The Actuarial Profession
making financial sense of the future

Modelling the Effects of Treatments for Heart Disease
Workshop D4

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Plan of Talk

1. Background
2. Model
3. Data
4. Parameter estimation
5. Applications
6. Questions

Background

Increasing life expectancy

Year	UK Males - Age			
	0	30	50	70
1981	70.8	42.7	24.1	10.1
1991	73.2	44.7	26.0	11.1
2001	75.7	46.9	28.3	12.5

Year	UK Females - Age			
	0	30	50	70
1981	76.8	48.2	29.2	13.3
1991	78.7	49.7	30.6	14.3
2001	80.4	51.2	32.1	15.2

(UK Office of National Statistics)

Background

UK actuarial profession (Faculty & Institute)

- Social Policy Board
  - Actuaries Panel on Medical Advances (APMA)
  - Terms of Reference:
    'To identify current and future medical advances that may affect future levels of mortality and health needs and the possible extent of the effect'
  - Research project:
    October 2004 → 2007, funded by EPSRC, supported by the UK actuarial profession

    Develop a continuous time/age model for an individual's life history incorporating significant events relating to IHD, Stroke and their risk factors
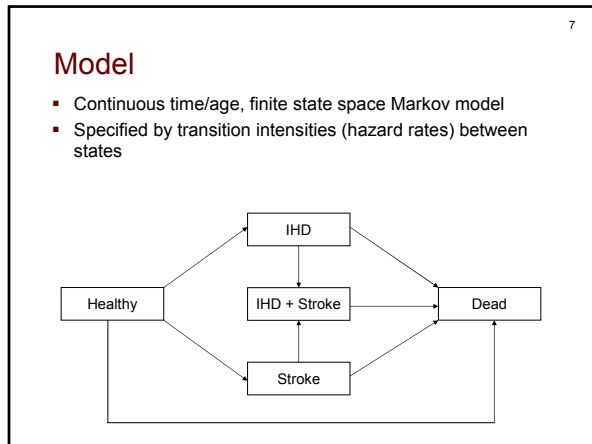
Background

- Ischaemic Heart Disease (IHD)
  Angina (Stable and Unstable)
  Myocardial Infarction (MI)
- Stroke
  Transient Ischaemic Attack
  Hard Stroke (HS) (Ischaemic and Haemorrhagic)
- Major risk factors
  Age
  Sex
  Smoking
  Hypertension
  Hypercholesterolaemia
  Diabetes
  Body Mass Index

Background

Uses of the model

- Quantify the effect of new treatments
  - Statins
- Quantify the effects of changes in behaviour
  - Smoking
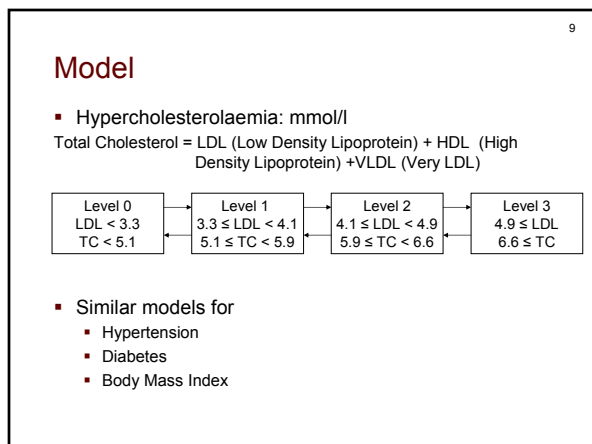- Quantify the effects of trends
  - Obesity

Model

- Continuous time/age, finite state space Markov model
- Specified by transition intensities (hazard rates) between states

