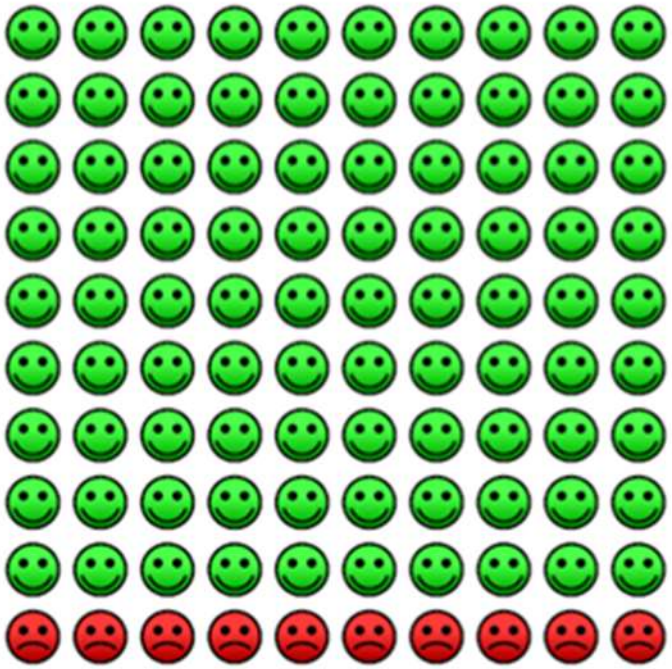
Risk of coronary heart disease and stroke 1

Cardiovascular risk 10% over 10 years: no treatment



If 100 people at this level of risk take no statin, over 10 years on average:

- 90 people will not develop CHD or have a stroke (the green faces)
- 10 people will develop CHD or have a stroke (the red faces).

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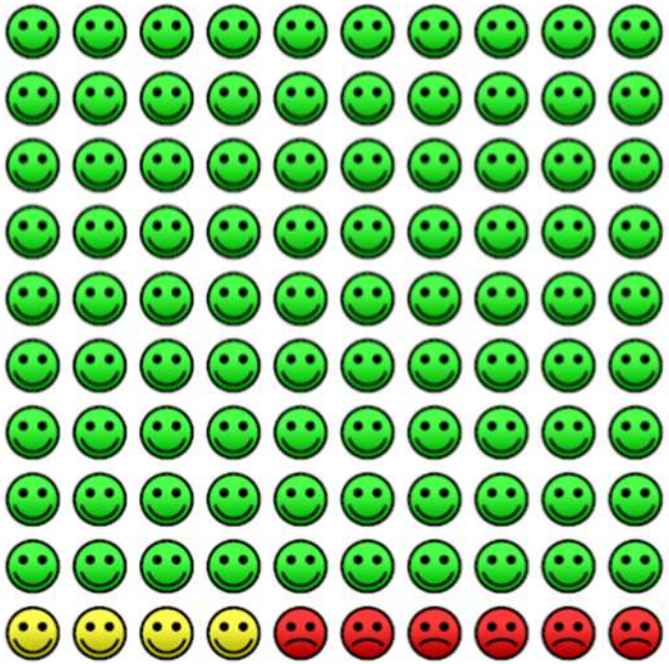
Risk of coronary heart disease and stroke 2

Cardiovascular risk 10% over 10 years: taking atorvastatin



If all 100 people take atorvastatin for 10 years, over that time on average:

- 4 people will be saved from developing CHD or having a stroke (the yellow faces)
- 90 people will not develop CHD or have a stroke, but would not have done anyway (the green faces)
- 6 people will still develop CHD or have a stroke (the red faces).

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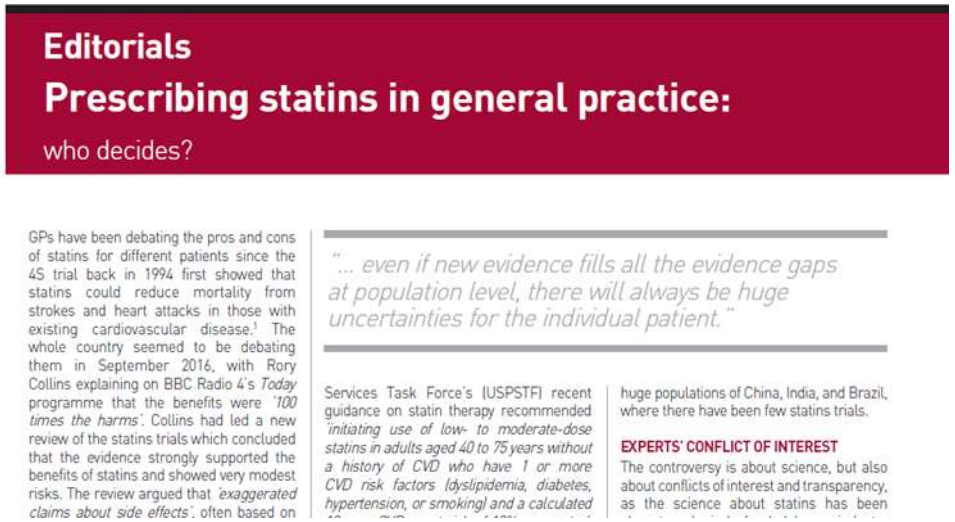
Value of observational data



Editorials

Prescribing statins in general practice:

who decides?

GPs have been debating the pros and cons of statins for different patients since the 4S trial back in 1994 first showed that statins could reduce mortality from strokes and heart attacks in those with existing cardiovascular disease.[1] The whole country seemed to be debating them in September 2016, with Rory Collins explaining on BBC Radio 4's *Today* programme that the benefits were *'100 times the harms'*. Collins had led a new review of the statins trials which concluded that the evidence strongly supported the benefits of statins and showed very modest risks. The review argued that *'exaggerated claims about side effects'*, often based on

"... even if new evidence fills all the evidence gaps at population level, there will always be huge uncertainties for the individual patient."

Services Task Force's (USPSTF) recent guidance on statin therapy recommended *'initiating use of low- to moderate-dose statins in adults aged 40 to 75 years without a history of CVD who have 1 or more CVD risk factors (dyslipidemia, diabetes, hypertension, or smoking) and a calculated*

huge populations of China, India, and Brazil, where there have been few statins trials.

EXPERTS' CONFLICT OF INTEREST

The controversy is about science, but also about conflicts of interest and transparency, as the science about statins has been

- longer follow up periods than the usual 3-5 years in trials
- lack of trial data on the elderly
- difficulty comparing baseline risk in trials with QRISK2
- generalisability from highly selected trial participants to the general population

Steel et al. *British Journal of General Practice* 2017

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Insurance and government

- Pricing and reserving for longevity risk (annuities, pension liabilities, etc.) and morbidity and mortality risk
- Predicting volumes of coverage of medical procedures
- Predicting changes in population life expectancy.

Individual

- Information on average life expectancy (and confidence limits)
- How to structure retirement funds
- Lifestyle changes can be made (e.g. stop smoking)
- Potential benefits and harms of treatments at population level

References

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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.

Questions

Comments

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

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