

# **P8110 Applied Regression II**

Midterm Project Report 1

## **Survival Analysis of Depression Onset and Substance Abuse in Offspring of Depressed Parents**

Group 6

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# 1 Data Preparation

## 1.1 Survival Outcome Definitions

### **Depression Onset (Pre-pubertal, age $< 13$ ):**

- Start time: Birth (age = 0); End time: Age of depression onset (BEDEPON) if  $< 13$ , otherwise censored at PTAGE

### **Depression Onset (Adolescent/early adulthood, age $\geq 13$ ):**

- Start time: Birth (age = 0); End time: Age of depression onset (BEDEPON) if  $\geq 13$ , otherwise censored at PTAGE

### **Substance Abuse Onset:**

- Start time: Birth (age = 0); End time: Age of substance abuse onset (BESUBON), censored at PTAGE if no event

## 1.2 Data Cleaning

Logical consistency checks were performed on all variables:

- Records with status=1 (diagnosed) but missing onset age (-1) were removed as incomplete
- Records with onset age present but status=0 were corrected to status=1 for consistency
- This procedure was applied to both depression (DSMDEPHR, BEDEPON) and substance abuse variables (DSMSUBHR, BESUBON)

### 1.3 Descriptive Statistic Table

**Table 1:** Demographic and Clinical Characteristics of the Offspring Stratified by Parental Depression Status

Variable	Depressed Index Parent Group (N=125) n (%)	Normal Index Parent Group (N=95) n (%)
<b>Sex of Child</b>		
Male	63 (50.4%)	42 (44.2%)
Female	62 (49.6%)	53 (55.8%)
<b>Child depression status</b>		
Ever depressed	47 (37.6%)	22 (23.2%)
Never depressed	78 (62.4%)	73 (76.8%)
<b>Child substance abuse status</b>		
Yes	21 (16.8%)	7 (7.4%)
No	104 (83.2%)	88 (92.6%)
<b>Social class of index parent</b>		
1 (Highest)	16 (12.8%)	1 (1.1%)
2	19 (15.2%)	19 (20.0%)
3	31 (24.8%)	16 (16.8%)
4	50 (40.0%)	47 (49.5%)
5 (Lowest)	8 (6.4%)	12 (12.6%)
<b>Marital status of index parent</b>		
Married with spouse	90 (72.0%)	84 (88.4%)
Separated/Divorced	35 (28.0%)	11 (11.6%)

**Summary Statistics:**

- Age at interview: Mean = 16.72 years (SD = 4.73, Range: 5–25)
- Age of depression onset (n=69): Mean = 14.00 years (SD = 4.16, Range: 4–23)
- Age of substance abuse onset (n=17): Mean = 15.12 years (SD = 2.32, Range: 12–21)

