Institute and Faculty of Actuaries

# Use of routinely collected primary care data to model longevity and longevity improvement

Elena Kulinskaya & Lisanne Gitsels,
University of East Anglia

7 September 2016

# Content

- Big Data and Statistics
- Big Data Research at UEA
- IFoA grant on modelling longevity
  - Aims
  - Methodology
- Case Study on Statins
  - Rationale
  - Study design & Methodology
  - Results
- Discussion

Institute and Faculty of Actuaries

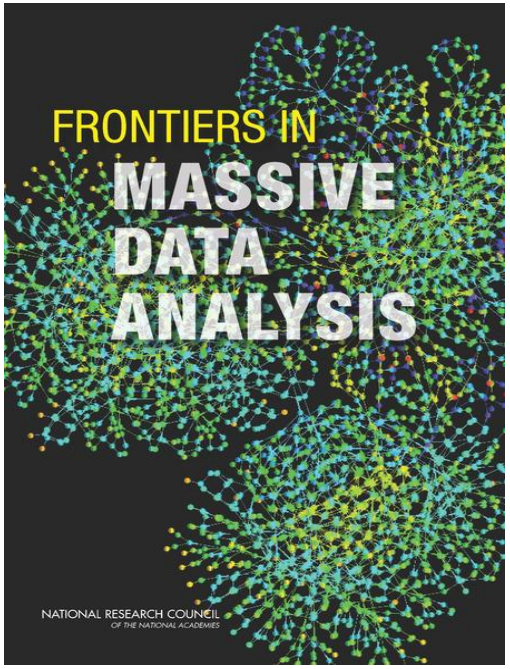
# Data explosion

“90% of the data in the world today has been created in the last two years alone. Some estimate that data production will be 44 times greater in 2020 than it was in 2009. Others estimate an additional 2.5 quintillion bytes of data is being generated every day.”

Australian Public Service Big Data Strategy, Commonwealth of Australia 2013.

“We now create as much information in two days as humans did from the beginning of history to 2003.”

Eric Schmidt, Google CEO, 2010.




Institute and Faculty of Actuaries

# Fields and Disciplines

Access to unprecedented volumes and complexity of data collected by government, businesses, and social media provides a seemingly unlimited resource for harvesting new knowledge.

Big Data arise in such fields  as genomics, public health, environmental sciences, neuroscience, and business.

Basic issues of management and storage have primarily implicated computer science, underpinning initiatives sometimes described as business analytics or data science.

Statistical science has not played a prominent role. Because practical problem solving has proceeded rapidly, the science has lagged behind and work to identify the statistical features associated with Big Data has been largely ad hoc.

The Alan Turing Institute:  Cambridge, Edinburgh, Oxford, Warwick and UCL.

Institute and Faculty of Actuaries

# Google Flu example

## Why Google Flu Is A Failure

**Steven Salzberg,** CONTRIBUTOR
*Fighting Pseudoscience* **FULL BIO**
Opinions expressed by Forbes Contributors are their own.

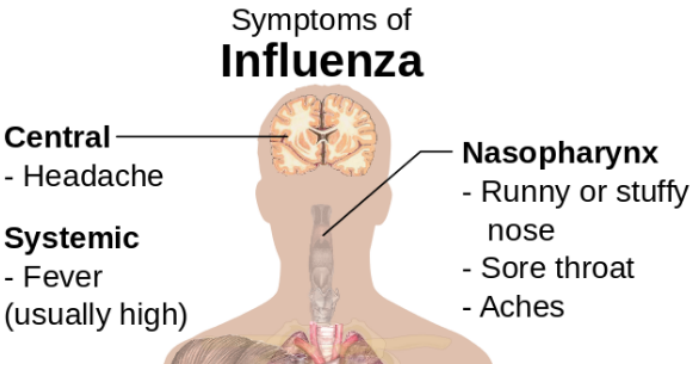
It seemed like such a good idea at the time.

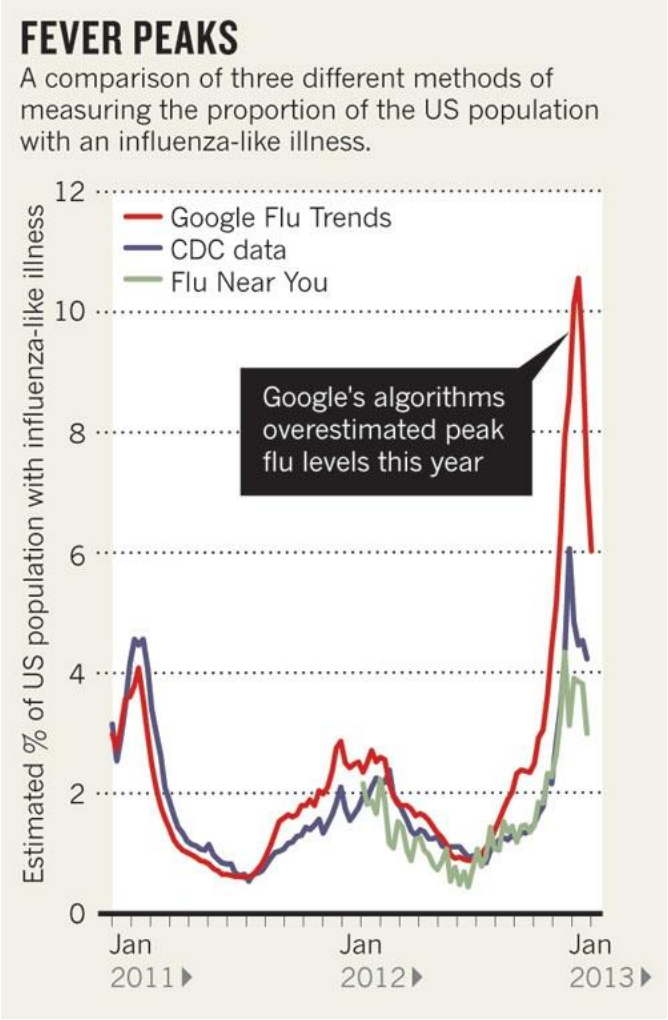
People with the flu (the influenza virus, that is) will probably go online to find out how to treat it, or to search for other information about the flu. So Google GOOG +0.58% decided to track such behavior, hoping it might be able to predict flu outbreaks even faster than traditional health authorities such as the Centers for Disease Control (CDC).

