STAT 6390: Analysis of Survival Data

Textbook coverage: Chapter 1

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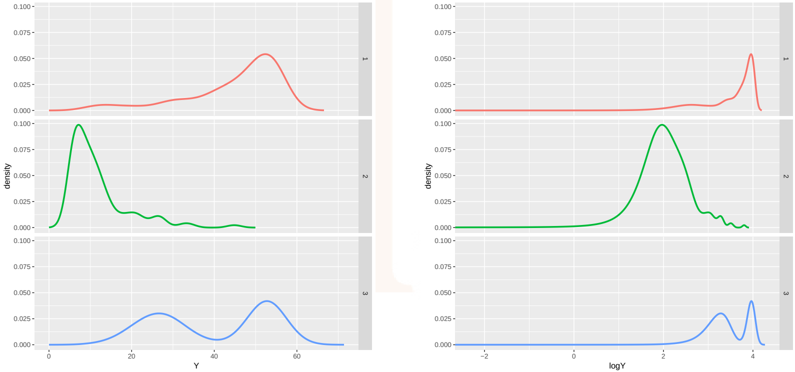
Survival analysis?

- Survival analysis aka
  - duration analysis
  - event history analysis
  - time to event analysis
- Models the relationship between duration (Y) and covariates (X).
  - time until graduation
  - time until failure of an electronic component
  - time until a patient dies
- Linear regression, e.g., ordinary least squares `lm(Y ~ X)`, is usually not feasible.

Why not use OLS?

- Inference for OLS assumes Y is normal.
    - Duration is always positive.
    - Duration is usually not-normal.
    - Log-transformation might not work.



Why not use OLS?

- OLS handles missing values via complete case analysis or imputation*.
  - Survival data consists of missing values that are meaningful, so dropping incomplete observations means losing information.
  - Imputation requires additional assumption from the distribution of Y.
  - Replacing missing values with mean or median would result in underestimation if the missingness are caused by *right censoring*.
- Common source of missing values in survival data: *censoring* and *truncation*.

Other reasons for survival models

- Survival models can handle time-varying covaraites.
- Probabilities associated with survival times is more relevant.
- Many existing packages make routine survival analysis more accessible.
- A partial list of `R` package can be found here: https://cran.r-project.org/web/views/Survival.html

Censoring

- The survival time of an individual is said to be *right censored* when the end-point of interest has not been observed for that individual.
- The “end-point” is a well-defined event, say death from a disease.
- The actually survival time can be regarded as right censored when
  - lost to follow-up
  - death from a different cause
  - no event had occurred by the end of the study

Loading `survMisc`, Ver 0.4.6.

- Most datasets in the book are available via `R` package **`survMisc`**
- Some datasets are only available in version 0.4.6 or eariler.
- Archived `R` package can be installed with

```
> ## install.package("devtools")
> library(devtools)
> install_version("survMisc", version = "0.4.6")
```

- `install.package()` installs the latest version.
- `install_version()` installs a specified package.

WHAS

- Load data from Worcester Heart Attach Study (WHAS) in Table 1.1:

```
> data(whas100, package = "survMisc")
```

- The above code only works with **survMisc** version ≤0.4.6.

```
Warning in readChar(con, 5L, useBytes = TRUE): cannot open compressed file
'whas100.RData', probable reason 'No such file or directory'
Error in readChar(con, 5L, useBytes = TRUE): cannot open the connection
```

```
> head(whas100)
Error in head(whas100): object 'whas100' not found
```

- A description of `whas100` can be called from

```
> ?whas100
> ?survMisc::whas100
```

- `whas100` is a `data.frame`.

```
> class(whas100)
Error in eval(expr, envir, enclos): object 'whas100' not found
```

WHAS

- A more effective way to manipulate data frame is through "`tibble`".
- Install **`tidyverse`** (https://www.tidyverse.org)

```
> ## install.package(tidyverse)
> library(tidyverse)
> whas100 <- as.tibble(whas100)
Error in as.tibble(whas100): object 'whas100' not found
> whas100
Error in eval(expr, envir, enclos): object 'whas100' not found
```

WHAS

- A transposed version to print `whas100`:

```
> ## install.package(tidyverse)
> glimpse(whas100)
Error in glimpse(whas100):  object 'whas100' not found
```

- See https://r4ds.had.co.nz/tibbles.html for details.

