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Impact of Diabetes Mellitus II on Longevity and Morbidity Risks: Full Case Analysis

Njabulo Ncube (PhD Candidate)

University of East Anglia (UK)

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Presentation Outline

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Introduction
Purpose of the Study

- To derive, analyse and model the impact of diabetes mellitus II (DM-II) on longevity and morbidity risks.
- Primary Outcome: all-cause mortality.
- Secondary Outcomes: amputation, cognitive impairment, Chronic Kidney Disease (CKD) Stages 3 to 5, heart failure (HF), myocardial infarction (MI), pulmonary vascular disease (PVD), stroke, cancer and cognitive impairment including dementia.

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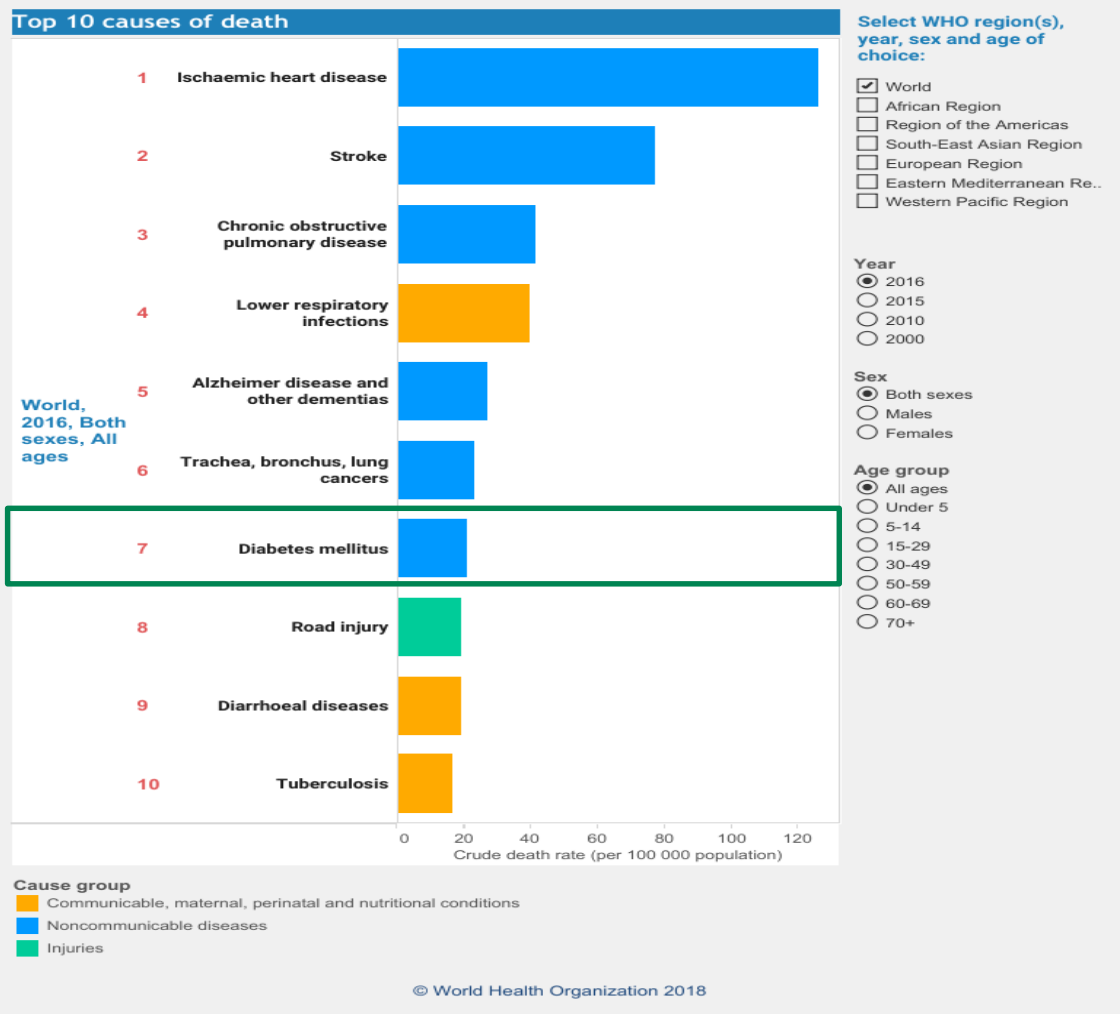
Why Diabetes Mellitus II (DM-II)