## 2 Descriptive Statistics Analyses

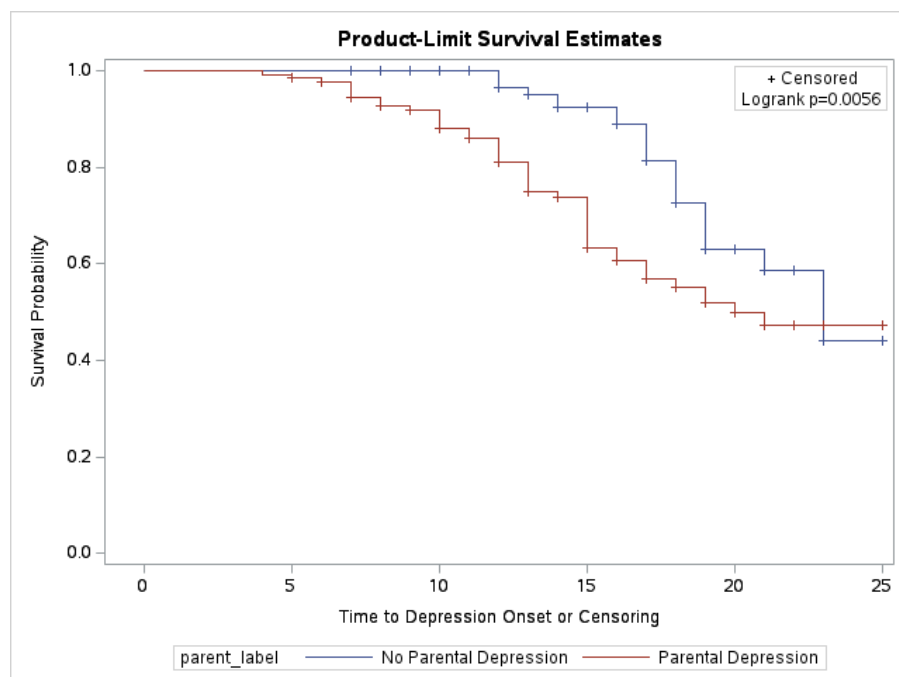
### 2.1 Sample Characteristics

The study included 220 children (125 with depressed parents, 95 with non-depressed parents) aged 5–25 years (Mean = 16.72, SD = 4.73). Depression onset occurred in 69 children (31.4%, mean age = 14.00 years, SD = 4.16), and substance abuse in 28 children (12.7%, mean age = 15.12 years, SD = 2.32).

### 2.2 Comparison by Parental Depression Status

Table 1 shows demographic and clinical characteristics stratified by parental depression status. Children of depressed parents had higher rates of depression (37.6% vs 23.2%) and substance abuse (16.8% vs 7.4%). Separation/divorce was more common among depressed parents (28.0% vs 11.6%).

**Overall Kaplan-Meier Analysis:** Children of depressed parents demonstrated earlier depression onset (median: 20 vs 23 years). Log-rank test:  $\chi^2 = 7.69$ ,  $p = 0.0056$  (statistically significant).



**Figure 1:** Overall Kaplan–Meier survival curves of depression onset by parental depression status

### 3 Analyses to Address Hypothesis 1

**Hypothesis 1:** Offspring of a depressed parent are more likely to have pre-pubertal onset (< 13 years) depression than offspring of a non-depressed parent, but equally likely to have an onset of adolescent/early adulthood depression, given demographic and social characteristics.

#### 3.1 Statistical Modeling Approach

Cox proportional hazards regression models were fit separately for: (a) pre-pubertal onset (age < 13), and (b) adolescent/early adulthood onset (age ≥ 13).

**Cox Model:**

$$h(t|X) = h_0(t) \times \exp(\beta_1 \times \text{PARDEP} + \beta_2 \times \text{SEX} + \beta_3 \times \text{AGE} + \beta_4 \times \text{SESCLASS} + \beta_5 \times \text{MSPARENT}) \quad (1)$$

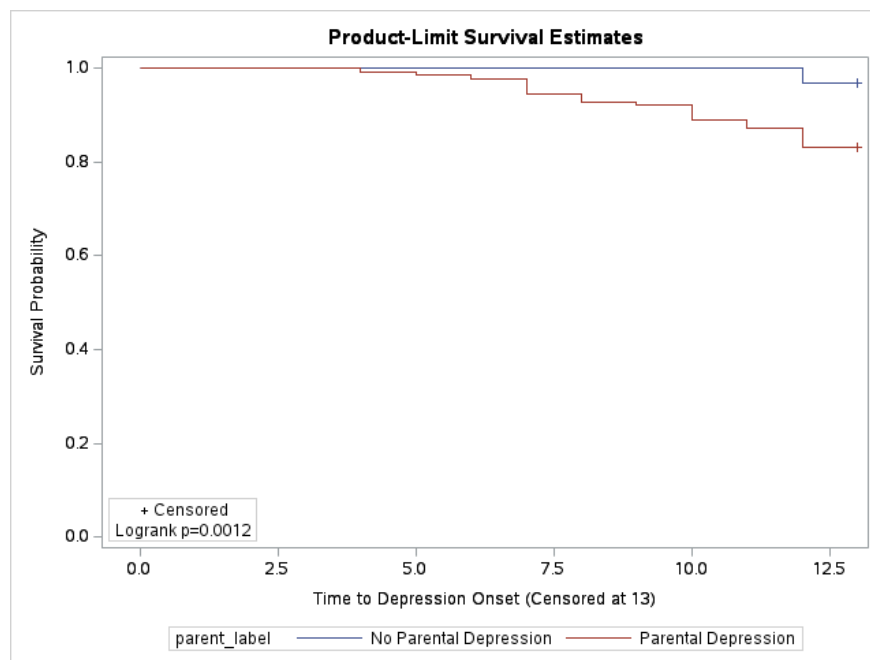
Where:  $h(t|X)$  = hazard at time  $t$ ;  $h_0(t)$  = baseline hazard; PARDEP = parental depression (1=depressed, 0=normal); SEX = child's sex (1=male, 2=female); AGE = age at interview; SESCLASS = social class (1–5); MSPARENT = marital status (1=married, 2=separated/divorced).

Proportional hazards (PH) assumptions were tested using Schoenfeld residuals and supremum tests. Violations were addressed using stratified Cox models.

