Applied Regression II Final - Part Two

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Model summaries and outcomes for both model one and model two are found in the summary section.

Model One: Parental depression independent of time

Model one uses a Cox model to model the time until a child experiences depression as a function of parental history of depression. I fit a crude and an adjusted model.

The crude model one is:

$$h(t, x) = h_0(t)h(\beta_1 x_{1i})$$

$$\text{where, } x_1 = \begin{cases} 0 \text{ if no history of parental depression} \\ 1 \text{ if history of parental depression} \end{cases}$$

The adjusted model one is:

$$h(t, x) = h_0(t)h(\beta_1 x_{1i} + \beta_2 x_{2i} + \beta_3 x_{3i} + \beta_4 x_{4i} + \beta_5 x_{5i} + \beta_6 x_{6i} + \beta_7 x_{7i})$$

$$\text{where, } x_1 = \begin{cases} 0 \text{ if no history of parental depression} \\ 1 \text{ if history of parental depression} \end{cases} \quad x_2 = \begin{cases} 0 \text{ if female} \\ 1 \text{ if male} \end{cases}$$

$$x_3 = \begin{cases} 1 \text{ if SES class is 2} \\ 0 \text{ otherwise} \end{cases} \quad x_4 = \begin{cases} 1 \text{ if SES class is 3} \\ 0 \text{ otherwise} \end{cases} \quad x_5 = \begin{cases} 1 \text{ if SES class is 4} \\ 0 \text{ otherwise} \end{cases}$$

$$x_6 = \begin{cases} 1 \text{ if SES class is 5} \\ 0 \text{ otherwise} \end{cases} \quad x_7 = \begin{cases} 1 \text{ if parents married} \\ 0 \text{ otherwise} \end{cases}$$

SAS code for the crude and adjusted model is as follows:

```
proc phreg data = depression;
    class parent_dep (ref = '0') / param = ref;
    model follow_time * child_dep(0) = parent_dep / ties = efron risklimits;
    assess ph / resample;
run;

proc phreg data = depression;
    class parent_dep (ref = '0')
          child_sex (ref = '1')
          ses_parent (ref = '1')
          mar_stat_parent (ref = '1') / param = ref;
    model follow_time*child_dep(0) = parent_dep child_sex ses_parent mar_stat_parent
      / ties = efron risklimits;
    assess ph / resample;
run;
```

I tested the proportional hazards assumption for all covariates and found that the assumption was violated for parental depression status ($p = 0.003$). Because the proportional hazards assumption is violated, parental depression is a time-dependent variable and needs to be adjusted for.

Checking Proportional Hazards Assumption for parent_dep1
Observed Path and First 20 Simulated Paths
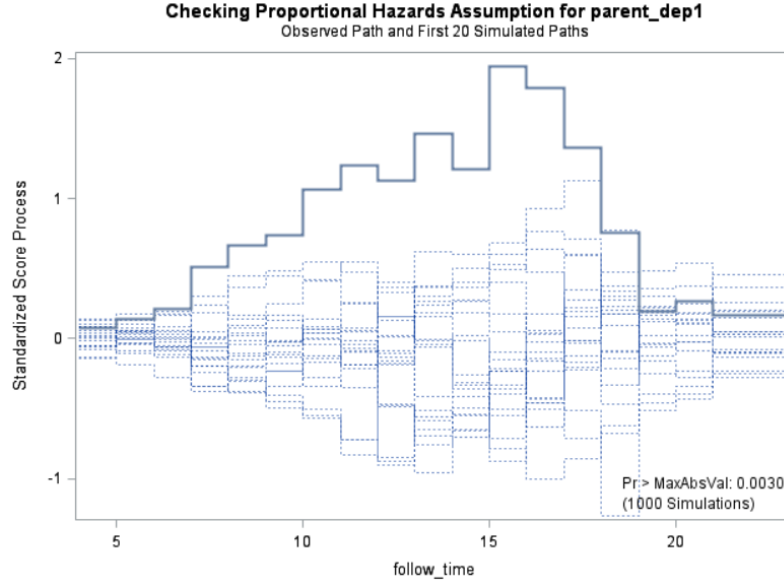
Model Two

A check of the proportional hazards assumption in model one showed that the effect of parental history on the time until a child experiences depression is not constant over time. As such, in model 2 I have introduced a time-dependent covariate ("early_onset") that indicates if the age that depression started or the age at which censoring occurred was pre-pubertal (< 13 years old) or not (13 years or older):

