In all cases, we restrict our analysis to the elderly observations in the dataset with non-missing values of serum LDL; this leaves 725 of the original 735 observations fit for analysis.

**(1)**

**Methods:** We present descriptive statistics and survival distributions using Kaplan-Meier estimates across 3 strata based on serum LDL level (<100 mg/dL, 100-159 mg/dL, and ≥160 mg/dL).. We define these strata based on the recommendations from the Mayo Clinic used for Homework 1 to correspond roughly to low, medium, and high levels of LDL. We compute a hazard ratio and accompanying Wald-based 95% CI using Cox proportional hazard regression with a Hubert-White sandwich estimator of corresponding standard errors. Our explanatory variable is a continuous measure of LDL. Our response variable is an indicator of all-cause mortality.

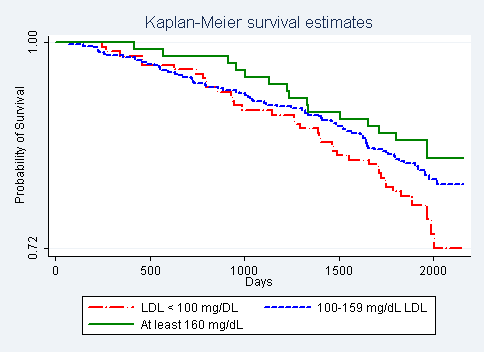


Figure 1: Kaplan-Meier Survival Curves by LDL group

|  |  |  |  |
| --- | --- | --- | --- |
| **Estimated Probability of Survival by LDL Group** | | | |
| **Year** | **< 100 mg/dL LDL**  **(N=165)** | **100-159 mg/dL LDL**  **(N=453)** | **≥ 160 mg/dL LDL**  **(N=107)** |
| 1 | 0.982 | 0.980 | 1.00 |
| 2 | 0.964 | 0.947 | 0.981 |
| 3 | 0.909 | 0.921 | 0.953 |
| 4 | 0.867 | 0.894 | 0.907 |
| 5 | 0.800 | 0.841 | 0.869 |

**Inference:** The maximum observed time in the study is 5.91 years. The Kaplan Meier curve estimates the probability of survival for the 165 individuals with LDL below 100 mg/dL, the 453 individuals with LDL between 100 mg/dL and 159 mg/dL, and the 107 individuals with LDL of at least 160 mg/dL. We can see that, for all observed times, the highest probability of survival belongs to the group with the highest LDL (≥160 mg/dL). By the end of the study, we see that the group with the lowest LDL (<100 mg/dL) has the lowest survival probability, although its survival probability did not start to differ from that of the medium LDL group (100-159 mg/dL) until after about 900 days.

From Cox proportional Hazards regression with a Hubert-White estimator of standard errors, we find that for each 1 mg/dL difference in serum LDL, the risk of death is 0.74% lower in the group with higher LDL. A Wald-based 95% CI suggests that this estimate would not be unusual if the true risk of death in the group with higher LDL were between 0.018% lower and 1.29% lower. We note that 0 is not contained in this interval. This estimate is statistically significant (two-sided p-value=0.009) at the 0.05 level so we have evidence to reject the null hypothesis that the instantaneous risk of death is the same for all observed levels of LDL.

**2.**

**Methods:** See problem 1 for descriptive statistics and survival distributions using Kaplan-Meier estimates across 3 strata based on serum LDL level (<100 mg/dL, 100-159 mg/dL, and ≥160 mg/dL). We also compute a hazard ratio and accompanying Wald-based 95% CI using Cox proportional hazard regression with a Hubert-White sandwich estimator of corresponding standard errors. In view of the possibility that LDL has a multiplicative effect on risk of death, we use a log transformation of continuous serum LDL as the explanatory variable in our proportional hazards regression. Our response variable is an indicator of all-cause mortality.

**Inference:** From Cox proportional hazards regression with a Hubert-White estimator of standard errors, we find that for each twofold increase in serum LDL, the risk of death is 43.6% lower in the group with higher LDL. A Wald-based 95% CI suggests that this estimate would not be unusual if the true risk of death in the group with higher LDL were between 26.2% lower and 56.9% lower. We note that 0 is not contained in this interval. This estimate is statistically significant (two-sided p-value <0.001) at the 0.05 level, so we have some evidence of an association between LDL and instantaneous risk of death under this model.

**3.**

**Methods:** See problem 1 for descriptive statistics and survival distributions using Kaplan-Meier estimates across 3 strata based on serum LDL level (<100 mg/dL, 100-159 mg/dL, and ≥160 mg/dL). Here, we estimate hazard ratios and accompanying Wald-based 95% CIs using a Cox proportional hazards regression with a quadratic in serum LDL as our explanatory variables. We use the Hubert-White sandwich estimator for corresponding standard errors. Our response variable is an indicator of all-cause mortality.

**Inference:** From Cox proportional Hazards regression, we find that for each 1 mg/dL difference in squared LDL, the risk of death is 0.008% lower in the group with higher LDL. We would like to use this point estimate to detect a non-linear association between LDL and mortality risk, suggesting that a linear model as used in problem 1 may not have been sufficient. A Wald-based 95% CI suggests that the coefficient estimate of the squared term would not be unusual if the true value were between mg/dL lower and mg/dL higher. Note that this 95% CI contains 0. The accompanying two-sided p-value of this estimate is 0.055 > 0.05, so we do not have sufficient evidence to conclude that the association between serum LDL and instantaneous risk of death is not linear, where our alternative model is that the association is quadratic.

**4.**

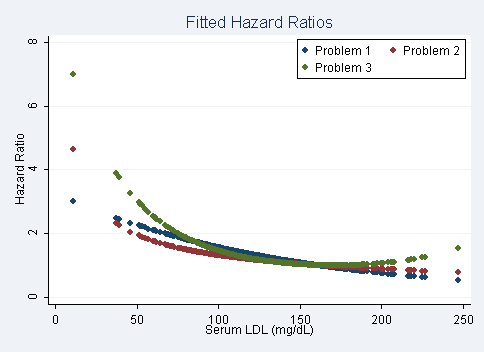


Figure 2: Comparison of fitted hazard ratios from problems 1-3

As shown in Figure 2, it appears that the fitted hazard ratios from problem 1 (with continuous LDL as the sole explanatory variable) are similar to those from problem 2 (with log-transformed LDL as the sole explanatory variable). Modeling an additive instead of a multiplicative association does not yield substantially different fitted values. The fitted hazard ratio from problem 3 (with a quadratic in LDL as the explanatory variables) seems to have a considerably steeper slope for levels of LDL below 75 mg/dL than the other two specifications. We also observe a slightly steeper slope for values of LDL above 200 mg/dL. The fitted values for all three specifications seem to be approximately the same for LDL between 100 mg/dL and 200 mg/dL, where we have 75% of the observations in our data.