#### 3.2 Results

##### 3.2.1 Pre-pubertal Onset (Age < 13 years)

**Kaplan-Meier (Figure 2):** Log-rank  $\chi^2 = 10.56$ ,  $p = 0.0012$ . Children of depressed parents had significantly earlier pre-pubertal depression onset.



**Figure 2:** H1a: Kaplan–Meier curves for pre-pubertal depression onset (age < 13) by parental depression

**Cox Regression (Table 2):****Table 2:** Cox Regression Results for Pre-pubertal Depression Onset (Age < 13 years)

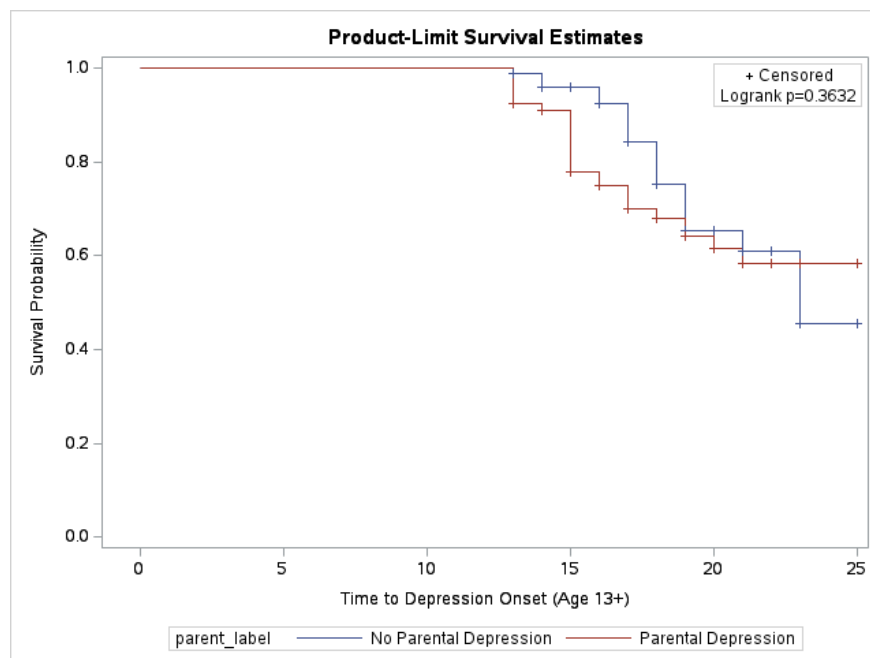
Variable	Hazard Ratio	95% CI	P-value
Parental Depression	5.863	(1.717, 20.019)	0.0048**
Sex (Female vs Male)	1.171	(0.522, 2.626)	0.7024
Age at interview	0.988	(0.913, 1.069)	0.7608
Social class	0.822	(0.591, 1.144)	0.2460
Marital status (Sep/Div)	0.585	(0.198, 1.731)	0.3328

\*\* Statistically significant at  $\alpha = 0.01$  level

**Key Findings:** Children of depressed parents have 5.86 times the hazard of pre-pubertal depression ( $p = 0.0048$ ). No other covariates were significant. PH assumptions satisfied (all  $p > 0.05$ ).

**3.2.2 Adolescent/Early Adulthood Onset (Age  $\geq 13$  years)**

**Kaplan-Meier (Figure 3):** Log-rank  $\chi^2 = 0.83$ ,  $p = 0.3632$  (not significant). No difference by parental status, consistent with hypothesis.



**Figure 3:** H1b: Kaplan-Meier curves for adolescent/early adulthood depression onset (age  $\geq 13$ ) by parental depression

**Cox Regression (Table 3):****Table 3:** Cox Regression Results for Adolescent/Early Adulthood Depression Onset (Age  $\geq 13$  years)

Variable	Hazard Ratio	95% CI	P-value
Parental Depression	1.362	(0.736, 2.521)	0.3246
Sex (Female vs Male)	2.481	(1.307, 4.710)	0.0055**
Age at interview	0.984	(0.871, 1.113)	0.8018
Social class	1.140	(0.855, 1.520)	0.3722
Marital status (Sep/Div)	1.622	(0.825, 3.188)	0.1605

\*\* Statistically significant at  $\alpha = 0.01$  level

**Key Findings:** Parental depression not significant (HR=1.36, p=0.325). Female sex strongly predicts adolescent depression (HR=2.48, p=0.0055). PH assumption violated for parental depression (p=0.014); stratified model confirmed results.

