Ixta-Report

Ixtaccihuatl Obregon

2024-12-13

Methods - COX PH ASSUMPTIONS

We used a cox proportional hazards model to assess the effect of the covariates on the hazard of developing cirrhosis. The assumption of the model is that hazard ratios between groups is constant over time. Additionaly, the effects of the covariates on the hazard are assumed to be proportional. To determine if the Cox PH model violated the proportional hazard assumptions we used the coxph() function in R.

Results - COX PH ASSUMPTIONS

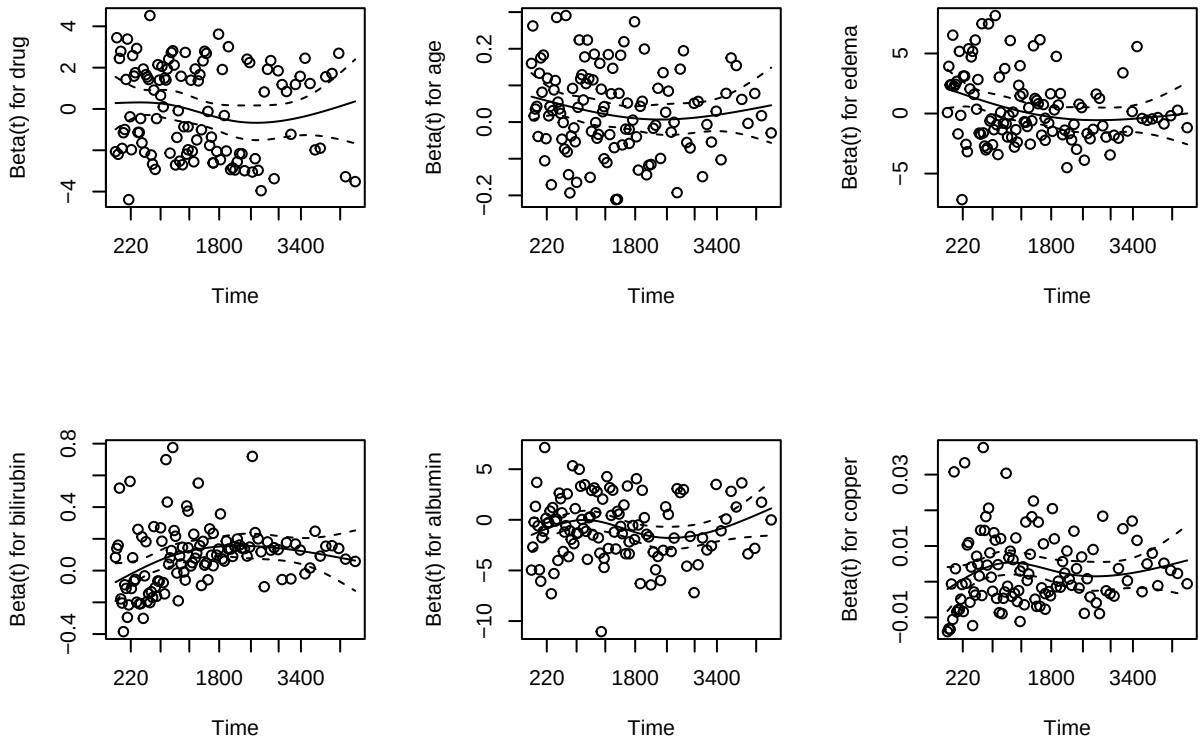
```
## Rows: 418 Columns: 20
## -- Column specification --------------------------------------------------------
## Delimiter: ","
## chr  (7): Status, Drug, Sex, Ascites, Hepatomegaly, Spiders, Edema
## dbl (13): ID, N_Days, Age, Bilirubin, Cholesterol, Albumin, Copper, Alk_Phos...
##
## i Use `spec()` to retrieve the full column specification for this data.
## i Specify the column types or set `show_col_types = FALSE` to quiet this message.
```

```
## Warning: There was 1 warning in `mutate()`.
## i In argument: `status = case_when(...)`.
## Caused by warning:
## ! NAs introduced by coercion
```

Table 1: Multivariate Cox Proportional Hazards Analysis - Stepwise Selection Model