Instead, as the authors of a new article in *Science* explain, we got "big data hubris." David Lazer and colleagues explain that:

> "Big data hubris" is the often implicit assumption that big data are a substitute for, rather than a supplement to, traditional data collection and analysis.

The folks at Google figured that, with all their massive data, they could outsmart anyone.




Institute and Faculty of Actuaries

# Statistical Problems in Big Data

- False positives arising from multiple exploratory analyses
- Biases due to peculiarities of units, outcomes or settings
- Missing data
- Inadequate linkage strategies
- Data gathered at varied levels such as transaction, person, organization, community, and state
- Causal Inference from (mostly) correlational data
- Modelling heterogeneity

Institute and Faculty of Actuaries

# ESRC Business and Local Government Data Research Centre (BLG DRC)

- Funded under the ESRC's Big Data Network, £5m, 2014-19
  - An Eastern ARC (Essex, UEA & Kent) partnership
- Exploitation of data to benefit researchers, data owners and society
- Facilitating access to data, stimulating innovative policy/practice-relevant research
- Highest ethical standards, anonymised data used non-disclosively
- Training for researchers and other users
- Business Engagement Programme
- Research programme including methodology of Big Data analytics
- Data can be safely accommodated at the UK Data Archive at Essex, and safe access is possible in different formats, including through the safe rooms at UEA and Essex.

ESRC Business and Local Government Data Research Centre

University of Essex

UEA University of East Anglia

University of Kent

LSE

Institute and Faculty of Actuaries

# 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, Senior Lecturer, CMP;

Prof Ruth Hancock, NMS, Prof Nick Steel, NMS.

**Aviva co-investigators**

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

Institute and Faculty of Actuaries

# Main objectives

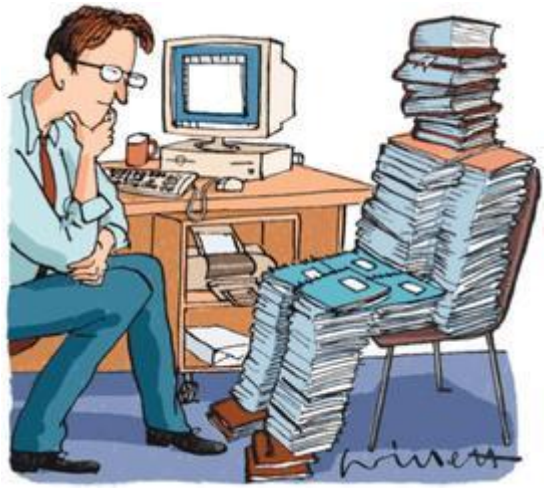
**Development of novel statistical and actuarial methods for:**

- Modelling mortality
- Modelling trends in morbidity and uptake of health interventions
- Assessing basis risk
- Evaluating longevity improvement based on Big Health and Actuarial Data
- Tools to forecast longevity risk of a book


Institute and Faculty of Actuaries

# 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 01.01.2015, this includes 3.4 million patients
- Added various social economic status variables such as IMD and Mosaic
- The Continuing Mortality Investigation (CMI) data



Institute and Faculty of Actuaries

# Aim 1: Identification and quantification of the key factors affecting mortality/ longevity

- 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 may include type 2 diabetes or heart failure.
- Health interventions may include an introduction of NICE guidelines on use of particular health sustaining drugs such as calcium-channel blockers, or targeted outcomes such as the blood pressure targets.
- Lifestyle factors may include obesity or smoking.

Institute and Faculty of Actuaries

# Design and methods

- For each of these conditions we will design a population-based prospective 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, and 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, multilevel modelling and multiple imputation will be used.