WHAS

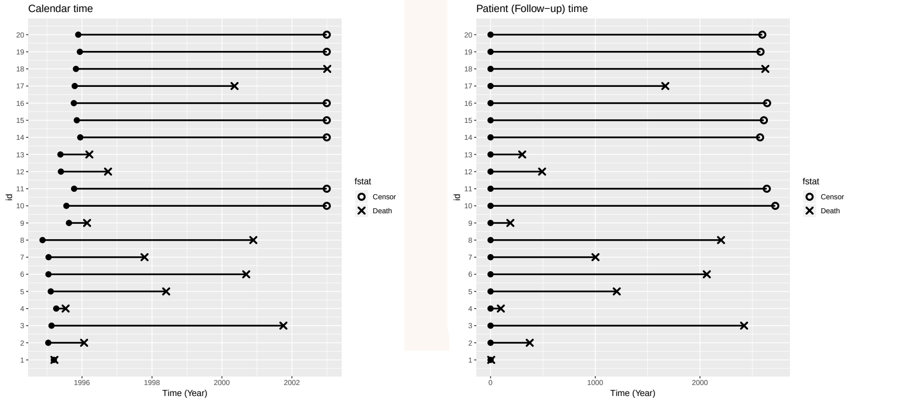
- Here is the screen shot of Table 1.1:

ID	Admission Date	Follow Up Date	Length of Stay	Follow Up Time	Vital Status	Age at Admission	Gender	BMI
1	3/13/95	3/19/95	4	6	Dead	65	Male	31.4
2	1/14/95	1/23/96	5	374	Dead	88	Female	22.7
3	2/17/95	10/4/01	5	2421	Dead	77	Male	27.9
4	4/7/95	7/14/95	9	98	Dead	81	Female	21.5
5	2/9/95	5/29/98	4	1205	Dead	78	Male	30.7
6	1/16/95	9/11/00	7	2065	Dead	82	Female	26.5
7	1/17/95	10/15/97	3	1002	Dead	66	Female	35.7
8	11/15/94	11/24/00	56	2201	Dead	81	Female	28.3
9	8/18/95	2/23/96	5	189	Dead	76	Male	27.1
10	7/22/95	12/31/02	9	2719	Alive	40	Male	21.8

- `los` corresponds to length of stay
- `fstat` corresponds to the vital status; this is also called the *status indicator*, or the *censoring indicator*.
  - It talks the value of 1 if an event has observed (death) and 0 otherwise.

WHAS

- There are two common ways to display follow-up times



WHAS

- Patients are *not* all recruited at exactly the same time.
- The end of study appear to be Jan. 05, 2003.

```
> max(strptime(whas100$foldate, format = "%m/%d/%Y"))
Error in strptime(whas100$foldate, format = "%m/%d/%Y") :  object 'whas100'
not found
```

- Patients remain alive at the end of study,
  - patient # 10, 11, 14, 15, 16, etc.
- or left the study by then are considered (right) censored.
  - none in this study.
- In the above figures, the **X** marks the events.
- There are two types of censoring:
  - Informative; dropout related to the outcome
  - Non-informative (indepndent); dropout not related to the outcome

`Surv` objects

- In this course, we will use t to denote the duration (right figure).
- The `Surv` function in the **survival** package produces a special structure for survival data:

```
> library(survival)
> args(Surv)
function (time, time2, event, type = c("right", "left", "interval",
    "counting", "interval2", "mstate"), origin = 0)
NULL
```

- Similar structure is adopted to several packages. For examples,

```
> args(reda::Survr)
function (ID, time, event, origin = 0, check = TRUE, ...)
NULL
> args(reReg::reSurv)
function (time1, time2, id, event, status, origin = 0)
NULL
```

`Surv` objects

- For the WHAS, the `Surv` object is

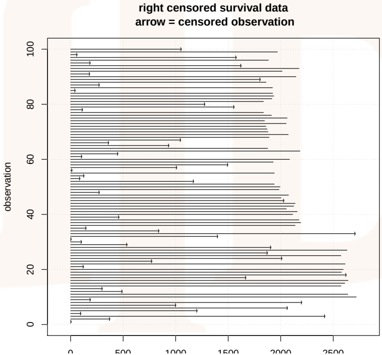
```
> whas100 %>% with(Surv(lenfol, fstat))
Error in eval(lhs, parent, parent):  object 'whas100' not found
```

- There are 100 observation times, e.g., $t_1, \ldots, t_{100}$.
- Censored events are accompanied with $+$.
- With the definition Y is the exact event time, C is the censoring time, then $T = \min(Y, C)$ is the *observed* event time.

Surv objects

- The Surv can be plotted with R 's generic function plot.
- When **survMisc** $\leq$ V0.4.6 is loaded, an event plot will be displayed.

```
> whas100 %>% with(Surv(lenfol, fstat)) %>% plot
```



- This feature has been deprecated with newer version of **survMisc**, where a *Kaplan-Meier* curve will be shown.

`reSurv` objects

- Although `whas100` does not contain recurrent event data, a similar event plot can be produced with package **`reReg`**.
- The latest (development) version of **`reReg`** can be installed via `GitHub`.

```
> ## devtools::install_github("stc04003/reReg")
> library(reReg)
```

- A `reSurv` object must be declared first.