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                    ┌───────┐
                    │  IHD  │
                    └───────┘
          ┌──────────┐  ┌────────────┐  ┌────────┐
          │ Healthy  │  │ IHD + Stroke│ │  Dead  │
          └──────────┘  └────────────┘  └────────┘
                    ┌────────┐
                    │ Stroke │
                    └────────┘
```

Model

- Healthy has 160 sub-states:

Risk Factor	Levels
Body Mass Index	5
Hypertension	4
Diabetes	2
Hypercholesterolaemia	4
Smoking	modelled deterministically

- Model allows for multiple cases of MI and HS
- IHD and/or Stroke = 10 separate states (x 160)
- Total number of states = 160 + 10 x 160 + 1 = 1761

Model

- Hypercholesterolaemia: mmol/l

Total Cholesterol = LDL (Low Density Lipoprotein) + HDL (High Density Lipoprotein) +VLDL (Very LDL)

Level 0	Level 1	Level 2	Level 3
LDL < 3.3	3.3 ≤ LDL < 4.1	4.1 ≤ LDL < 4.9	4.9 ≤ LDL
TC < 5.1	5.1 ≤ TC < 5.9	5.9 ≤ TC < 6.6	6.6 ≤ TC

- Similar models for
  - Hypertension
  - Diabetes
  - Body Mass Index

Data

Framingham data sets

	Sex	Original Cohort	Offspring & Spouses
Dates No. of Examinations		1948 – 1986 20	1971 – 1998 6
Total exposure (in years)	M	57,911	42,779
	F	77,545	45,449
Median age for exposure (years)	M	58	48
	F	59	47
No. cases of IHD	M	416	263
	F	322	105
No. cases of Stroke	M	279	51
	F	373	41
No. of deaths	M	1606	288
	F	1532	140

Parameter estimation

- Raw transition intensities
  - Occurrence/Exposure rates
- Smoothed transition intensities
  - Generalised linear model
    - Poisson errors
    - Log link
  - Include factors if significant
    - Statistically
    - Medically
  - Total number of parameters = 153

Parameter estimation

Significant factors

Transition	Age	Sex	Smoking	BMI	H'tens	H'chol	Diabetes	Cohort effect	IHD	Stroke
→ MI (1st)	(1)	(2)	(4)		(5)	(3)	(6)	(7) 1.60	-	
→ HS (1st)	(1)		(3)		(2)			(4) 2.05		-
H'tens → ←	•	•		•	-			-		
H'chol → ←	•	•				-		•		
Diabetes →	•	•		•			-	•		
←	•						-	•		
BMI → ←		•	•	-				-		
→ Dead	(1)	(6)	(5)	(7)	(2)	(10)	(9)	(8) 0.58	(3)	(4)

Parameter estimation

Transition intensities for Hard Stroke transition for Offspring Cohort, Current Smoker for different levels of Blood Pressure

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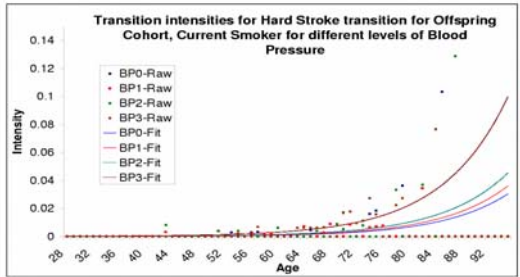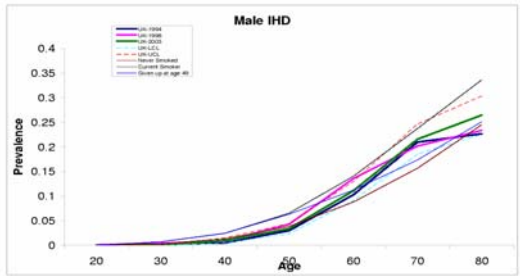
Parameter estimation

Parameterise model to reflect UK experience
- Adjustments to the coefficients from Framingham data
  - Age
  - Sex
  - Age-Sex interaction
  - Age Squared
  - Age Squared-Sex interaction
- No adjustments to other coefficients

Parameter estimation

Male IHD

Applications - Treatment

- Statins
  - Cholesterol lowering drugs
  - First licensed in the UK in 1987
  - Rosuvastatin licensed in 2003
- Effect
  - Standard dose reduces cholesterol by 1.8 mmol/l
  - Reduction in IHD risk increases over 5 years
  - Reduction in stroke risk is constant