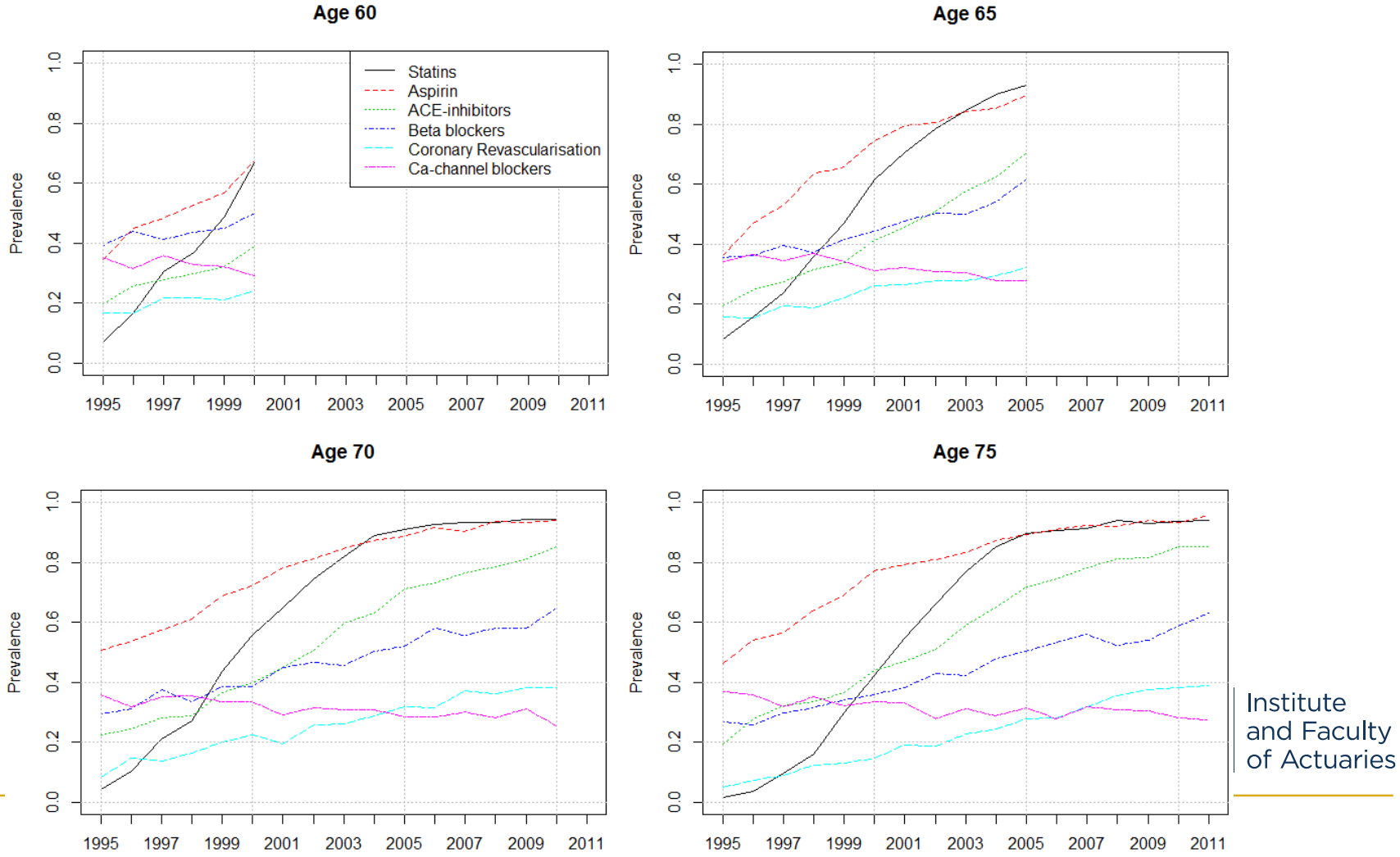
Institute and Faculty of Actuaries

# Aim 2. Modelling of temporal changes in the factors affecting morbidity and mortality

- Trends in the incidence and/or prevalence of particular medical conditions and/or lifestyle factors will also be obtained from the primary care data.
- This will enable us to establish patterns due to social or geographic inequalities, such as socio-economic status (SES), age or postcode lottery.
- For instance, the patients in the more deprived areas may be disadvantaged in regards to the latest interventions and/or public health campaigns at least initially. This will result in widening the gap in longevity between individuals from different backgrounds.
- Thus 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.

