Survival analysis after a first Ischaemic stroke event: a case-control study in the adult population of England.

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1 Introduction

- Stroke is a severe and wide-spread disease. In the UK, there are **152,000** strokes per year (that is, one every 3 minutes 27 seconds) accounting for 53,004 deaths [1].

- Stroke can be categorised as haemorrhagic stroke, HS (rupture of blood vessel in the brain) and ischaemic stroke, IS (blood clot disrupting the blood supply to the brain). IS stroke type is considered in this study.

- A stroke may cause long-term problems such as disability which can necessitate rehabilitation and further care. Stroke survivors can also experience significant psychological impacts, repeat strokes, transient ischaemic attacks (TIAs) and/or death within a year of stroke.

- It is no longer regarded as the "disease of the old age" due to the worrying trend of younger people being affected by it. It is expected to double by 2030 unless proper strategies are devised. The economic burden of stroke in UK is estimated to be around £9 billion a year [2].
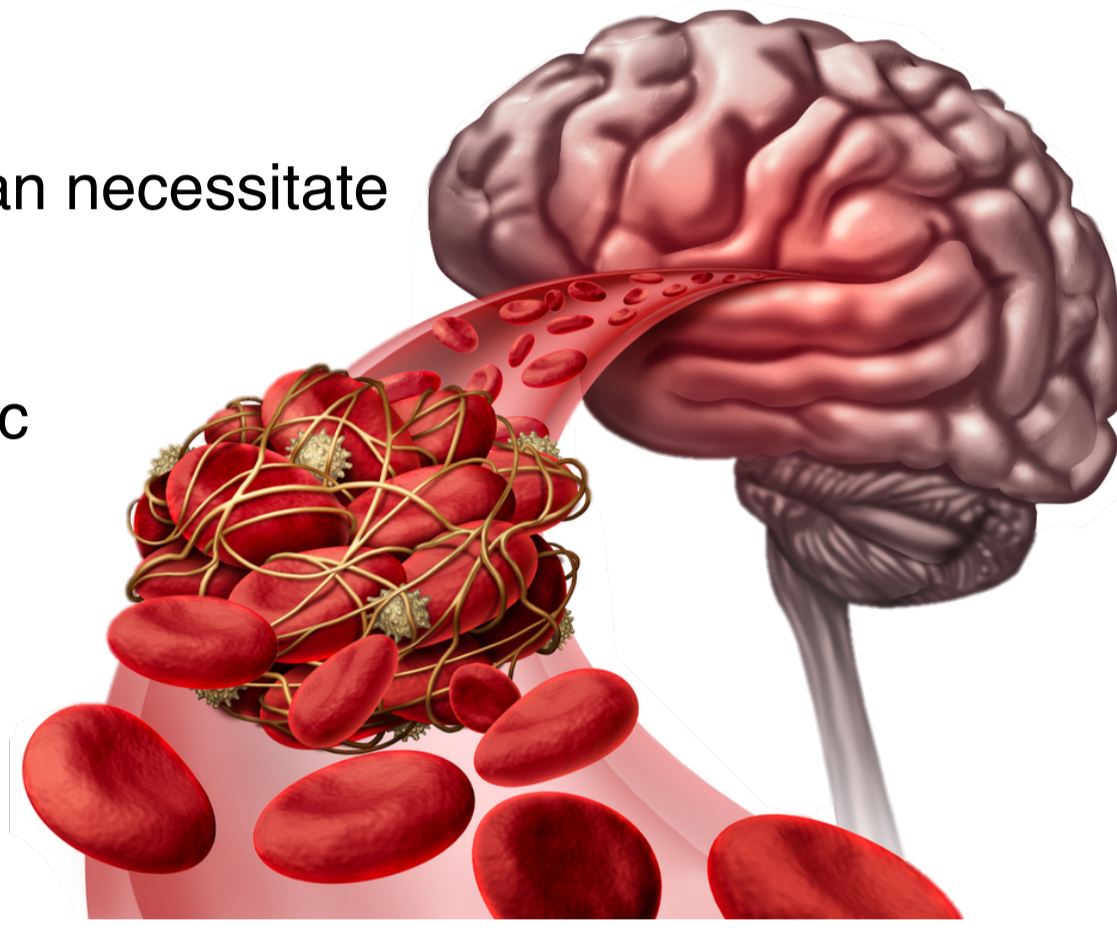