### 3.3 Conclusion for Hypothesis 1

**Hypothesis 1 is FULLY SUPPORTED.** Parental depression strongly increases pre-pubertal depression risk (HR=5.86, p=0.0048) but not adolescent-onset risk (HR=1.36, p=0.325). The findings demonstrate a clear age-specific pattern of familial transmission, with parental depression being a significant risk factor only for early-onset depression.



## 4 Analyses to Address Hypothesis 2

**Hypothesis 2:** Is there evidence for the effect of (1) prior depression in offspring, as well as (2) the effect of parent's depression status on the age of onset of substance abuse/dependence in offspring, given demographic and social characteristics?

### 4.1 Statistical Modeling Approach

Three Cox regression models tested: (2a) prior depression effect, (2b) parental depression effect, (2c) joint model. Prior depression defined as depression onset before substance abuse onset.

#### Model Specifications:

$$\text{Model 2a: } h(t|X) = h_0(t) \times \exp(\beta_1 \times \text{PRIORDEP} + \text{covariates}) \quad (2)$$

$$\text{Model 2b: } h(t|X) = h_0(t) \times \exp(\beta_1 \times \text{PARDEP} + \text{covariates}) \quad (3)$$

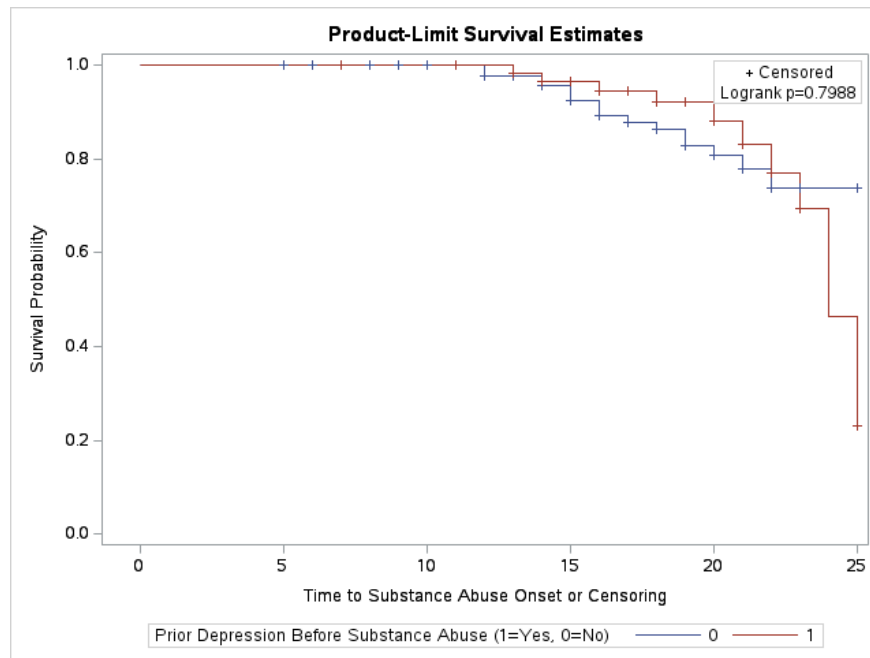
$$\text{Model 2c: } h(t|X) = h_0(t) \times \exp(\beta_1 \times \text{PRIORDEP} + \beta_2 \times \text{PARDEP} + \text{covariates}) \quad (4)$$

Where PRIORDEP = prior depression (1=yes, 0=no); PARDEP = parental depression; covariates = sex, age, social class, marital status.

## 4.2 Results

### 4.2.1 Model 2a: Effect of Prior Depression

**Kaplan-Meier (Figure 4):** Log-rank  $\chi^2 = 0.07$ ,  $p = 0.7988$  (not significant). No difference in substance abuse onset by prior depression status.