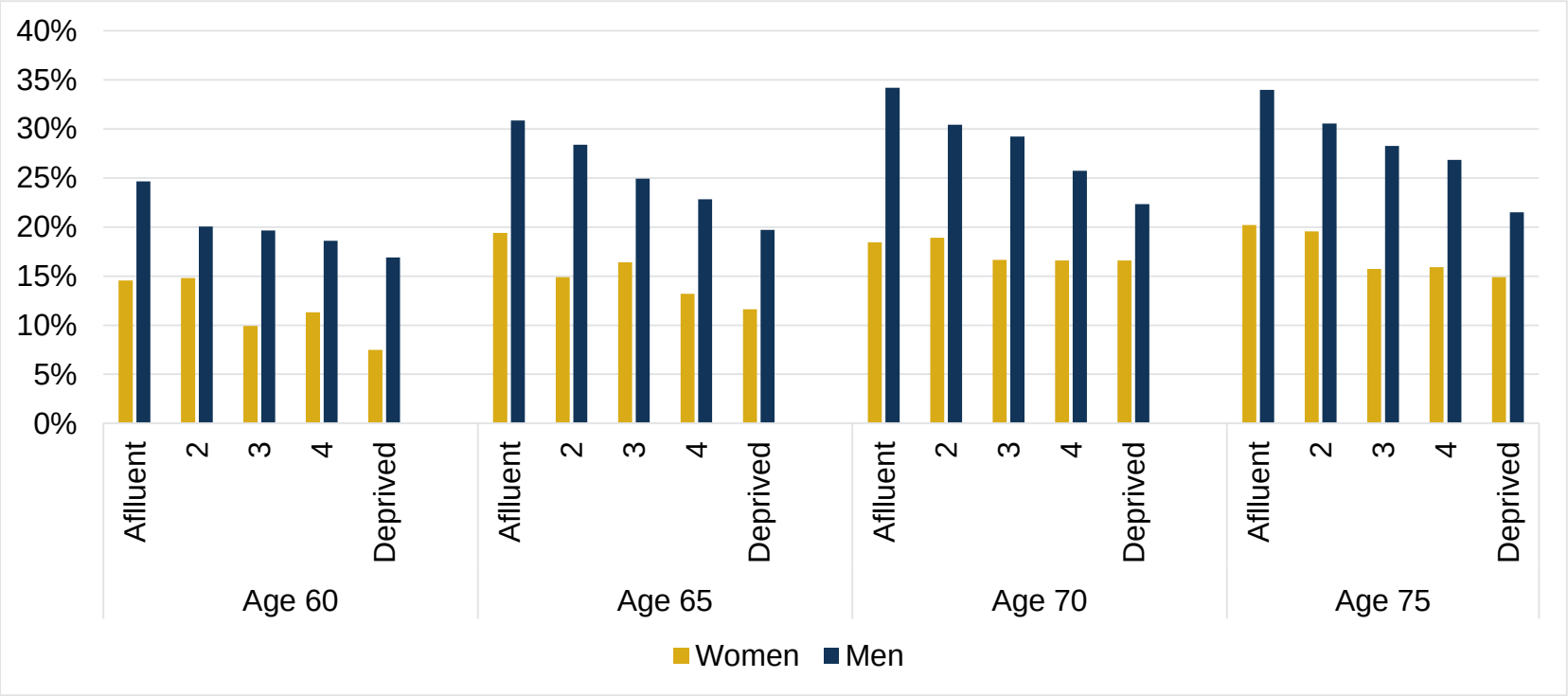
Institute and Faculty of Actuaries

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




Institute and Faculty of Actuaries

# Example: Coronary Revascularisation given IHD




Institute and Faculty of Actuaries

# Aim 3. Evaluation of plausible scenarios in mortality trends due to particular medical advances or lifestyle changes on the population of insureds

As often happens with the existing portfolio of insured lives, the minute health details of a life are not available.  Instead, the interest lies in the mortality trends of the whole book.

To be able to provide this information, three components are required:

- established in Aim 1 model for survival differentials associated with a particular disease or intervention;
- developed in Aim 2 model for the incidence/ prevalence of this condition or uptake of this intervention over time,
- and the sufficient knowledge of the population to which it is desired to translate trends in longevity established in general population to be able to assess the basis risk.

Institute and Faculty of Actuaries

# Aim 4. Tools to forecast longevity risk of a book

- We will develop an R package incorporating our models and providing analytical and graphical means to forecast longevity of a general UK population, and also of a population of a user defined composition under a number of scenarios for changes in disease incidence, health behaviours and treatments.
- This will be an open source software available from the project website along with an accompanying manual for its use.
- We also intend to develop teaching materials for the actuarial community on the modelling techniques used in the project, and the use of the developed R package. These materials will be available from the project website.

Institute and Faculty of Actuaries

Institute and Faculty of Actuaries

# Case Study

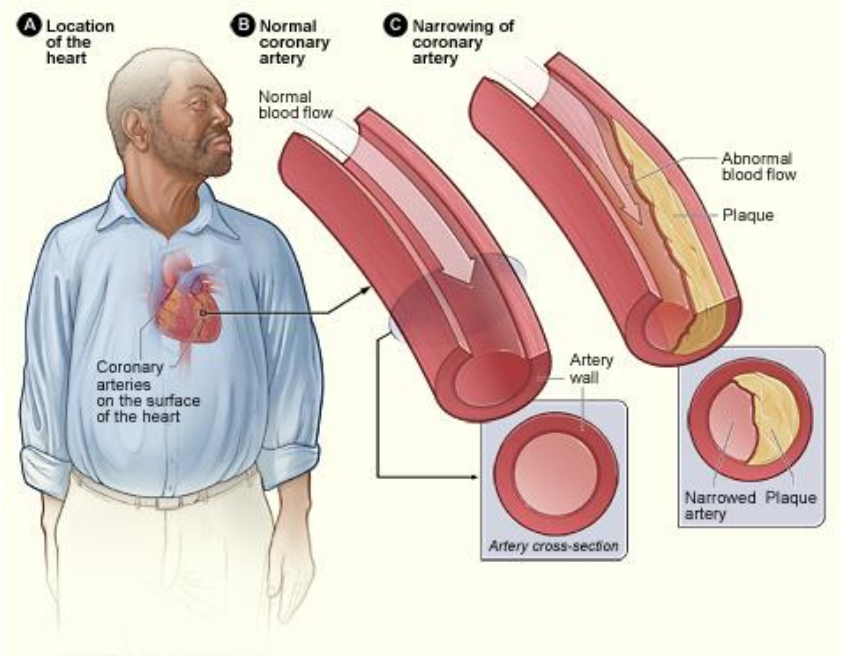
## Statins and Life Expectancy



7 September 2016

# Cardiovascular disease (CVD)

- Disease of the heart or blood vessels, e.g. heart attack and stroke
- Leading cause of global and UK death: 33%
- Risk factors for CVD:
  - High blood pressure (hypertension)
  - Smoking
  - High blood cholesterol
  - Diabetes
  - Lack of exercise
  - Being overweight or obese
  - Family history / ethnic background