Figure 1: Illustration of a blood clot travelling to the brain.
Image source : nydisability

The aim of the study was to study the impact of a first IS event on the survival of patients in England by estimating the influence of various risk factors (demographical data, treatments, co-morbidities and lifestyle interventions) on the hazards of all-cause mortality after stroke.

2 Methodology

- In this retrospective case-control study, data was obtained from the THIN database of patients in England, aged 18 years or older at entry, with a **first-ever** ischaemic stroke diagnosis between January 1986 and January 2017.

- They were matched on to at least 3 controls on age, gender and GP practice.

- The primary outcome was all-cause mortality.

- Variables of interest :

  Drugs : antihypertensive drugs, anticoagulants, statins and antiplatelets.

  Medical conditions : asthma, atrial fibrillation, chronic kidney disease, chronic obstructive pulmonary disorder, diabetes type II, peripheral vascular disease, hypercholesterolemia and hypertension.

  Other : BMI, gender, date of birth, age ... stroke diagnosis/at study entry, smoking status, IMD deprivation.

The Cox's parametric regression model

$$\mu(t|u) = \mu_0(t|u)\,exp^{(\beta * u)}$$

Baseline hazard function

β is a vector of unknown parameters and u is a vector of covariates

Weibull model assumes the Weibull baseline hazard. Two parameters (shape, k and scale, λ) must be estimated to describe the underlying hazard function over time.

Additional regression model to allow varying shape depending on covariates

$$\mu_0(t) = \frac{k}{\lambda}\left(\frac{t}{\lambda}\right)^{k-1}$$

$$k(u)$$

Figure 2: Cox-Weibull model parametric model.

- The hazards of all-cause mortality were estimated using a Cox-Weibull survival model with a random statistical frailty effect of GP practice, which included both scale and shape effects.

- A total of **20,250** eligible patients with first-ever IS event and their **55,519** controls were followed up to **30** years.