Source: WHO (2018)

DM-II: Rankings among the Top Ten

Year	All Ages	50-59	60-69	70+
2016	7	6	5	6
2015	7	6	5	6
2010	10	7	5	7
2000	15	9	6	7

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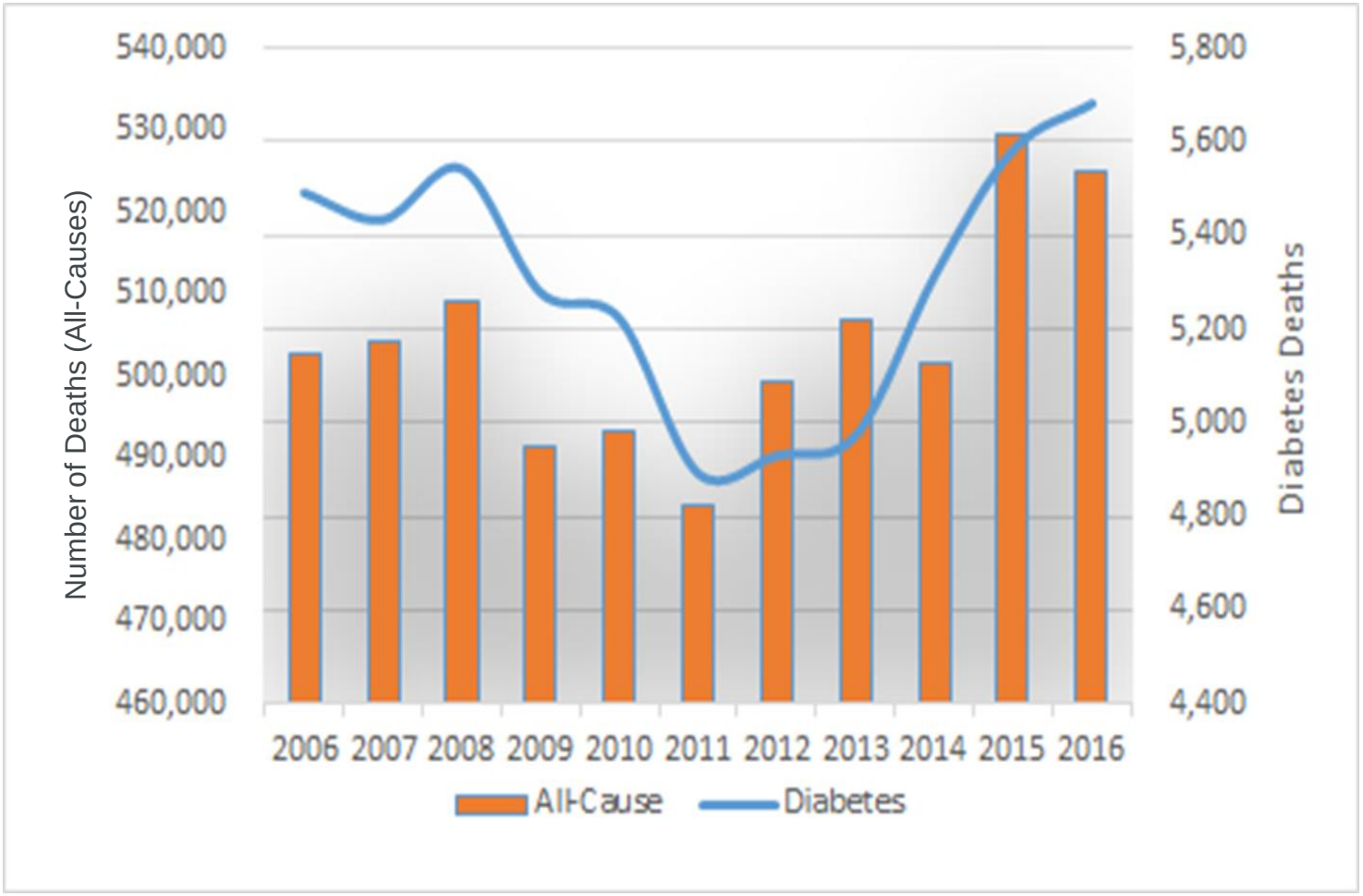
Why DM-II (cntd.)



