# STAT 6390: Analysis of Survival Data

Textbook coverage: Chapter 1

Steven Chiou

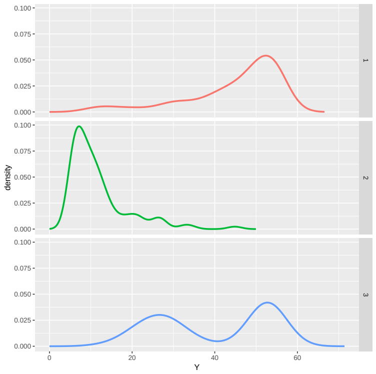
Department of Mathematical Sciences,
University of Texas at Dallas

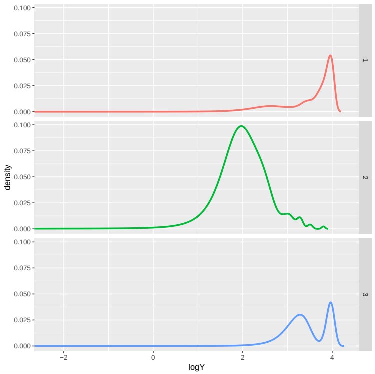
## Survival analysis?

- 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 $\leq$0.4.6.

```
> head(whas100)
  id admitdate   foldate los lenfol fstat age gender      bmi
1  1 3/13/1995 3/19/1995   4      6     1  65      0 31.38134
2  2 1/14/1995 1/23/1996   5    374     1  88      1 22.65790
3  3 2/17/1995 10/4/2001   5   2421     1  77      0 27.87892
4  4  4/7/1995 7/14/1995   9     98     1  81      1 21.47878
5  5  2/9/1995 5/29/1998   4   1205     1  78      0 30.70601
6  6 1/16/1995 9/11/2000   7   2065     1  82      1 26.45294
```

- A description of `whas100` can be called from

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

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

```
> class(whas100)
[1] "data.frame"
```

## 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)
> whas100
# A tibble: 100 x 9
      id admitdate  foldate      los lenfol fstat   age gender   bmi
   <int> <fct>      <fct>      <int>  <int> <int> <int>  <int> <dbl>
 1     1 3/13/1995  3/19/1995      4      6     1    65      0  31.4
 2     2 1/14/1995  1/23/1996      5    374     1    88      1  22.7
 3     3 2/17/1995  10/4/2001      5   2421     1    77      0  27.9
 4     4 4/7/1995   7/14/1995      9     98     1    81      1  21.5
 5     5 2/9/1995   5/29/1998      4   1205     1    78      0  30.7
 6     6 1/16/1995  9/11/2000      7   2065     1    82      1  26.5
 7     7 1/17/1995  10/15/1997     3   1002     1    66      1  35.7
 8     8 11/15/1994 11/24/2000    56   2201     1    81      1  28.3
 9     9 8/18/1995  2/23/1996      5    189     1    76      0  27.1
10    10 7/22/1995  12/31/2002     9   2719     0    40      0  21.8
# ... with 90 more rows
```

## WHAS

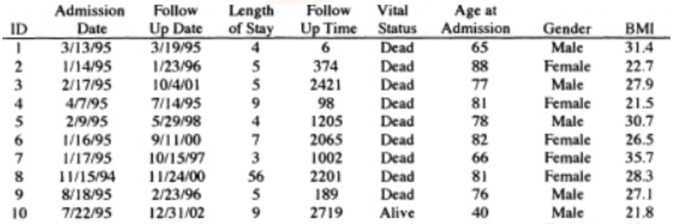
- A transposed version to print `whas100`:

```
> ## install.package(tidyverse)
> glimpse(whas100)
Observations: 100
Variables: 9
$ id        <int> 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 1...
$ admitdate <fct> 3/13/1995, 1/14/1995, 2/17/1995, 4/7/1995, 2/9/1995,...
$ foldate   <fct> 3/19/1995, 1/23/1996, 10/4/2001, 7/14/1995, 5/29/199...
$ los       <int> 4, 5, 5, 9, 4, 7, 3, 56, 5, 9, 6, 11, 6, 10, 7, 5, 6...
$ lenfol    <int> 6, 374, 2421, 98, 1205, 2065, 1002, 2201, 189, 2719,...
$ fstat     <int> 1, 1, 1, 1, 1, 1, 1, 1, 1, 0, 0, 1, 1, 0, 0, 0, 1, 1...
$ age       <int> 65, 88, 77, 81, 78, 82, 66, 81, 76, 40, 73, 83, 64, ...
$ gender    <int> 0, 1, 0, 1, 0, 1, 1, 1, 0, 0, 1, 0, 1, 0, 0, 0, 0, 0...
$ bmi       <dbl> 31.38134, 22.65790, 27.87892, 21.47878, 30.70601, 26...
```

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

## WHAS

- Here is the screen shot of Table 1.1:

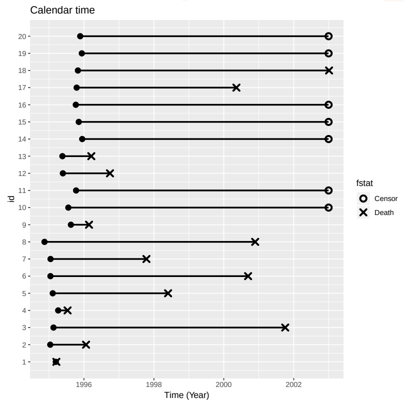


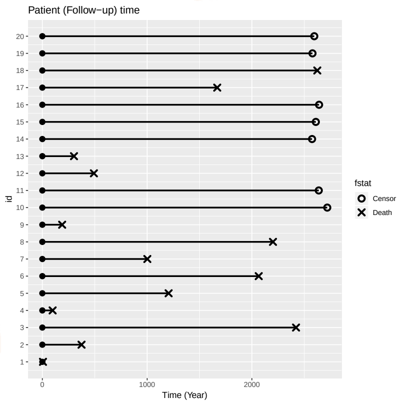
| ID | Admission Date | Follow Up Date | Length of Stay | Follow Up Time | Vital Status | Age at Admission | Gender | BMI |
|---|---|---|---|---|---|---|---|---|
| 1 | 3/13/95 | 3/19/95 | 4 | 6 | Dead | 65 | Male | 31.4 |
| 2 | 1/14/95 | 1/23/96 | 5 | 374 | Dead | 88 | Female | 22.7 |
| 3 | 2/17/95 | 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"))
[1] "2003-01-05 CST"
```