Institute and Faculty of Actuaries

# Primary prevention of CVD

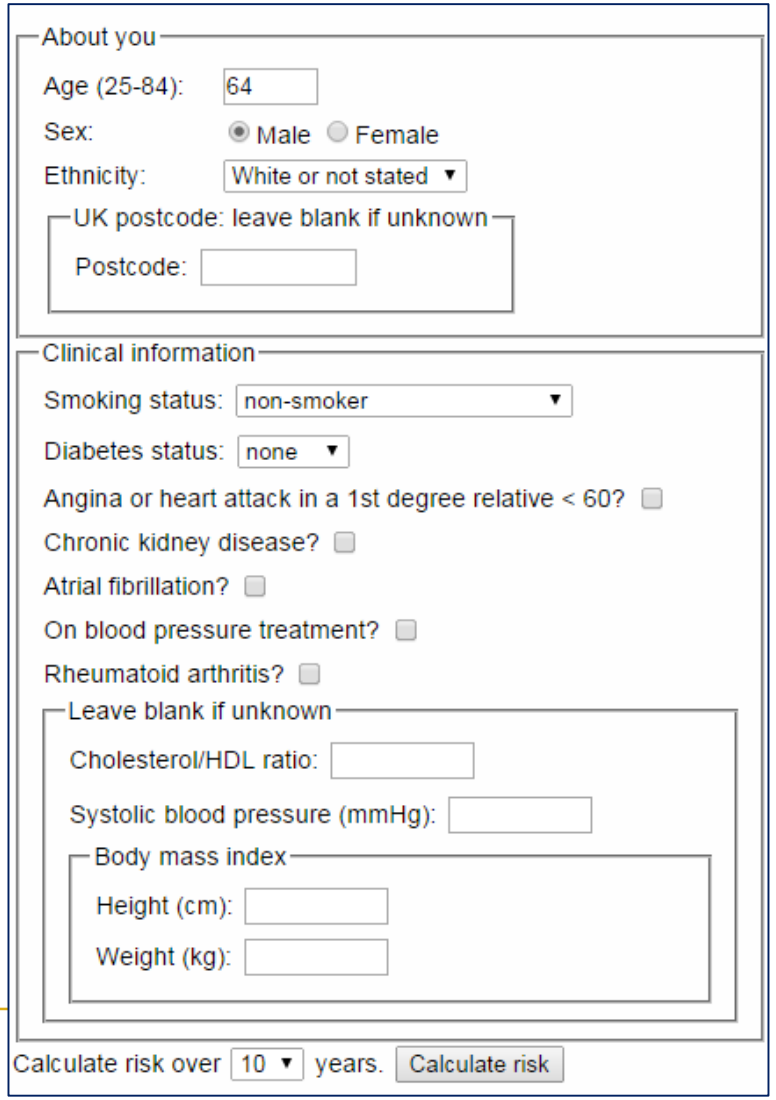
Primary prevention: no previous history of CVD

- Example: lipid-lowering therapy - statins

National Institute of Health and Clinical Excellence (NICE):

- *Offer atorvastatin 20 mg for the primary prevention of CVD to people who have a 10% or greater 10-year risk of developing CVD.*
- *Estimate the level of risk using the QRISK2 assessment tool*
- www.nice.org.uk/guidance/cg181/
- www.qrisk.org/2016/

Up to 17 million UK residents eligible for statins



# Previous research on effectiveness of statins

Meta-analysis of 27 randomised clinical trials by Cholesterol Treatment Trialists' (CTT) Collaborators, The Lancet 2015 (http://dx.doi.org/10.1016/S0140-6736(14)61368-4)

- Overall 9% relative reduction in all-cause mortality with statins
- Equivalent to absolute reduction of 1 per 1,111 patients per year per mmol – others no benefit

**Webfigure 9: Effects on any deaths per 1.0 mmol/L reduction in LDL cholesterol at different levels of risk, by history of vascular disease and overall**

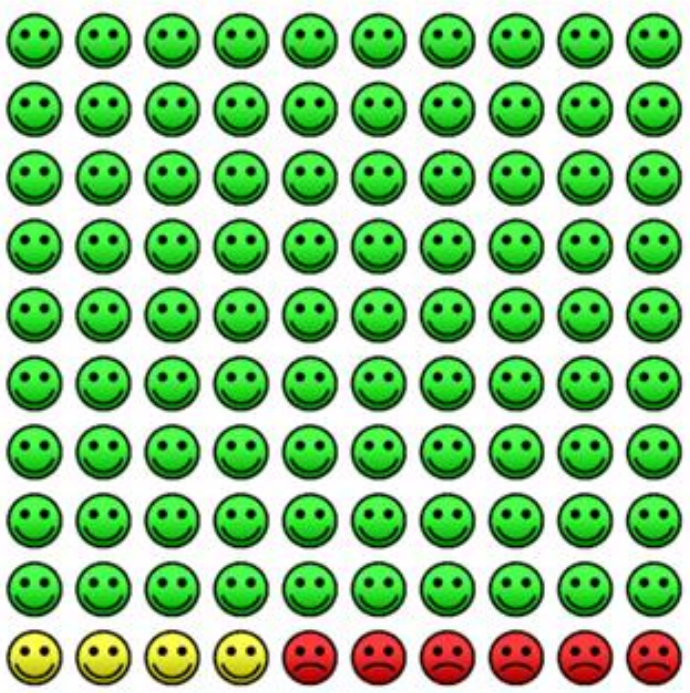
| 5−year MVE risk at baseline | Deaths (% per annum) Statin/more | Control/less | RR (CI) per 1.0 mmol/L reduction in LDL cholesterol | Trend test |
|---|---|---|---|---|
| **Participants without vascular disease** | | | | |
| < 5% | 164 (0.38) | 177 (0.41) | 0.94 (0.71 − 1.26) | |
| ≥ 5%,<10% | 372 (0.77) | 446 (0.93) | 0.83 (0.69 − 0.99) | |
| ≥ 10%,<20% | 703 (1.99) | 778 (2.19) | 0.88 (0.76 − 1.02) | $\chi^2_1$=1.57 |
| ≥ 20%,<30% | 363 (5.13) | 339 (4.73) | 1.06 (0.86 − 1.32) | (p=0.2) |
| ≥ 30% | 192 (10.76) | 192 (11.44) | 0.94 (0.70 − 1.25) | |
| **Subtotal** | **1794 (1.33)** | **1932 (1.42)** | **0.91 (0.85 − 0.97) p= 0.007** | |