Source: ONS (2017)

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Study Design

Selection Criteria

- UK THIN database.

- Patients diagnosed with DM-II (cases) from 1984 and, aged 40 years and above were matched (1:3) to non – diabetics (controls) by practice, age and sex.
- Excluded patients with severe medical conditions diagnosed (e.g. cancer) before entry date.
- The follow up period is from 1984 up to 2017.

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Study Design

- Variables of Interest – at entry

Demographic
1. Age Group
2. Birth Year
3. Gender
4. General Practice (Frailty)

Life Style and Socio-economic
1. Smoking Status
2. Townsend Deprivation Index
3. Body Mass Index (BMI)

Medical Conditions
1. Case-Control Indicator
2. Angina
3. Atrial Fibrillation (AF)
4. HF
5. Hypercholesterolemia
6. Hypertension
7. MI
8. PVD

✚

Interactions e.g. Age Group and Gender, Case-Control and Smoking status

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Study Design

Full Case Analysis - Selection Criteria

Included Patients with complete records on

- Smoking status,
- Alcohol consumption status,
- Townsend deprivation score,
- BMI,
- Blood Pressure (BP),
- Blood lipid ratio and
- High-density lipoproteins (HDL).

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Study Sample

Total Study Sample

- 108 282 (57% Males) Cases.
- 253 800 (55% Males) Controls.

Full Case Study Sample

- 20 213 (57.7% Males) Cases.
- 28 693 (56.2% Males) Controls.