- 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

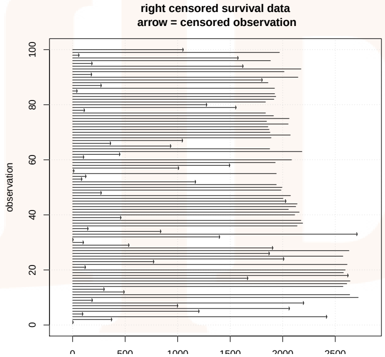
```
> whas100 %>% with(Surv(lenfol, fstat))
  [1]    6   374  2421    98  1205  2065  1002  2201   189  2719+ 2638+
 [12]  492   302  2574+ 2610+ 2641+ 1669  2624  2578+ 2595+  123  2613+
 [23]  774  2012  2573+ 1874  2631+ 1907   538   104     6  1401  2710
 [34]  841   148  2137+ 2190+ 2173+  461  2114+ 2157+ 2054+ 2124+ 2137+
 [45] 2031  2003+ 2074+  274  1984+ 1993+ 1939+ 1172    89   128  1939+
 [56]   14  1011  1497  1929+ 2084+  107   451  2183+ 1876+  936   363
 [67] 1048  1889+ 2072+ 1879+ 1870+ 1859+ 2052+ 1846+ 2061+ 1912+ 1836+
 [78]  114  1557  1278  1836+ 1916+ 1934+ 1923+   44  1922+  274  1860+
 [89] 1806  2145+  182  2013+ 2174+ 1624   187  1883+ 1577    62  1969+
[100] 1054
```

- 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))
# A tibble: 100 x 5
     id recTime recType temTime temStatus
  <int> <lgl>   <lgl>     <dbl>     <dbl>
1     1 NA      NA            6         1
2     2 NA      NA          374         1
3     3 NA      NA         2421         1
4     4 NA      NA           98         1
5     5 NA      NA         1205         1
# ... with 95 more rows
```

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

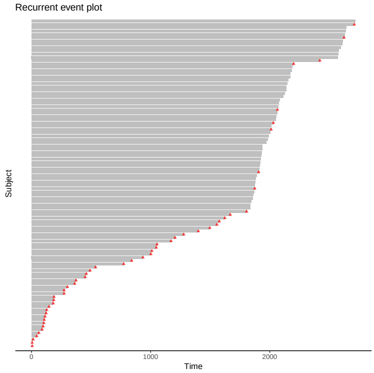
```
> plotEvents(reSurv(lenfol, id, rep(0, 100), fstat) ~ 1, data = whas100)
```

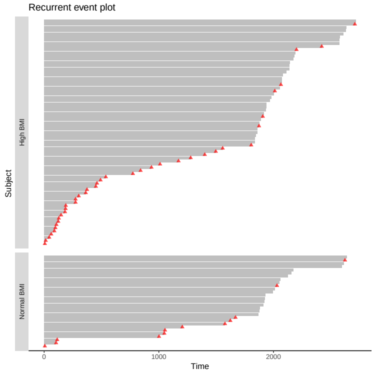
- The function plotEvents also allows stratifications.

```
> 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 ($\infty$ 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.

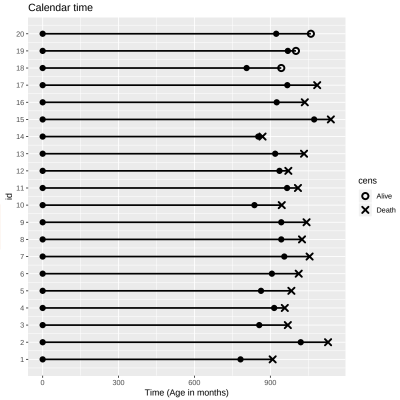
```
> data(channing, package = "boot")
> head(channing)
   sex entry exit time cens
1 Male   782  909  127    1
2 Male  1020 1128  108    1
3 Male   856  969  113    1
4 Male   915  957   42    1
5 Male   863  983  120    1
6 Male   906 1012  106    1
```

- 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 *i*th patient, respectively. Left truncation implies $T_i < Y_i$.
- Standard survival analysis methods require independent censoring and *quasi-independence* of failure and truncation.