- Multiple Imputation method was used to impute for missing records of lifestyle factors.
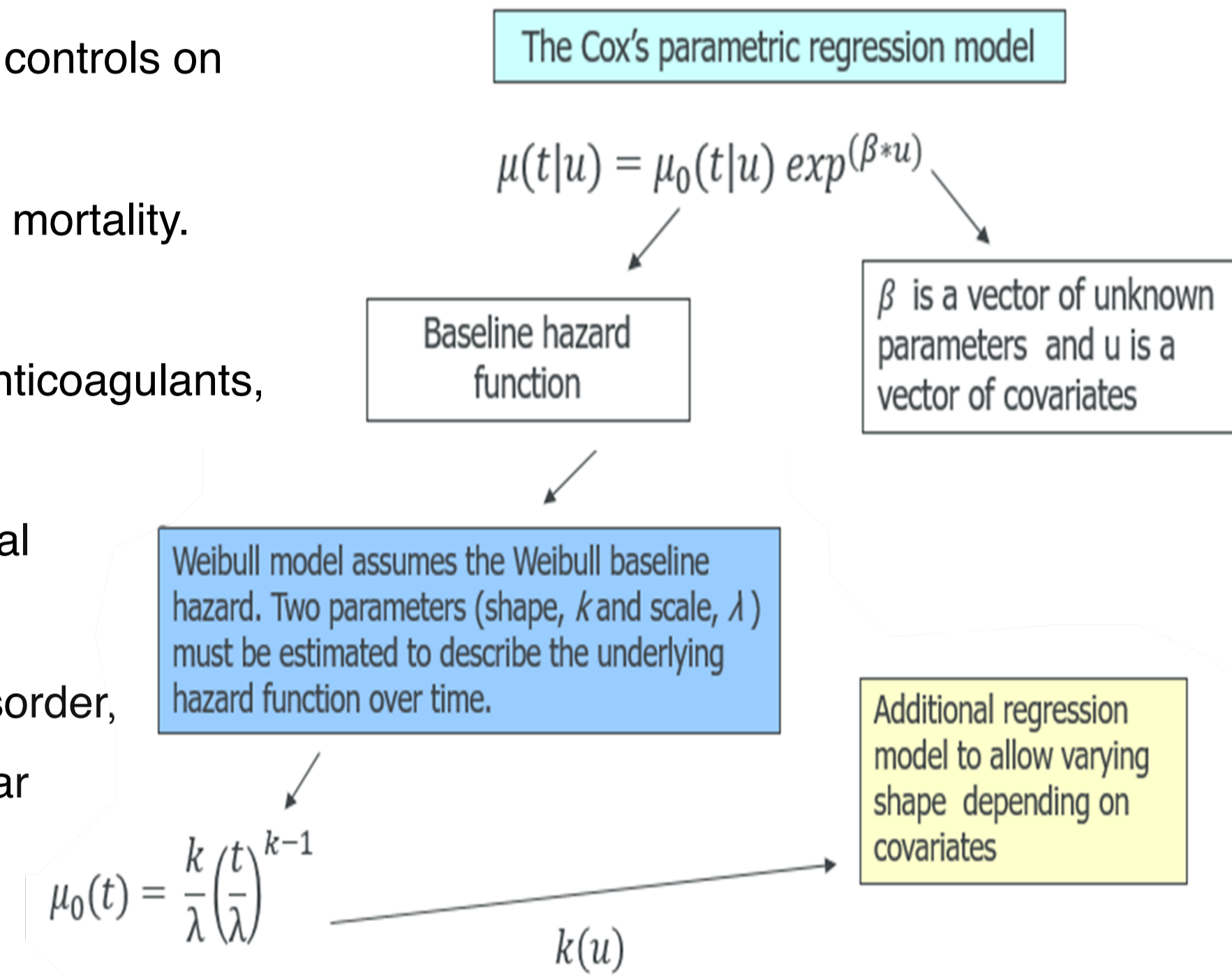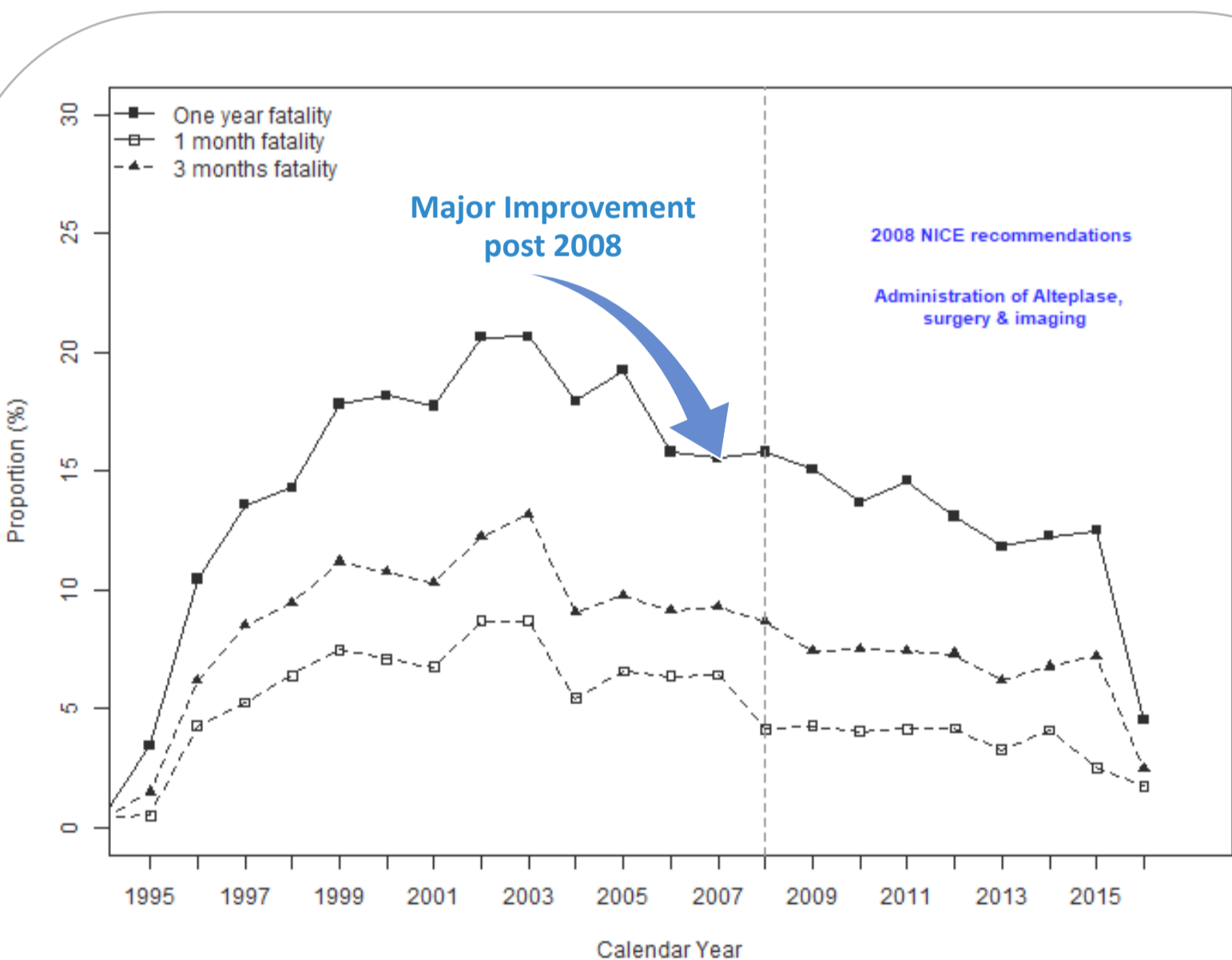
3 Results