Institute and Faculty of Actuaries

# Cates plot for benefits of statin treatment

https://www.nice.org.uk/guidance/cg181/resources/patient-decision-aid-243780157

**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).



Institute and Faculty of Actuaries

# Limitations of statin trials

- Randomised clinical trials are the ‘gold standard’ for evidence of effectiveness
  - Confounders randomized equally to both groups (in theory)
- Generalisability from trial participants to general population
  - Exclusion on grounds of age, comorbidity, intolerance to intervention
- Short follow-up
  - Maximum 5 years
- Commercial trial data not available for individual scrutiny
  - Lack of transparency
- Large observational datasets can fill these gaps with robust statistical analyses

Institute and Faculty of Actuaries

# Research question

What is the survival benefit associated with statin prescription as primary prevention of cardiovascular disease for different risk groups at various ages in the general population?

Institute and Faculty of Actuaries

# Design and Data Selection

- Population-based prospective cohort study
- Restrictions data:
  - Medical records from 1987 to 2011 of people born between 1920 and 1940
- Target ages:
  - 60, 65, 70, and 75
- Exclusion:
  - Patients with a history of cardiovascular disease

Institute and Faculty of Actuaries

# Missing Data

Incomplete records in: BMI, smoking status, and risk of cardiac event

Multiple imputation

- Joint modelling
  - Linear regression for BMI and risk of cardiac event
  - Ordered probit regression for smoking status
- Multilevel on GP practice
- MCMC (Monte Carlo Markov Chain) 500 iterations resulting in 10 imputed datasets
- REALCOM-Imputation software

# Model specification

Cox's proportional hazard regression estimates the hazard $\lambda_{ij}$ for patient *i* from GP practice *j*: $\lambda_{ij} = \lambda_0(t)\, Z_j\, e^{\beta X_{ij}}$

where $\lambda_0$ = baseline hazard (function of time),
$Z_j$ = shared frailty term on GP practice (constant),
$\beta$ = coefficients (constant),
and $X_{ij}$ = exposures, e.g. statins (constant).

Models specified:

- Ages: 60, 65, 70, and 75
- Risk groups:
  - Low <10% risk of cardiac event
  - Moderate 10-19% risk of cardiac event
  - High ≥20% risk of cardiac event

