Effect of Intensive Glycemic Control on Progression of Retinopathy in Patients with Type 2 Diabetes

STAT/BIOSTAT 7XX

Invalid Date

Instructions

This exam is **open-book** but must be completed **independently**.
You may not discuss the problems with anyone other than the instructor:
Email: lmao@biostat.wisc.edu

The **Action to Control Cardiovascular Risk in Diabetes (ACCORD)** trial was conducted from **1999 to 2012** to evaluate the health effects of specific strategies for managing blood glucose levels, serum lipid levels, and blood pressure in patients with type 2 diabetes. Here, we focus on the glycemia substudy, which investigated whether **intensive glycemic control** slows **progression of diabetic retinopathy** compared to standard control.

Diabetic retinopathy is a major **microvascular complication of diabetes** and a leading cause of blindness in the U.S. The study enrolled **10,251 diabetic patients**, with **5,128 randomized** to intensive control and **5,123 to standard control**, followed over **7 years** for indications of **retinopathy progression** (e.g., loss of vision, cataract extraction, vitrectomy, etc.).

Our primary research question is:
- *Does intensive glycemic control reduce the risk of retinopathy progression compared to standard glycemic control?*

Also of interest are risk factors such as **age, sex, race, medical history, and clinical measurements like HbA1c**.

Data Description

The dataset `accord_glyc.txt` contains the following variables:

- **MaskID**: Patient identifier
- **time**: Time (years) from randomization to retinopathy progression or censoring
- **status**: Event indicator (1 = retinopathy progression, 0 = censored)
- **trt**: Treatment group (1 = intensive glycemic control, 0 = standard glycemic control)
- **female**: Sex (1 = female, 0 = male)
- **age**: Baseline age (years)
- **race**: Race (White, Black, Hispanic, Other)
- **hba1c**: Glycosylated hemoglobin (%)
- **cvd**: History of cardiovascular disease (1 = yes, 0 = no)
- **chol**: Total cholesterol (mg/dL)
- **ldl**: Low-density lipoprotein (mg/dL)
- **hdl**: High-density lipoprotein (mg/dL)

Exam Questions

1. Descriptive Statistics (20 points)

Summarize key baseline characteristics **by treatment group** and **overall**, including:

- Demographic variables: **Sex, age, and race**
- Medical history: **Cardiovascular disease (CVD)**
- Biochemical measurements: **HbA1c, total cholesterol, LDL, HDL, etc.**
- **Calculate the event rates** of retinopathy progression in each treatment arm.

---

2. Graphical Analysis (20 points)

To explore treatment effects visually:

- **Compute and plot Kaplan-Meier survival curves** for retinopathy progression-free probabilities, stratified by:
  - **Treatment group**
  - **Sex**
  - **Race**

- **Interpretation:**
  - Which **sex and race group** appears to benefit most from intensive glycemic control?

---

3. Multiple Regression Analysis (40 points)

Construct a **Cox proportional hazards model** to analyze how intensive glycemic control and other factors affect **retinopathy progression**, adjusting for key covariates.

Steps to Follow:

1. **Covariate Selection:** Based on results from **Questions 1 & 2**, choose relevant risk factors.

2. **Proportionality Assumption:**
   - Check whether each covariate satisfies the **proportional hazards assumption**.
   - If violated, apply appropriate corrections (e.g., time-dependent covariates, stratification).

3. **Functional Form of Continuous Covariates:**
   - Check whether continuous variables (e.g., age, HbA1c) are correctly specified.
   - Consider transformations (e.g., splines, quadratic terms) if necessary.

4. **Statistical Inference:**

- Interpret the effects of **intensive glycemic control** and **other significant risk factors**.

- Perform a formal **global test** for race group differences (degrees of freedom: 3).

---

4. Reporting Findings (20 points)

Write a **short press release (3–4 sentences)** summarizing the **most important findings** in **nontechnical language**, suitable for a general audience.

Ensure the summary is:
- **Concise**
- **Scientifically accurate**
- **Understandable to non-experts**

Grading Rubric

Question	Points	Key Aspects for Full Credit
1	20	Correct summary of patient characteristics and event rates
2	20	Proper Kaplan-Meier plots and clear interpretation
3	40	Well-specified Cox model, assumption checks, and interpretation
4	20	Clear and engaging press release summary