Figure 3 : One-year, 1 month and 3 months all-cause mortality for IS stroke patients, 1995– 2016. A considerable decline is observed post 2008. The NICE guidelines were amended for better management of post stroke complications , secondary prevention and rehabilitation[4].
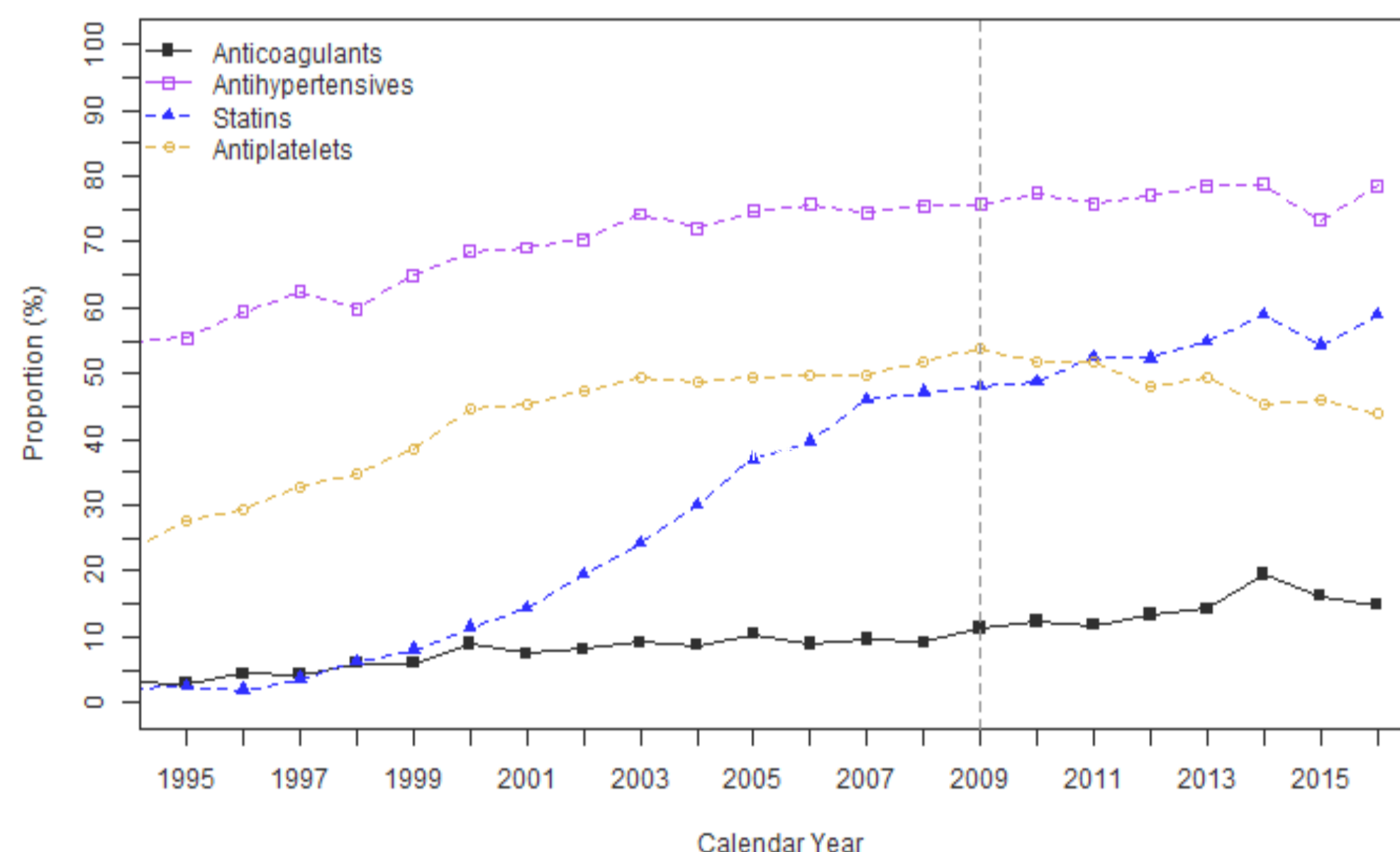