The crude model one is:

$$h(t,x) = h_0(t)h(\beta_1 x_{1i} + \beta_2 x_{2i} + \beta_3 x_{1i} x_{2i})$$

$$\text{where, } x_1 = \begin{cases} 0 \text{ if no history of parental depression} \\ 1 \text{ if history of parental depression} \end{cases}$$

$$x_2 = \begin{cases} 0 \text{ if follow time is } \geq \ 13 \text{ years} \\ 1 \text{ if follow time is } < \ 13 \text{ years} \end{cases}$$

The adjusted model two is:

$$h(t,x) = h_0(t)h(\beta_1 x_{1i} + \beta_2 x_{2i} + \beta_3 x_{3i} + \beta_4 x_{4i} + \beta_5 x_{5i} + \beta_6 x_{6i} + \beta_7 x_{7i} + \beta_8 x_{8i} + \beta_9 x_{1i} x_{2i})$$

$$\text{where, } x_1 = \begin{cases} 1 \text{ if history of parental depression} \\ 0 \text{ if no history of parental depression} \end{cases}$$

$$x_2 = \begin{cases} 1 \text{ if follow time is } < \ 13 \text{ years} \\ 0 \text{ if follow time is } \geq \ 13 \text{ years} \end{cases} \quad x_3 = \begin{cases} 1 \text{ if Male} \\ 0 \text{ if Female} \end{cases} \quad x_4 = \begin{cases} 1 \text{ if SES class is 2} \\ 0 \text{ otherwise} \end{cases}$$

$$x_5 = \begin{cases} 1 \text{ if SES class is 3} \\ 0 \text{ otherwise} \end{cases} \quad x_6 = \begin{cases} 1 \text{ if SES class is 4} \\ 0 \text{ otherwise} \end{cases}$$

$$x_7 = \begin{cases} 1 \text{ if SES class is 5} \\ 0 \text{ otherwise} \end{cases} \quad x_8 = \begin{cases} 1 \text{ if parents married} \\ 0 \text{ otherwise} \end{cases}$$

SAS code for the crude and adjusted model two, as well as the survival plot is as follows:

```
data depression;
    set depression;
```

```
    if follow_time >= 13 then early_onset = 0;
        else early_onset = 1;
run;

proc phreg data = depression;
    class parent_dep (ref = '0')
            early_onset (ref = '0') / param = ref;
    model follow_time * child_dep(0) = parent_dep early_onset parent_dep*early_onset / ties = efron;
    hazardratio parent_dep / diff = ref;
run;

proc phreg data = depression;
    class parent_dep (ref = '0')
            early_onset (ref = '0')
            child_sex (ref = '1')
            ses_parent (ref = '1')
            mar_stat_parent (ref = '1') / param = ref;
    model follow_time * child_dep(0) = parent_dep early_onset child_sex ses_parent
            mar_stat_parent parent_dep*early_onset / ties = efron risklimits;
    hazardratio parent_dep / diff = ref;
run;

data plot;
    input Strata parent_dep early_onset child_sex ses_parent mar_stat_parent;
    datalines;
    1 1 1 1 1 1
    2 0 1 1 1 1
    3 1 0 1 1 1
    4 0 0 1 1 1
    ;
run;

proc phreg data = depression plots(overlay) = survival;
    model follow_time * child_dep(0) = parent_dep early_onset parent_dep*early_onset / ties = efron;
    hazardratio parent_dep / diff = ref;
    baseline covariates = plot / rowid = Strata;
    title "Survival curves of different child categories";
run;
```

Summary

Using likelihood ratio tests, at the 5% significance level both adjusted model one and adjusted model two were statistically significant (Model one: $\chi^2_1 = 20.02, p = 0.006$, Model two: $\chi^2_3 = 107.06, p < 0.0001$).

Table 1 provides hazard ratios and corresponding 95% confidence intervals for model one. Based on model one, children with parental history of depression have 2.28 times the risk of experiencing depression themselves compared to children without parental history of depression, adjusting for sex, SES class of parents, and marital status of parents (95% CI: 1.209, 3.332). However, a check of the proportional hazards assumption for model one revealed that the effect of parental depression was not constant over time (p = 0.002).