Distribution of the Study Sample by Age Group, Sex and Case-Control Status

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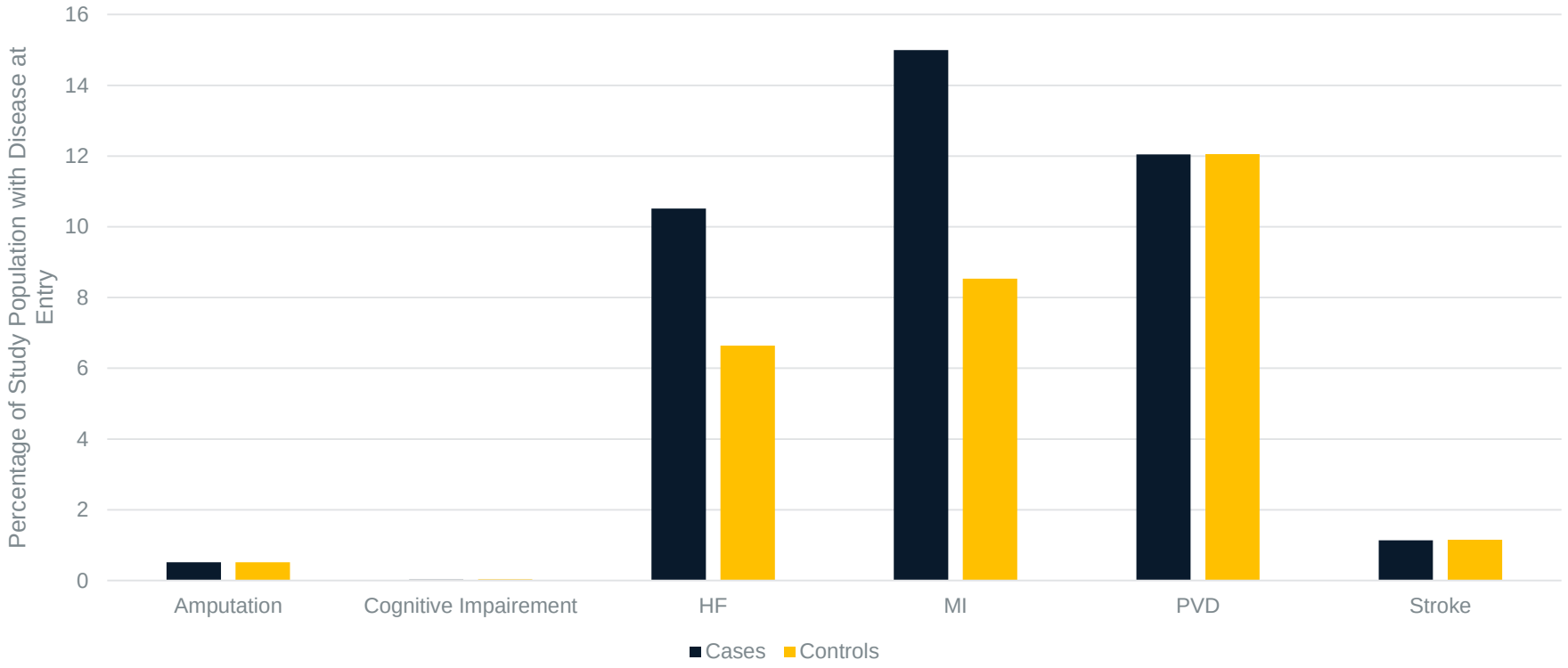
Prevalence of Some Medical Conditions at Entry Date



Cases	560 (0.52%)	27 (0.02%)	11,388 (10.52%)	16,242 (15.00%)	13,048 (12.05%)	1,230 (1.14%)
Controls	1,317 (0.52%)	73 (0.03%)	16,857 (6.64%)	21,665 (8.54%)	30,595 (12.05%)	2,920 (1.15%)

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Statistical Models for All-Cause Mortality

- Cox Regression for DM – II

Backward elimination was used for variable selection ($\alpha_{main} = 0.05$, $\alpha_{interactions} = 0.01$)

- Case-control indicator,
- Age group,
- Birth Year,
- Gender,
- Smoking status,
- Townsend deprivation index,
- HF,
- Hypercholesterolemia,
- Hypertension,
- MI,
- PVD,
- BMI

and interactions

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Assessing PH Assumption $(\alpha = 0.05)$