Figure 4: Prescriptions of pre-stroke drugs to IS patients by calendar year. A rise in the use of statins, antiplatelet agents, anticoagulants and antihypertensives is observed. However, after year 2010, a decline of the use of antiplatelet agents was detected.
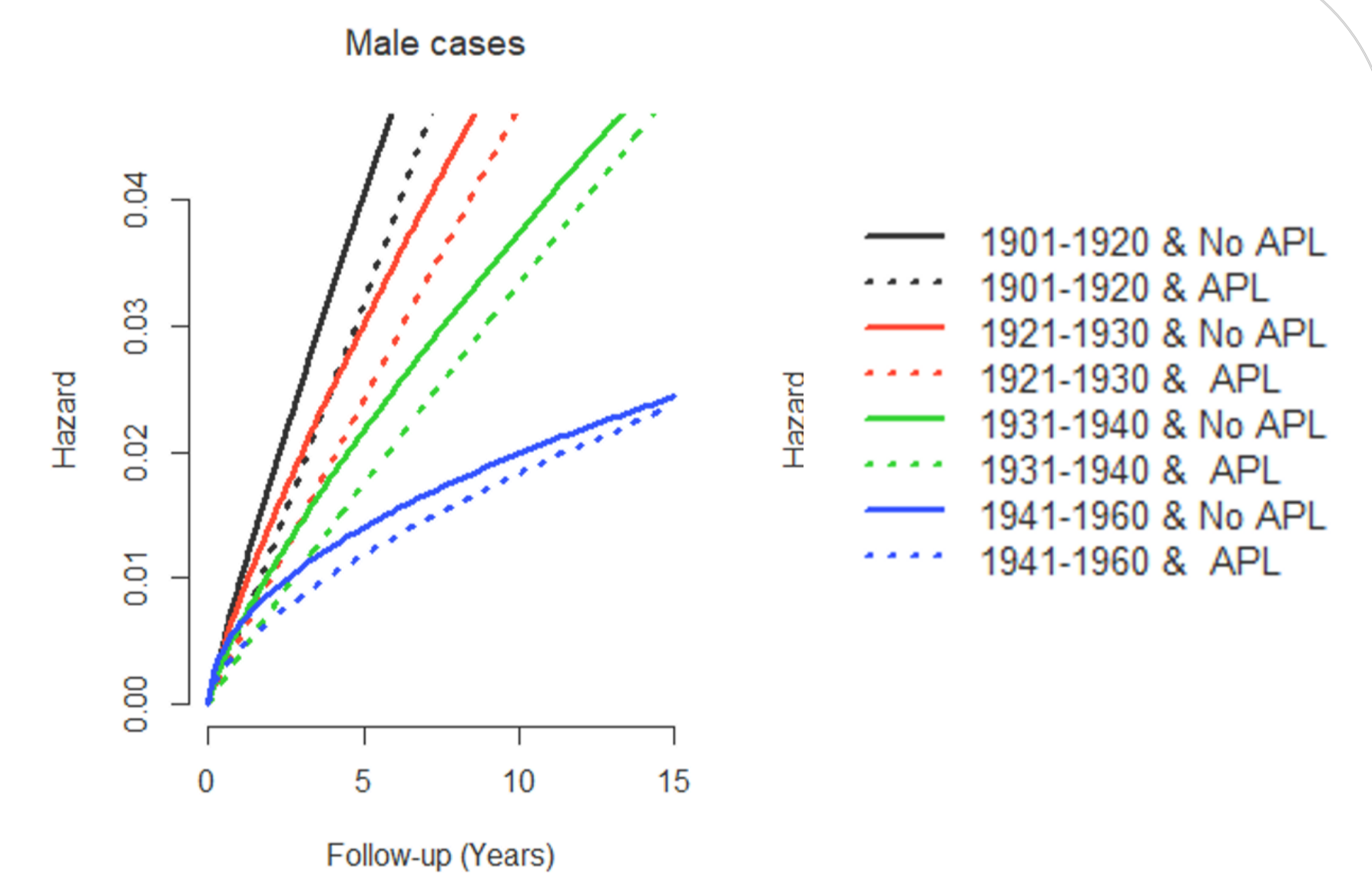