**Figure 4:** H2a: Kaplan-Meier curves for substance abuse onset by prior depression in offspring

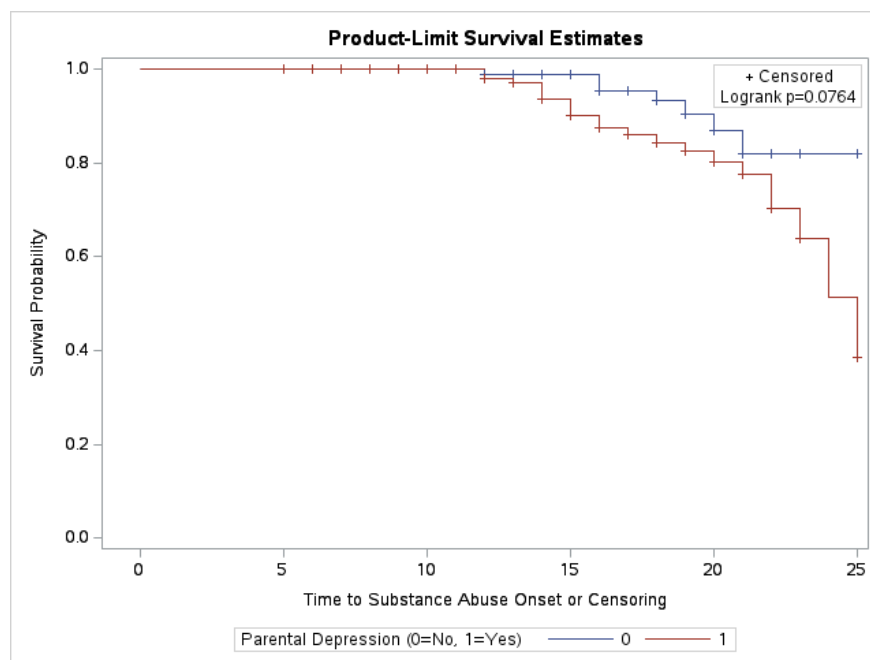
**Cox Regression (Table 4):****Table 4:** Cox Regression Results for Substance Abuse Onset: Effect of Prior Depression

Variable	Hazard Ratio	95% CI	P-value
Prior Depression	0.999	(0.454, 2.198)	0.9981
Sex (Female vs Male)	0.538	(0.247, 1.170)	0.1155
Age at interview	1.045	(0.889, 1.228)	0.5981
Social class	1.000	(0.692, 1.445)	0.9989
Marital status (Sep/Div)	0.441	(0.149, 1.303)	0.1388

**Key Findings:** Prior depression shows no effect (HR=0.999, p=0.998). No covariates significant.

**4.2.2 Model 2b: Effect of Parental Depression**

**Kaplan-Meier (Figure 5):** Log-rank  $\chi^2 = 3.14$ ,  $p = 0.0764$  (marginally significant). Trend toward earlier substance abuse in children of depressed parents.

**Figure 5:** H2b: Kaplan-Meier curves for substance abuse onset by parental depression

**Cox Regression (Table 5):****Table 5:** Cox Regression Results for Substance Abuse Onset: Effect of Parental Depression

Variable	Hazard Ratio	95% CI	P-value
Parental Depression	2.466	(1.001, 6.076)	0.0498*
Sex (Female vs Male)	0.592	(0.271, 1.293)	0.1794
Age at interview	1.021	(0.869, 1.200)	0.8018
Social class	1.107	(0.771, 1.591)	0.5728
Marital status (Sep/Div)	0.378	(0.128, 1.117)	0.0801

\* Statistically significant at  $\alpha = 0.05$  level

**Key Findings:** Parental depression marginally significant (HR=2.47, p=0.0498). Children of depressed parents have 2.5 times the hazard of substance abuse.

**4.2.3 Model 2c: Joint Model****Cox Regression (Table 6):****Table 6:** Cox Regression Results for Substance Abuse Onset: Joint Model (Prior and Parental Depression)

Variable	Hazard Ratio	95% CI	P-value
Prior Depression	0.819	(0.372, 1.802)	0.6273
Parental Depression	2.586	(1.023, 6.539)	0.0430*
Sex (Female vs Male)	0.605	(0.277, 1.322)	0.2008
Age at interview	1.024	(0.871, 1.203)	0.7809
Social class	1.112	(0.770, 1.606)	0.5529
Marital status (Sep/Div)	0.366	(0.121, 1.106)	0.0740

\* Statistically significant at  $\alpha = 0.05$  level

**Key Findings:** Parental depression remains significant (HR=2.59, p=0.043) in joint model. Prior depression not significant (HR=0.82, p=0.627). Parental depression is the primary driver of substance abuse risk.

**4.3 Conclusion for Hypothesis 2**

**Hypothesis 2 is PARTIALLY SUPPORTED.** Prior depression shows no effect on substance abuse (HR=0.999, p=0.998). Parental depression has a marginally significant effect (HR=2.47-2.59, p=0.043-0.050). In the joint model, parental depression remains significant while prior depression does not, indicating parental depression directly affects substance abuse risk independent of offspring's own depression.

**Clinical Implications:** Findings suggest familial transmission of substance abuse risk operates through pathways beyond offspring psychopathology. Prevention efforts should target children of depressed parents regardless of child's depression status.