	rho	chisq	p
Case-Control [Cases]	0.001202	0.007556	0.930731
Age Group [50-59]	0.002855	0.042302	0.837045
Age Group [60+]	-0.01454	1.12216	0.289454
Birth Year [1930-1939]	0.048563	13.64601	0.000221
Birth Year [1940-1949]	0.027559	4.442733	0.03505
Gender [Male]	-0.00143	0.010588	0.918042
Smokes [Former]	-0.00845	0.3666	0.544863
Smokes [Smoker]	-0.02358	2.866207	0.090458
Townsend [Less Deprived]	-0.01738	1.583886	0.208202
Townsend [2]	-0.01299	0.872694	0.350211
Townsend [4]	-0.01032	0.554632	0.456431
Townsend [Most Deprived]	-0.00078	0.00316	0.955175
HF [Yes]	-0.00032	0.000549	0.981302
Hypercholesterolemia [Treated]	0.033125	5.858287	0.015504
Hypercholesterolemia [Untreated]	-0.03202	5.509689	0.018911
Hypertension [Treated]	0.036188	6.896064	0.008639
Hypertension [Untreated]	-0.01671	1.454762	0.227765
MI [Yes]	-0.01977	2.116238	0.145744
PVD [Yes]	-0.00438	0.099198	0.752794
BMI [Overweight]	-0.01086	0.605801	0.436373
BMI [Obese]	-0.00255	0.033734	0.854273
Case-Control [Cases]:Smokes [Former]	0.025331	3.357494	0.0669
Case-Control [Cases]:Smokes [Smoker]	0.02132	2.33379	0.126593
Case-Control [Cases]:Hypercholesterolemia [Treated]	-0.03117	5.062485	0.024449
Case-Control [Cases]:Hypercholesterolemia [Untreated]	-0.01483	1.147207	0.284135
Case-Control [Cases]:MI [Yes]	0.018921	1.870298	0.171441
Case-Control [Cases]:PVD [Yes]	0.005052	0.132072	0.716293
Case-Control [Cases]:BMI [Overweight]	-0.01035	0.555738	0.455983
Case-Control [Cases]:BMI [Obese]	-0.02668	3.697196	0.054504
Age Group [50-59]:Gender [Male]	0.004786	0.118789	0.730352
Age Group [60+]:Gender [Male]	0.013832	1.006281	0.315796
Birth Year [1930-1939]:Gender [Male]	-0.02832	4.510593	0.033686
Birth Year [1940-1949]:Gender [Male]	-0.01775	1.778759	0.182302
Smokes [Former]:BMI [Overweight]	-0.00518	0.138134	0.710143
Smokes [Smoker]:BMI [Overweight]	0.005923	0.18299	0.668816
Smokes [Former]:BMI [Obese]	-0.00536	0.149176	0.699324
Smokes [Smoker]:BMI [Obese]	-0.00344	0.060556	0.805619
Townsend [Less Deprived]:BMI [Overweight]	0.002167	0.024508	0.8756
Townsend [2]:BMI [Overweight]	0.00821	0.349348	0.554483
Townsend [4]:BMI [Overweight]	0.006623	0.228463	0.632666
Townsend [Most Deprived]:BMI [Overweight]	0.002618	0.035617	0.850308
Townsend [Less Deprived]:BMI [Obese]	0.017672	1.63206	0.201418
Townsend [2]:BMI [Obese]	0.01169	0.707889	0.400146
Townsend [4]:BMI [Obese]	0.010126	0.53434	0.464788
Townsend [Most Deprived]:BMI[Obese]	0.008117	0.341958	0.558701
GLOBAL	NA	103.2145	0.0000018

Variables violating the PH Assumption

- Year of Birth
- Hypercholesterolemia
- Hypertension

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Validating PH Assumption results using timecox $(\alpha = 0.05)$

Test for Time Invariant Effects		
	Kolmogorov-Sminorv Test	p-value: $H_0: \beta(t) = \beta$
Intercept	2.72	0.207
Birth Year [1930-1939]	2.99	0.25
Birth Year [1940-1949]	2.53	0.217
Hypercholesterolemia [Treated]	2.52	0.735
Hypercholesterolemia [Untreated]	3.16	0.029
Hypertension [Treated]	4.9	0.159
Hypertension [Untreated]	2.31	0.558
Birth Year [1930-1939]:const(Gender) [Male]	5.2	0.127
Birth Year [1940-1949]:const(Gender) [Male]	4.5	0.324