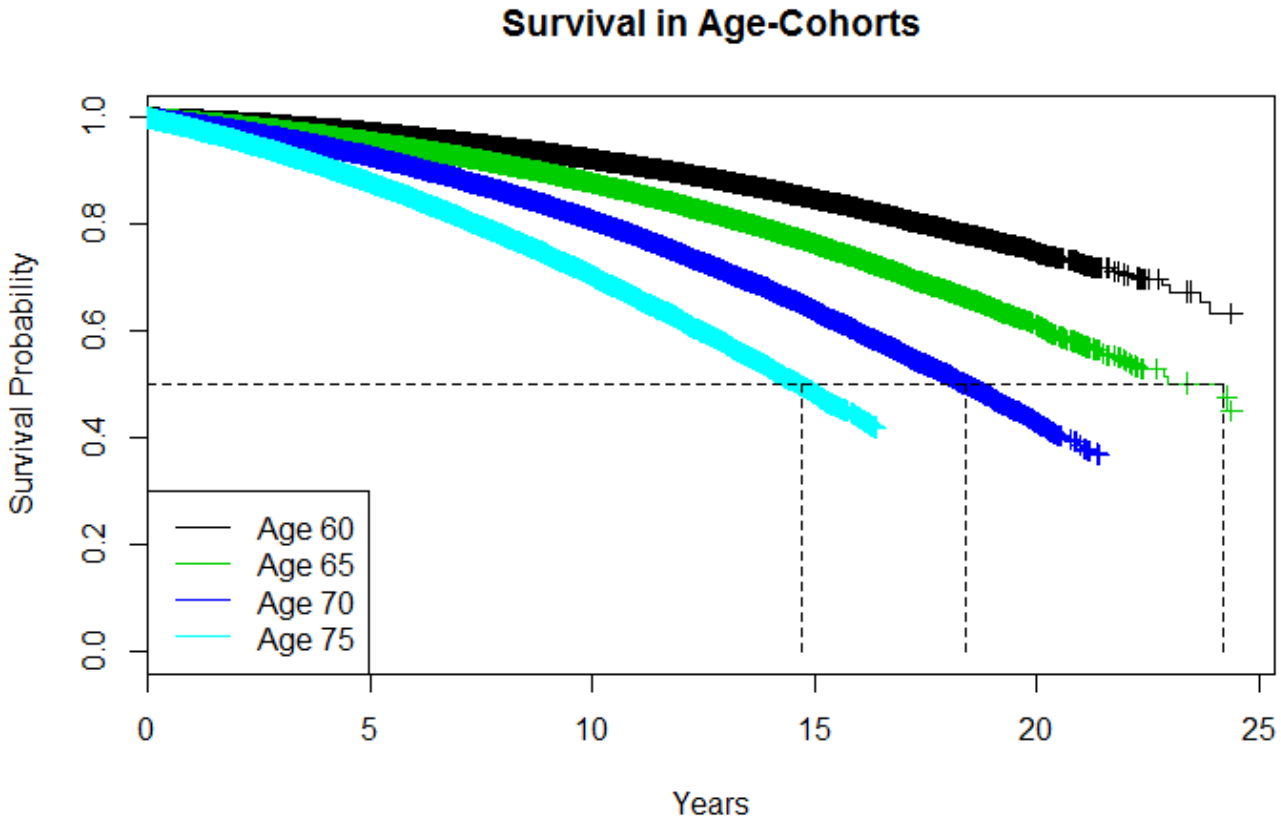
Institute and Faculty of Actuaries

# Cohorts' characteristics

| Cohort | Number of patients | Number of deaths | Average follow-up time | Maximum follow-up time |
|---|---|---|---|---|
| Age 60 | 118,700 | 15,296 (12.8%) | 12 years | 24 years |
| Age 65 | 199,574 | 28,848 (14.5%) | 10 years | 24 years |
| Age 70 | 247,149 | 40,699 (16.5%) | 7 years | 21 years |
| Age 75 | 194,085 | 37,356 (19.2%) | 6 years | 16 years |

Institute and Faculty of Actuaries

# Kaplan-Meier Plot



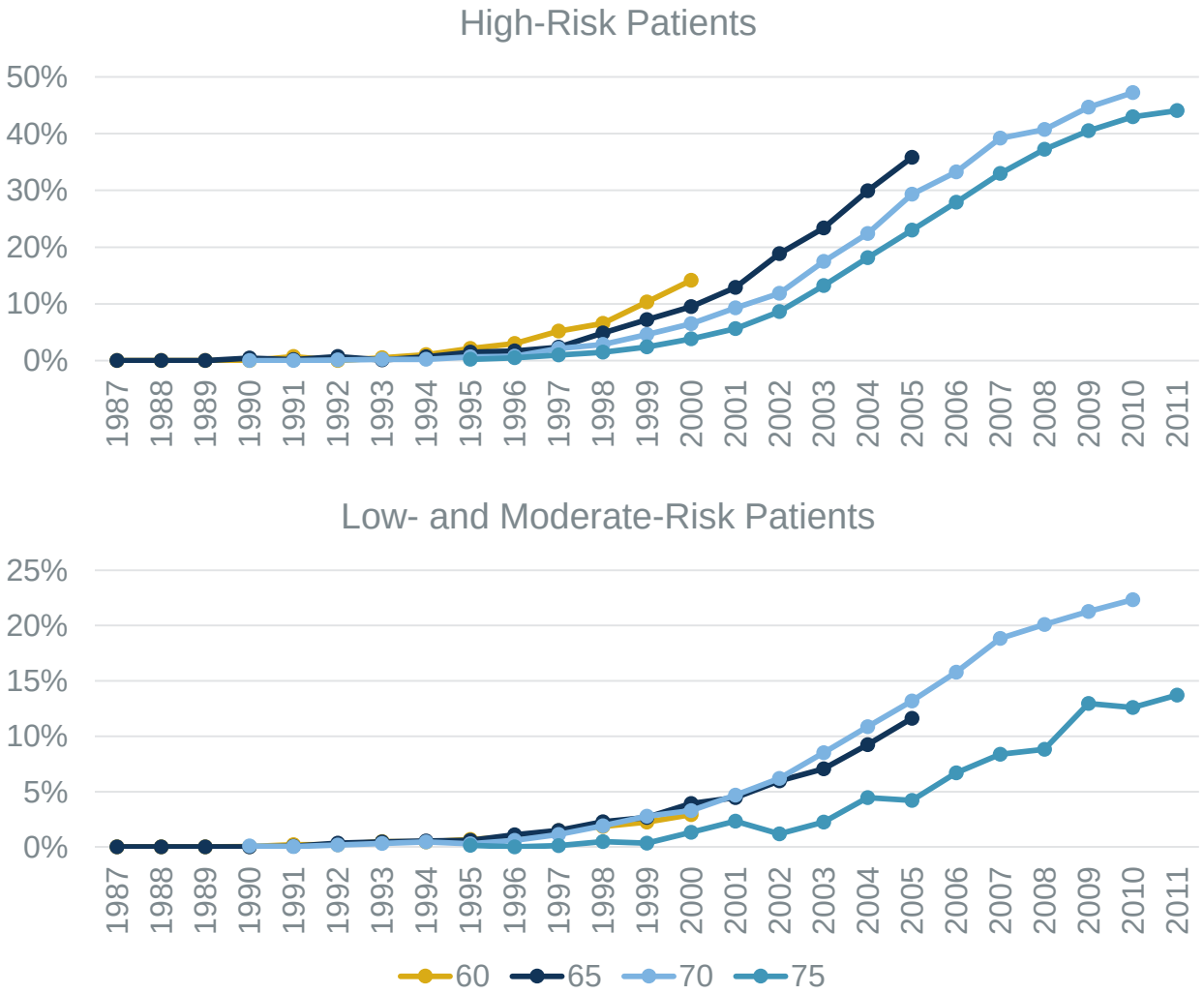

Institute and Faculty of Actuaries

# Distribution men and women across risk group

| Cohort | Cardiac risk | Women % (Statins %) | Men % (Statins %) |
|---|---|---|---|
| Age 60 | Low | 83 (1.2) | 16 (0.4) |
| | Moderate | 16 (3.7) | 78 (1.3) |
| | High | 1 (11.9) | 6 (5.2) |
| | | | |
| Age 65 | Low | 40 (2.2) | 0 (0.0) |
| | Moderate | 55 (7.4) | 72 (3.2) |
| | High | 5 (26.9) | 28 (12.4) |
| | | | |
| Age 70 | Moderate | 80 (9.5) | 17 (5.4) |
| | High | 20 (28.2) | 83 (17.4) |
| | | | |
| Age 75 | Moderate | 15 (4.6) | 0 (0.0) |
| | High | 85 (19.6) | 100 (19.1) |