`reSurv` objects

- `reSurv` prints a list-column tibble.

```
> with(whas100, reSurv(lenfol, id, rep(0, 100), fstat))
Error in with(whas100, reSurv(lenfol, id, rep(0, 100), fstat)):  object
'whas100' not found
```

- One way to plot the event plot with **`reReg`** is through `plotEvents`

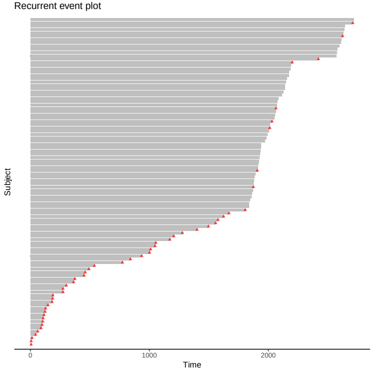
```
> plotEvents(reSurv(lenfol, id, rep(0, 100), fstat) ~ 1, data = whas100)
```

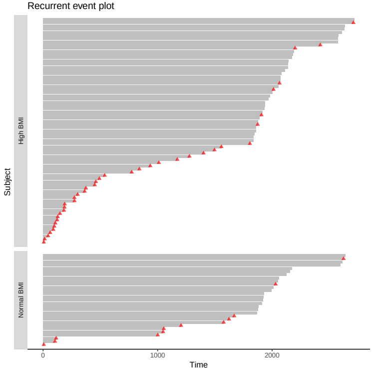
- The function `plotEvents` also allows stratifications.

```
> plotEvents(reSurv(lenfol, id, rep(0, 100), fstat) ~ bmi2,
+            data = whas100 %>% mutate(bmi2 = factor(bmi > 30, labels = c("High
```

reSurv objects

- The following are the event plots produced with the on the last page.





- See https://github.com/stc04003/reReg for mroe details.

Surv objects

- Another example that is subject to right censoring is the Stanford Heart Transplant Data

```
> data(heart)
> head(heart)
  start stop event        age      year surgery transplant id
1     0   50     1 -17.155373 0.1232033       0          0  1
2     0    6     1   3.835729 0.2546201       0          0  2
3     0    1     0   6.297057 0.2655715       0          0  3
4     1   16     1   6.297057 0.2655715       0          1  3
5     0   36     0  -7.737166 0.4900753       0          0  4
6    36   39     1  -7.737166 0.4900753       0          1  4
> heart %>% with(Surv(start, stop, event)) %>% head(14)
 [1] ( 0, 50]  ( 0,  6]  ( 0,  1+] ( 1, 16]  ( 0, 36+] (36, 39]  ( 0, 18]
 [8] ( 0,  3]  ( 0, 51+] (51,675]  ( 0, 40]  ( 0, 85]  ( 0, 12+] (12, 58]
```

- In this dataset, `start` is the entry time, `stop` is the exit time, and `event` is the censoring indicator where death is indicated by `event = 1`.
- In this example, `Surv` displays the "calendar time".

Other censoring

- *Left censoring* is encountered when the event of interest has already occurred when observation begins.
  - Less common.
  - If the event of interest has already occurred when observation begins, the subject is usually not selected in the study. If these subjects are left out, this is referred to *length biased sampling* or a special type of *left truncation*.
- *Interval censoring* is when individuals are known to have experienced an event within an interval of time.
  - When either end of the interval is undefined (∞ or 0), this reduced to either the left censoring or right censoring.
  - When the length of interval is small (e.g., $\rightarrow 0$), one might treats events as uncensored.

Left truncation (Section 7.4)

- After right censoring, the next most common source of incomplete observation is *left truncation* or *delayed entry*.
- An example is the Channing House Data, which can be loaded from the **boot** package.

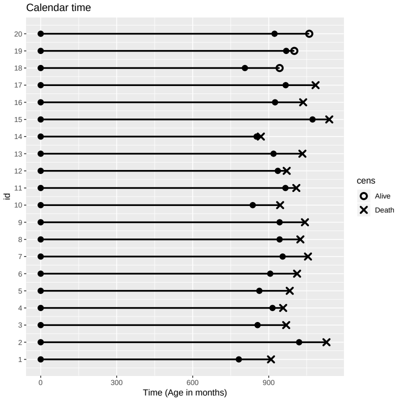
```
> data(channing, package = "boot")
> head(channing)
   sex entry exit time cens
1 Male   782  909  127    1
2 Male  1020 1128  108    1
3 Male   856  969  113    1
4 Male   915  957   42    1
5 Male   863  983  120    1
6 Male   906 1012  106    1
```

- The variables are:

entry	age (months) of entry into the retirement home
exit	age (months) of exiting the retirement home
cens	death status at exit (1 = dead, 0 = alive)

Left truncation

- The data were collected between 1964 and 1975 and feature 52% (right) censoring, as well as left truncation.
- The observed age at death has to be higher than the age at which the subject entered the Channing House retirement house.



Left truncation

- Data that are truncated are unobservable.
- The survival experiences of subjects with delayed entry do not contribute to the analysis until time exceeds an intermediate event.
- If T_i and Y_i are the truncation time and the failure time for the ith patient, respectively. Left truncation implies $T_i < Y_i$.
- Standard survival analysis methods require independent censoring and *quasi-independence* of failure and truncation.