Only hypercholesterolemia has time variant effects

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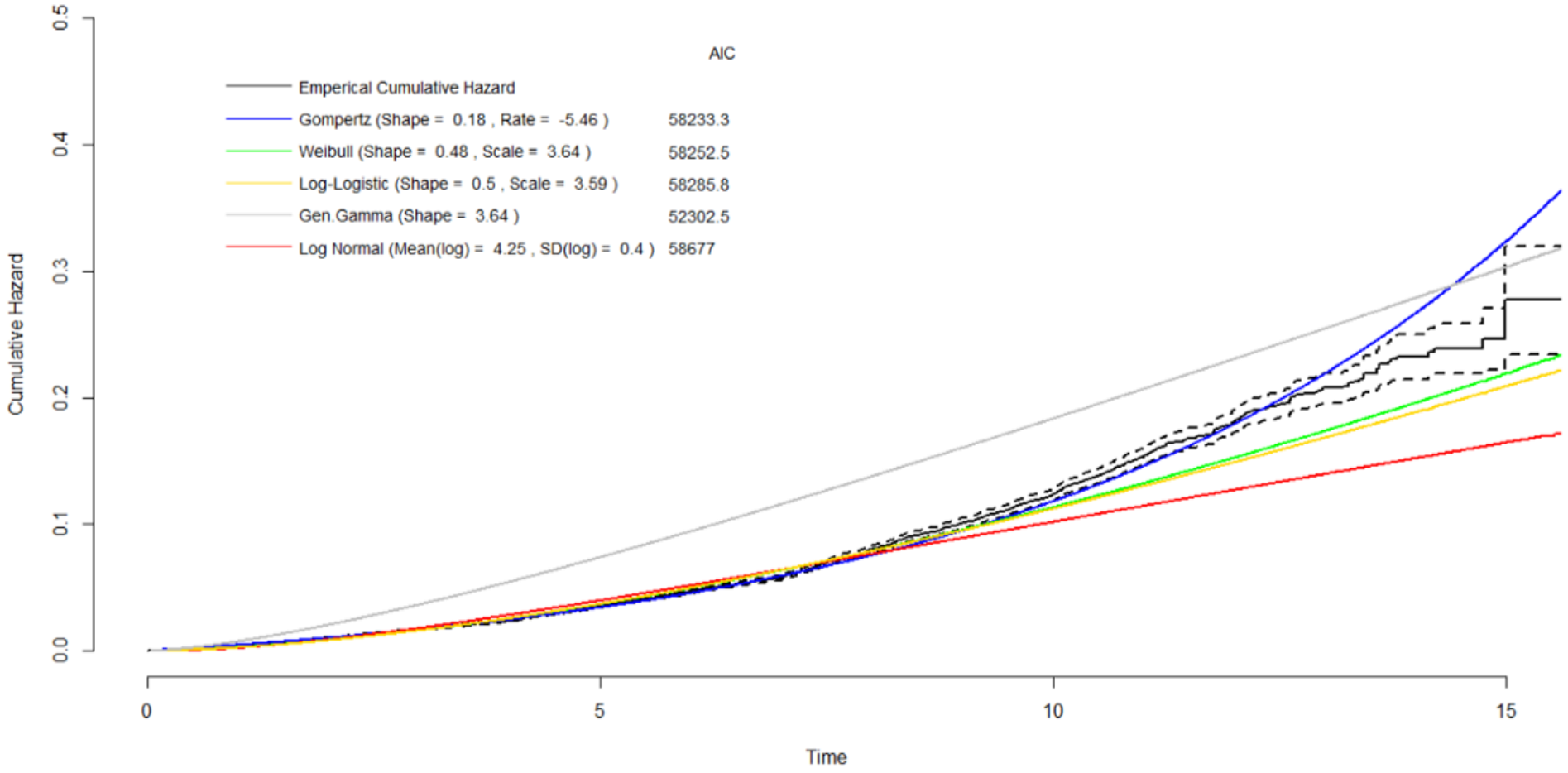
Estimating the Baseline Function using flexsurvreg package