Characteristic	**HR**[1]	**95% CI**[1]	**p-value**
drug			
D-penicillamine	—	—	
Placebo	0.94	0.63, 1.40	0.7
age	1.03	1.01, 1.05	0.004
edema			
No	—	—	
Yes	1.47	0.88, 2.47	0.14
bilirubin	1.09	1.05, 1.13	<0.001
albumin	0.47	0.28, 0.82	0.007
copper	1.00	1.00, 1.00	0.002
sgot	1.00	1.00, 1.01	0.015
prothrombin	1.33	1.07, 1.64	0.010
stage			
1	—	—	
2	3.88	0.47, 32.1	0.2
3	5.29	0.68, 41.1	0.11
4	8.02	1.04, 61.8	0.046

[1]HR = Hazard Ratio, CI = Confidence Interval



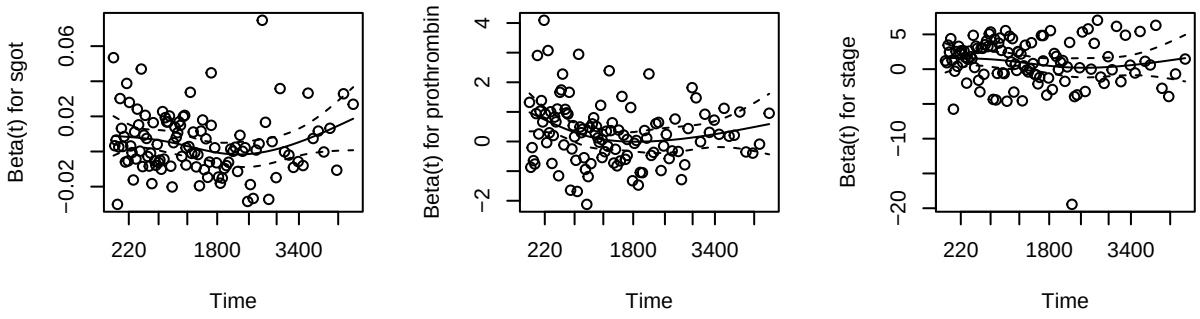


Table 2: Proportional Hazards Assumption Test for Cox PH Model - Stepwise Selection

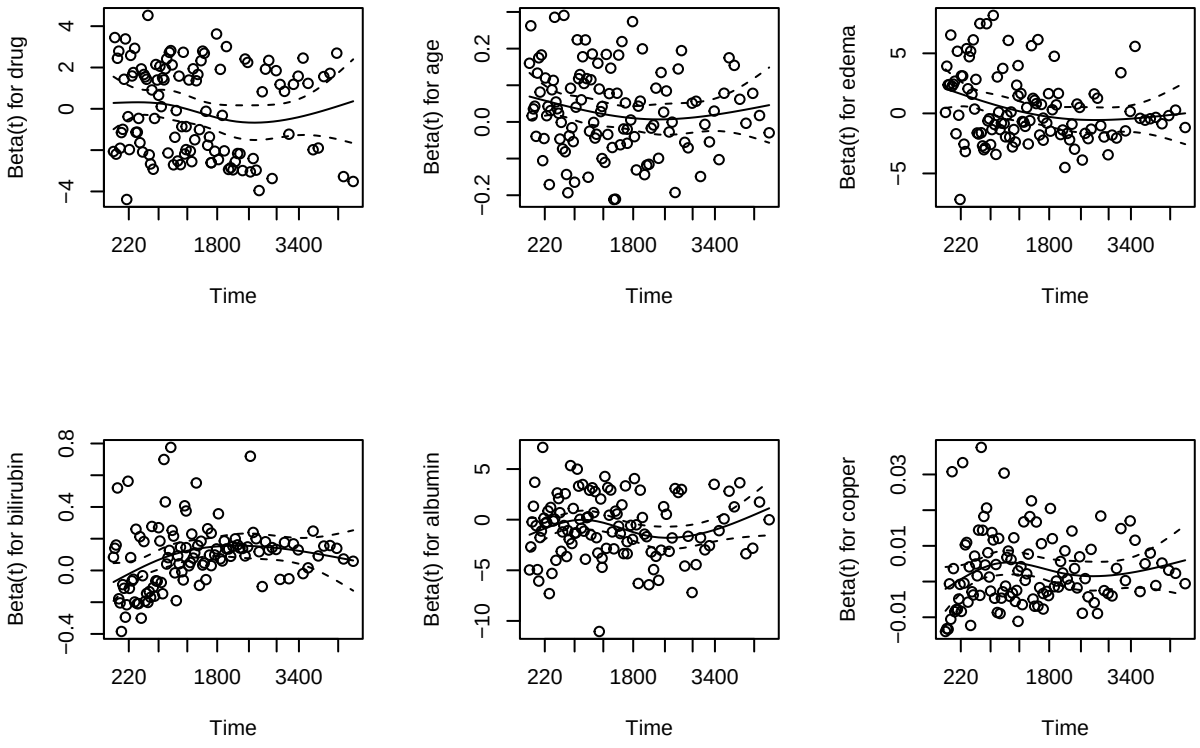
	chisq	df	p
drug	0.1600772	1	0.6890854
age	2.6909476	1	0.1009198
edema	6.1134319	1	0.0134158
bilirubin	8.3071868	1	0.0039489
albumin	0.6258766	1	0.4288719
copper	0.1021024	1	0.7493211
sgot	1.3384725	1	0.2473035
prothrombin	5.0189196	1	0.0250718
stage	4.5185052	3	0.2106456
GLOBAL	24.6087203	11	0.0103973