Table two provides hazard ratios and 95% confidenc intervals for model two. Model two includes a time dependent covariate that indicates if depression onset was pre-pubertal or not (depression onset occurs before 13) and an interaction term between this variable and parental depression ($\chi^2_1 = 3.51, p = 0.06$). Assessing risk of depression using this interaction term revealed that children with a parental history of depression have 1.45 (95% CI: 0.78, 2.69) times the risk of experiencing non-pre-pubertal depression compared to children without a parental history of depression, adjusting for sex, SES status of parents, and marital status of

parents. However, children with parental history of depression have 5.31 (95% CI: 1.55, 18.26) times the risk of experiencing pre-pubertal depression than children without a parental history of depression, adjusting for all other covariates.

Based on these analysis, children of depressed parents do experience a higher risk of depression themselves before the age of 13 compared to children without depressed parents. However, the risk of depression after the age of 13 is the same among both groups of children. Survival curves for model two can be found in Figure 1.

Table 1: Model one crude and adjusted hazards ratio

Covariate	HR (95% CI)	p-Value
Crude		
Parent Dep. vs. None	2.01 (1.21, 3.33)	0.007
Adjusted		
Parent Dep vs. None	2.28 (1.34, 3.88)	0.002
Female vs. Male	1.84 (1.10, 3.07)	0.02
SES 1	Reference	
SES 2	1.75 (0.47, 6.62)	0.41
SES 3	2.60 (0.74, 9.16)	0.14
SES 4	2.08 (0.61, 7.07)	0.24
SES 5	1.05 (0.24, 4.50)	0.95
Not married vs. Married	0.91 (0.50, 1.62)	0.74

Table 2: Model two crude and adjusted hazard ratios

| Covariate	HR (95% CI)	p-Value
Crude Model		
Parent Dep. vs. None		0.36
Parent Dep., Pre-pubertal interaction		
Parent Dep. vs. None, pre-pubertal onset	5.16 (1.53, 17.42)	
Parent Dep. vs. None, not pre-pubertal onset	1.32 (0.73, 2.38)	
Adjusted Model		
Parent Dep. vs. None		0.23
Parent Dep., Pre-pubertal interaction		
Parent Dep. vs. None, pre-pubertal onset	5.31 (1.55, 18.26)	
Parent Dep. vs. None, not pre-pubertal onset	1.45 (0.78, 2.69)	
Female vs. Male	1.71 (1.02, 2.88)	0.04
SES Class		
1	Reference	
2	1.52 (0.41, 5.71)	0.54
3	2.34 (0.67, 8.15)	0.18
4	2.09 (0.62, 7.06)	0.24
5	1.47 (0.34, 6.39)	0.61
Not married vs. Married	1.25 (0.70, 2.24)	0.46
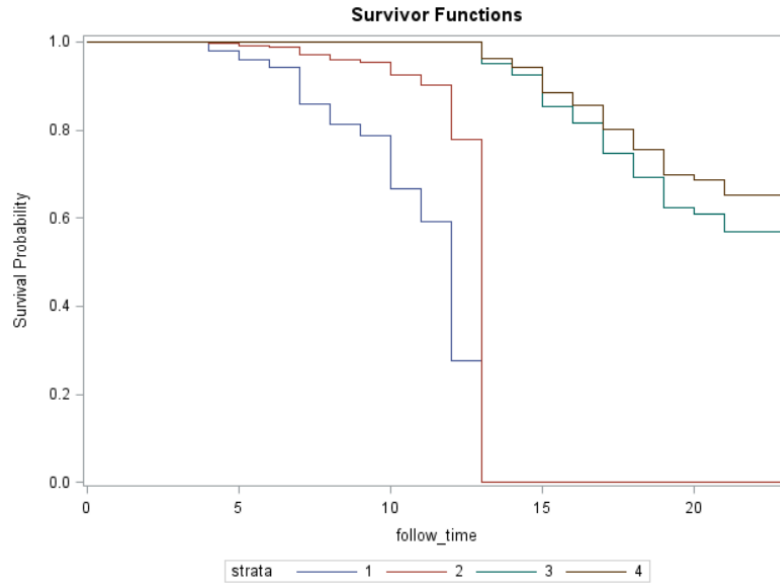
Figure 1: Strata 1: history of parental depression, pre-pubertal onset of depression; Strata 2: no history of parental depression, pre-pubertal depression; Strata 3: history of parental depression, no pre-pubertal onset; Strata 4: no history of parental depression, no pre-pubertal onset