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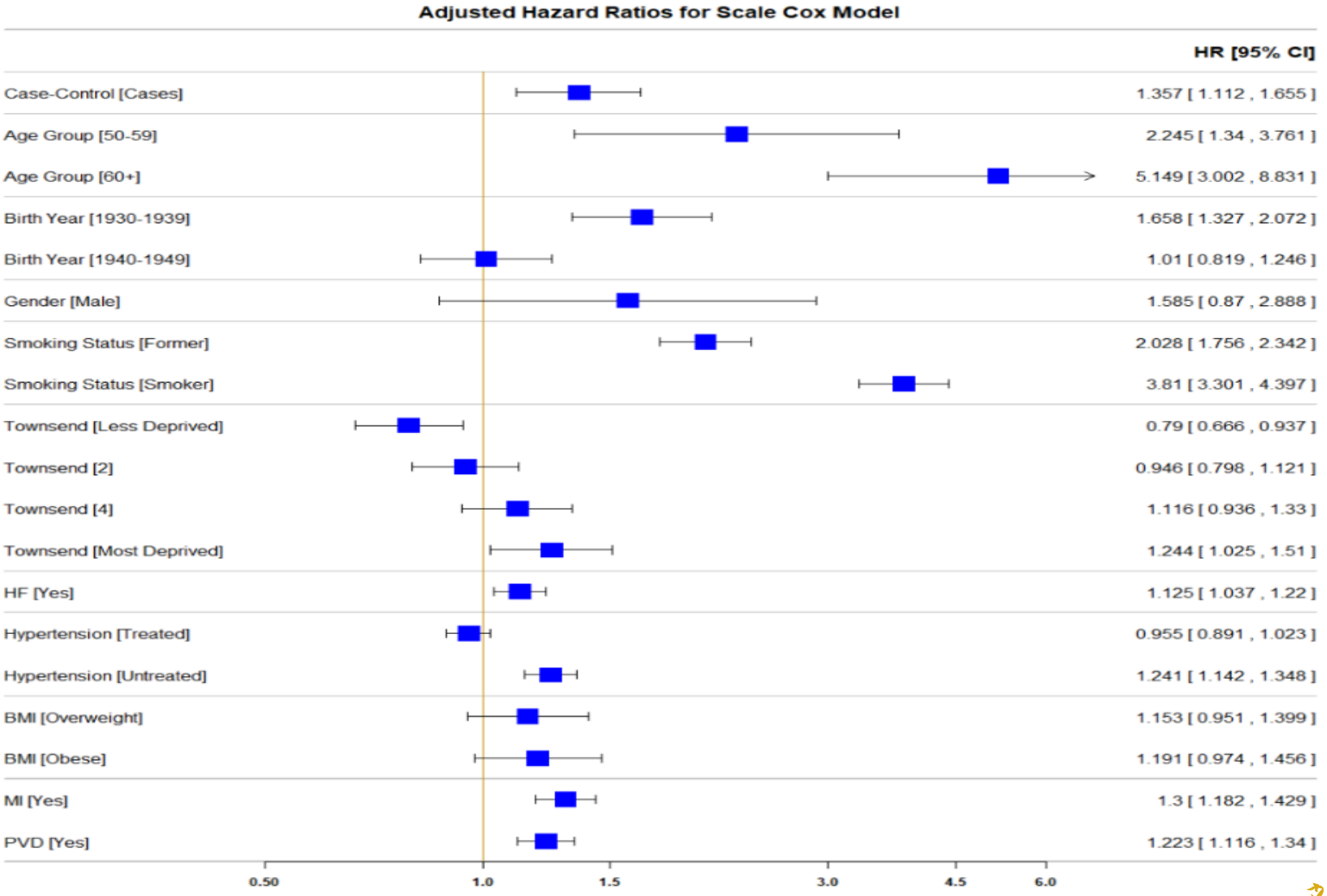
Gompertz-Cox Regression

- Distribution
  - Gompertz distribution.
- Shape Model
  - Hypercholesterolemia.
- Scale Model
  - All covariates and interactions as in Cox Model.

