

Cox Model With Time Varying Covariates

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Introduction

The Cox Proportional Hazards Model is an important model in *event history and survival analysis*. One important aspect of the Cox Model is its ability to include *time varying covariates*, covariates whose value changes over time.

The example below draws heavily from—but is slightly adapted from—the Stata `help stcox` file.

Get Data

```
. use https://www.stata-press.com/data/r17/drugtr2, clear // simulated drug data
```

Per the Stata documentation:

“Consider a dataset consisting of 45 observations on recovery time from walking pneumonia. Recovery time (in days) is recorded in the variable `time`, and there are measurements on the covariates `age`, `drug1`, and `drug2`, where `drug1` and `drug2` interact a choice of treatment with initial dosage level. The study was terminated after 30 days, so those who had not recovered by that time were censored (`cured = 0`).”

Look At The Data

It may be useful to take a quick look at the data.

```
. list in 1/10
```

	age	drug1	drug2	time	cured	_st	_d	_t	_t0
1.	36	0	50	20.6	1	1	1	20.6	0
2.	14	0	50	6.8	1	1	1	6.8000002	0
3.	43	0	125	8.6	1	1	1	8.6000004	0
4.	25	100	0	10	1	1	1	10	0
5.	50	100	0	30	0	1	0	30	0
6.	26	0	100	13.6	1	1	1	13.6	0
7.	21	150	0	5.4	1	1	1	5.4000001	0
8.	25	0	100	15.4	1	1	1	15.4	0
9.	32	125	0	8.6	1	1	1	8.6000004	0
10.	28	150	0	8.5	1	1	1	8.5	0

stset The Data

```
. stset time, failure(cured) // set up data for survival analysis
Survival-time data settings
    Failure event: cured!=0 & cured<.
```

Observed time interval: (0, time]
Exit on or before: failure

```

45 total observations
0 exclusions

```

```

45 observations remaining, representing
36 failures in single-record/single-failure data
677.9 total analysis time at risk and under observation
      At risk from t =      0
      Earliest observed entry t =      0
      Last observed exit t =     30

```

Model 1: Drugs Are *Time Invariant* Covariates

```

. stcox age drug1 drug2 // Cox model
      Failure _d: cured
      Analysis time _t: time
Iteration 0: Log likelihood = -116.54385
Iteration 1: Log likelihood = -102.77311
Iteration 2: Log likelihood = -101.92794
Iteration 3: Log likelihood = -101.92504
Iteration 4: Log likelihood = -101.92504
Refining estimates:
Iteration 0: Log likelihood = -101.92504
Cox regression with Breslow method for ties
No. of subjects =      45          Number of obs =      45
No. of failures =      36
Time at risk    = 677.9
Log likelihood = -101.92504          LR chi2(3)    = 29.24
                                          Prob > chi2   = 0.0000

```

_t	Haz. ratio	Std. err.	z	P> z	[95% conf. interval]
age	.8759449	.0253259	-4.58	0.000	.8276873 .9270162
drug1	1.008482	.0043249	1.97	0.049	1.000041 1.016994
drug2	1.00189	.0047971	0.39	0.693	.9925323 1.011337

```
. est store M1 // store estimates
```

Model 2: Drugs Are *Time Varying* Covariates

Option `tv` allows us to model time varying covariates. By including `, tvc(drug1 drug2)` in the `stcox` command below, we allowing `drug1` and `drug2` to have a *linear* interaction with time. Essentially, we are providing a *formula* for how the association of these variables with the hazard changes over time. We can estimate more complex interactions of time varying covariates with time. See `help stcox` for information.

```

. stcox age, tvc(drug1 drug2) // Cox model
      Failure _d: cured
      Analysis time _t: time
Iteration 0: Log likelihood = -116.54385
Iteration 1: Log likelihood = -104.50191
Iteration 2: Log likelihood = -103.87961
Iteration 3: Log likelihood = -103.87525
Iteration 4: Log likelihood = -103.87525
Refining estimates:
Iteration 0: Log likelihood = -103.87525
Cox regression with Breslow method for ties
No. of subjects =      45          Number of obs =      45
No. of failures =      36
Time at risk    = 677.9

```


age	.8786593	.0250789	-4.53	0.000	.8308552	.9292139
drug1emt	1.000272	.000335	0.81	0.416	.9996161	1.000929
drug2emt	.9998618	.000364	-0.38	0.704	.9991486	1.000576

. est store M3 // store estimates

Nice Table of Estimates to Compare Models

. est table M1 M2 M3, star equations(1)

Variable	M1	M2	M3
#1			
age	-.13245204***	-.12935802***	-.12935802***
drug1	.00844606*		
drug2	.00188866		
drug1emt			.0002724
drug2emt			-.00013819
tvc			
drug1		.0002724	
drug2		-.00013819	

Legend: * p<0.05; ** p<0.01; *** p<0.001