We can see from the Table **??** that edema(p=0.013), bilirubin (p=0.003), and prothrombin (p=0.025) violate the ph assumptions. To reduce bias, stratification and a time interactions on the violating covariates was conducted.

Table 3: Multivariate Cox Proportional Hazards Analysis - Stratification of Edema Model

Characteristic	**HR**[1]	**95% CI**[1]	**p-value**
drug			
D-penicillamine	—	—	
Placebo	0.88	0.59, 1.31	0.5
age	1.03	1.01, 1.05	0.005
bilirubin	1.08	1.04, 1.13	<0.001
albumin	0.50	0.29, 0.86	0.011
copper	1.00	1.00, 1.00	0.004
sgot	1.00	1.00, 1.01	0.033
prothrombin	1.36	1.09, 1.70	0.006
stage			
1	—	—	
2	4.64	0.55, 39.4	0.2
3	6.55	0.83, 52.0	0.075
4	9.43	1.20, 74.3	0.033

[1]HR = Hazard Ratio, CI = Confidence Interval



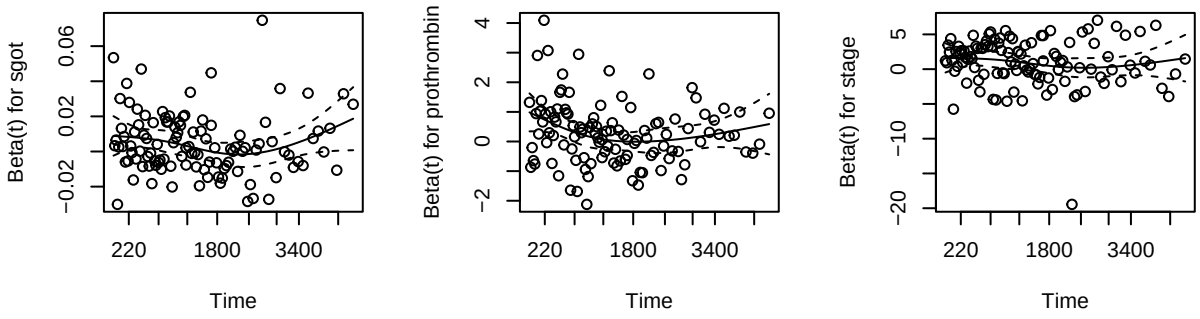


Table 4: Proportional Hazards Assumption Test COX PH Model Stratified for Edema

	chisq	df	p
drug	1.4344763	1	0.2310353
age	1.8937409	1	0.1687806
bilirubin	11.5075689	1	0.0006931
albumin	0.0049180	1	0.9440915
copper	0.3914633	1	0.5315312
sgot	1.0484233	1	0.3058705
prothrombin	2.6117691	1	0.1060734
stage	3.0850010	3	0.3787045
GLOBAL	18.9514038	10	0.0408843

We can see from the Table **??** that bilirubin (p=0.0006) violates the ph assumptions.

Limitations

There were several limitations within the project including missing data, imbalanced data, and a high censoring rate. Regarding missing data, 147 observation had missing values, which may require the application of imputations techniques to address potential bias. Furthermore, the data imbalance was attributed to the distribution of sex, where we had about 80-90% female participants and the right-skwedness of bilirubin. Lastly, with more than 50% of data being censored, high censoring data was a major limitation on the survival analysis and the robustness of the results.