Adjusted Hazard Ratios



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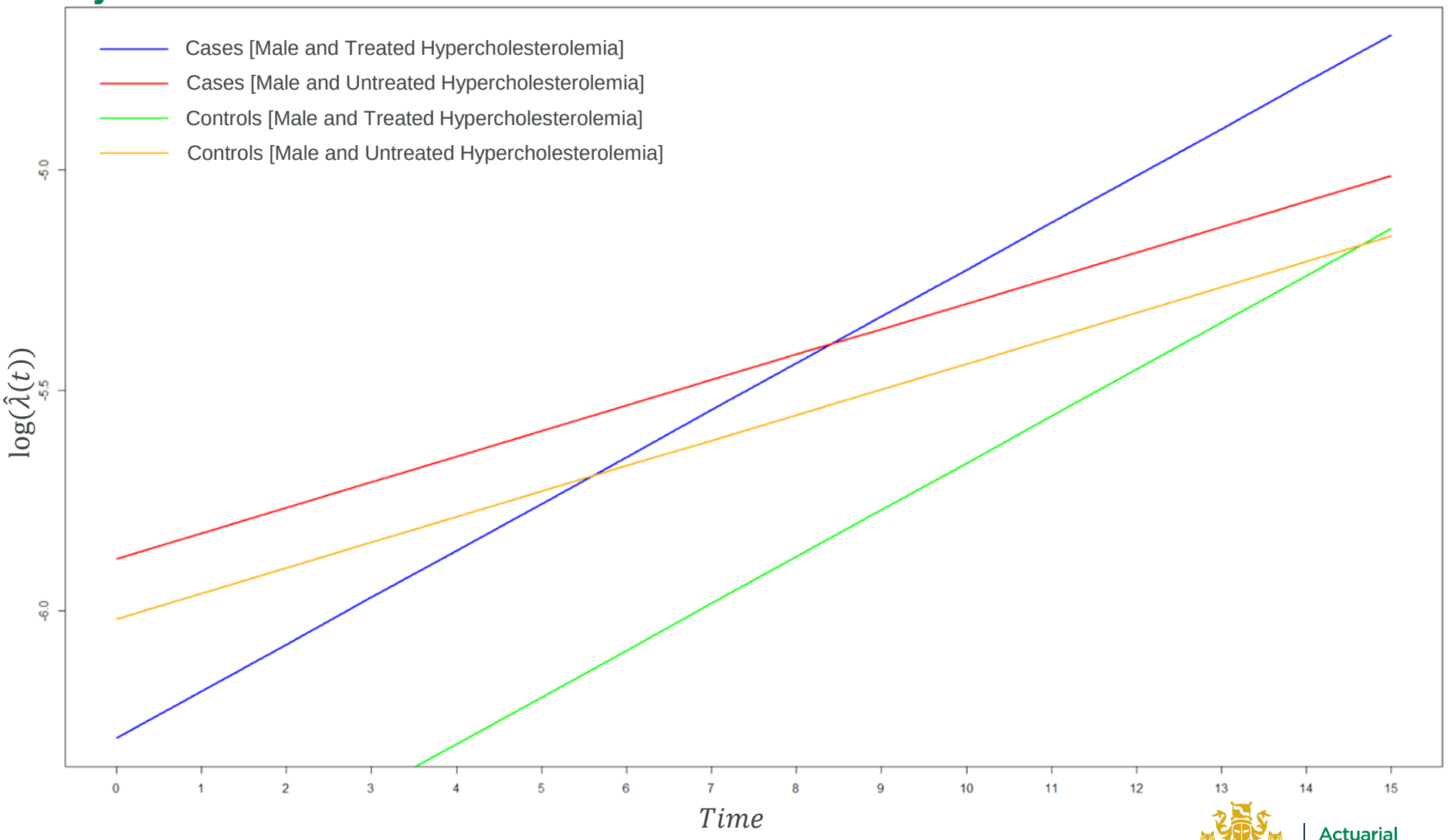
Adjusted Hazard Function



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Further Work

1. Imputed Data Model (Mortality)
2. Translation into Actuarial Models (Mortality)
3. Morbidity Models (Cancer, CKD Stages 3 – 5)
4. Translation into Actuarial Models
5. Publish at least 2 papers

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