Figure 5 : Survival of male patients across different birth cohorts and uptake of antiplatelet. APL : Antiplatelets.
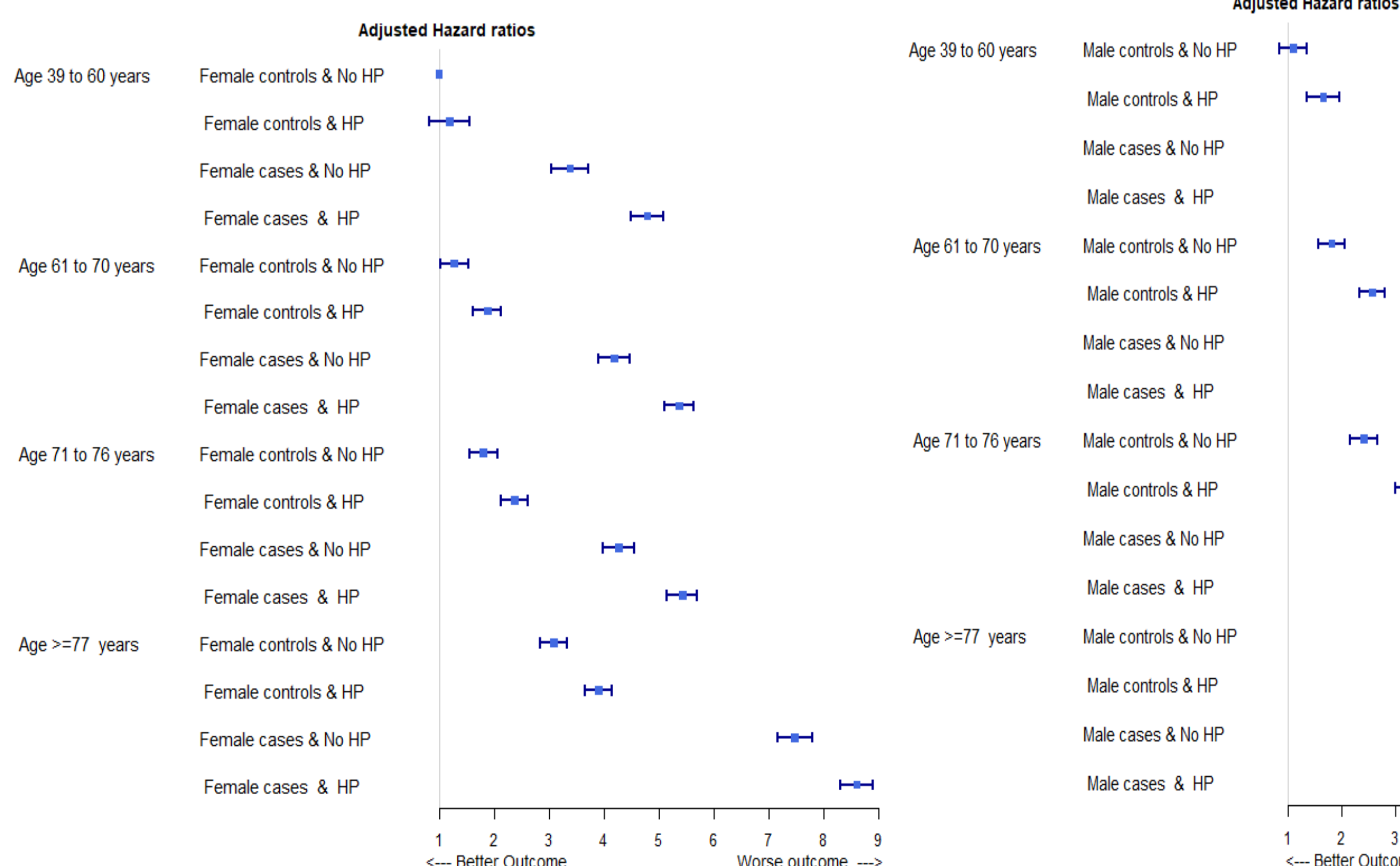

Figure 6: Forest plot of the hazard ratios of all-cause mortality by IS stroke diagnosis and associated interactions with gender, age category and hypertension diagnosis. The baseline category is the group of young (39 - 60 years) female controls with no hypertension. HP refers to hypertension diagnosis.

4 Conclusion

- Stroke outcome in England has improved over time.

- Pre-morbid use of preventive antiplatelet treatment declined after year 2010 and our finding shows that it is associated with improved survival outcome.

- Hypertension is not only a major risk factor for stroke but our study shows that it is also associated with poor survival outcomes, even after surviving a first-ever ischaemic stroke.

- Advancing age, male gender and a history of hypertension were associated with impaired survival in all patient groups and especially in IS patients. Stroke patients still face high mortality risk after having survived the first stroke event.

References:

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