  - % reduction in IHD/stroke risk is independent of baseline cholesterol level

Applications - Treatment

Condition	Years of treatment	% reduction in risk	
		1 mmol/l	1.8 mmol/l
IHD	1	11%	19%
	2	24%	39%
	3-5	33%	51%
	6 +	36%	55%
Stroke	All durations	10%	17%

Duration dependence → Semi-Markov model

Applications - Treatment

- Regimes
  - No treatment
  - Treated according to NCEP guidelines
  - Treated according to NCEP guidelines as well as everyone over the age of 55
  - Treated according to NCEP guidelines but with 30% take up rate
  - Treated on being diagnosed with IHD and/or Stroke
- Population profile
  - Starting age = 20
  - UK prevalence at age 20
  - Deterministic smoking profile (never, started before age 20 and given up at age 49 (Ex), current)

Applications - Treatment

Expected time to	Sex	Smoking category	Treatment regime				
			1	2	3	4	5
IHD, stroke or death	Male	Never	51.51	52.53	52.68	52.45	51.51
		Ex	48.51	49.72	49.85	49.59	48.51
		Current	44.25	45.85	46.03	45.69	44.25
	Female	Never	56.16	56.85	56.94	56.80	56.16
		Ex	53.63	54.34	54.43	54.28	53.63
		Current	49.32	50.32	50.49	50.23	49.32
Death	Male	Never	57.78	58.41	58.47	58.36	58.00
		Ex	54.93	55.66	55.71	55.59	55.15
		Current	50.18	51.20	51.29	51.11	50.41
	Female	Never	61.05	61.43	61.46	61.40	61.20
		Ex	58.55	58.96	58.99	58.92	58.71
		Current	54.01	54.60	54.67	54.54	54.17

Applications - Smoking

Relative risk at any time t (RR(t)) of MI and HS decreases with time since giving up smoking

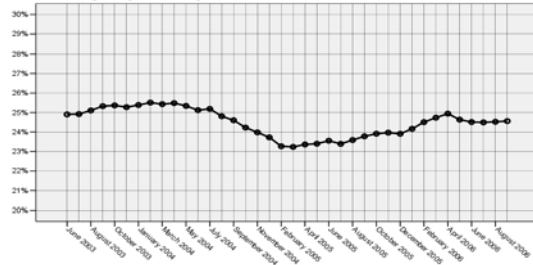$$RR(t) = [RR(0) - RR(\infty)] \, e^{-t/\tau} + RR(\infty)$$

where,	MI	HS
RR(0)	3.436	2.15
RR(∞)	1.1	1.1
τ years	1.59	1.35

Applications - Smoking

- Effect of ban on smoking in enclosed places
  - Republic of Ireland (2004)
  - Scotland (2006)
  - England (2007)
- Change in behaviour?

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Applications - Smoking

All Smokers: Cigarette Smoking Prevalence (as a % of the Population)
12 month moving average trend ending September 2006

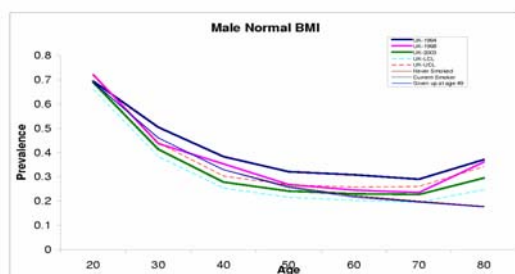Source: Office of Tobacco Control, Republic of Ireland

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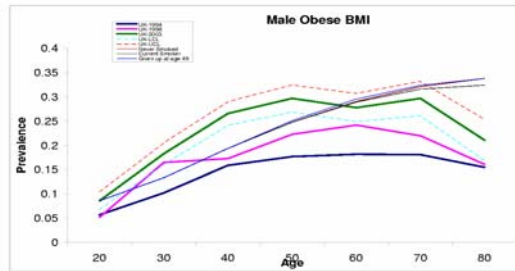
Applications - Obesity

Obesity
- Indicated by BMI
- BMI = Weight (*kgs*) / (Height (*mtrs*))^2
- Usual Classification:

Category	Range
Normal	BMI ≤ 25
Overweight	25 < BMI ≤ 30
Obese	30 < BMI

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Applications - Obesity

Applications - Obesity

Male Obese BMI

Applications - Obesity

Body Mass Index
- More detailed classification

Category	Range	Mortality rate as a multiple of base
Underweight (base)	BMI ≤ 18.5	1
Normal	18.5 < BMI ≤ 25	0.5875
Overweight	25 < BMI ≤ 30	0.4588
Moderately Obese	30 < BMI ≤ 35	0.5263
Morbidly Obese	35 < BMI	0.5868

- Not a significant risk factor for MI or HS
- Significant risk factor for
  - Diabetes and Hypertension
  - Death

Questions?