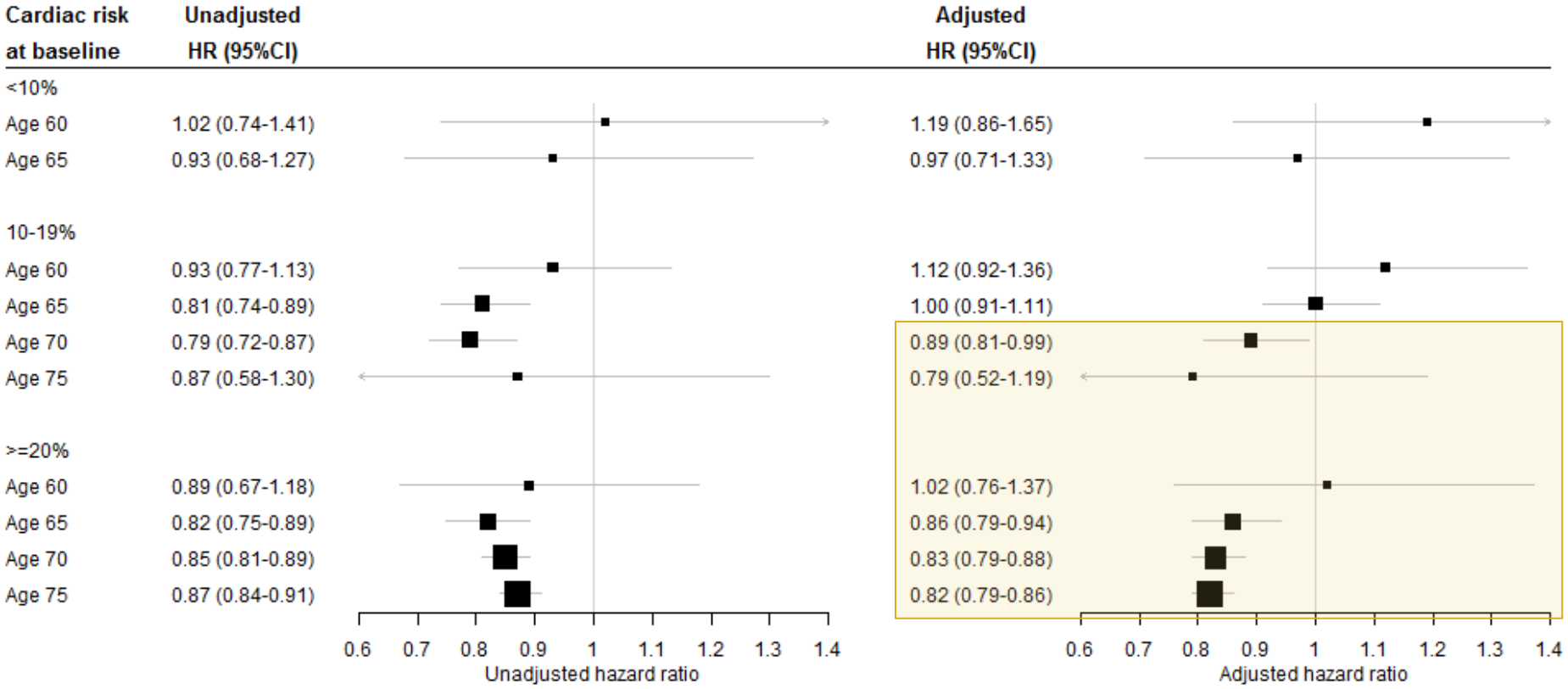
Institute and Faculty of Actuaries

# Uptake of statins by risk group




Institute and Faculty of Actuaries

# Hazard of mortality associated with statin prescription




The adjusted hazard ratios (HR) take into account sex, year of birth, postcode, diabetes, high cholesterol level, blood pressure regulating drugs, body mass index, smoking status, and general practice.

Institute and Faculty of Actuaries

# Impact

## Medicine and Public Health

Are current guideline thresholds for statin therapy for primary CVD prevention too low?

- Overtreatment of people under 60 and at <10% risk?
- Recent extension of guidelines to younger and lower risk groups may need to be reconsidered?
- Clinicians discuss risks and benefits of statin initiation with their patients

## Further research

Needed on statins for primary prevention:

- People under 65
- People with 10-year cardiac risk <10%
- Individual data on low risk patients in clinical trials

Institute and Faculty of Actuaries

# Impact cont.

## 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.

## Personal

- Information on average life expectancy (and confidence limits)
- How to structure retirement funds
- Lifestyle changes can be made (e.g. stop smoking)
- Potential benefits of statins after age 70 at population level

Institute and Faculty of Actuaries

# Questions

# Comments

Expressions of individual views by members of the Institute and Faculty of Actuaries and its staff are encouraged.

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

Institute and Faculty of Actuaries