Survival Analysis

Seval Kul, PhD Student
Research Assistant of Biostatistics
Department of Biostatistics
Faculty of Medicine
Mersin University / Turkey

Outline

- What is survival analysis
- Why special methods are needed to analyze survival data?
- Descriptive measures of survival experience.
- Goals of survival analysis.
  Goal 1: Kaplan Meier Estimate: To estimate and interpret survival function from survival data.
  Goal 2: Log rank test: To compare survival functions.
  Goal 3: Hazard Regression: To assess the relationship of explanatory variables to survival time

What is survival analysis?

- Survival analysis is a collection of statistical procedures for data analysis for which the outcome variable of interest is time until an event occurs.

Start follow up → **TİME** → **Event**

Outcome variable: Time until an event occurs

Event?

- Death
- Disease incidence
- Relapse from remission
- Recovery (e.g., return to work)

Time?

- Time to death
- Time to relapse of a disease
- Time to recovery from illness
- Length of stay in a hospital
- Time to finish an intervention

Time ≡ Survival Time

Examples

- Leukemia patients /time in remission (weeks)
- Disease-free cohort/time until heart disease (years)
- Elderly (60+) population/time until death (years)
- Heart transplants/time until death (months)

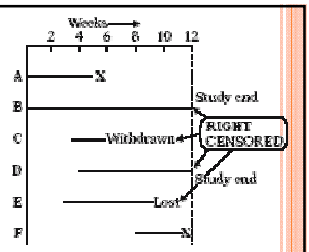
Is it always possible to record the time to event ?

Censoring occurs when we have some information about individual survival time, but we don't know the survival time exactly.

Censoring: Incomplete observation of the time to event.

Why censor?

- Study ends-no event
- Lost to follow up
- Withdraws



How we work with censored data:
Use all informaton up to time of censorship; don't throw away information.

Why special methods are needed to analyze survival data?

- 1. Why not compare mean time-to-event between your groups using a t-test or linear regression?

-- ignores censoring

- 2. Why not compare proportion of events in your groups using risk/odds ratios or logistic regression?

--ignores time

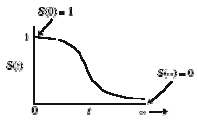
Terminology

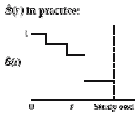
- S(t)=Survival function
- S(t) gives the probability that a person survives longer than some specified time **t:**

$S(t) = P(T > t)$

t	$S(t)$
1	$S(1) = P(T > 1)$
2	$S(2) = P(T > 2)$
3	$S(3) = P(T > 3)$
.	.
.	.
.	.

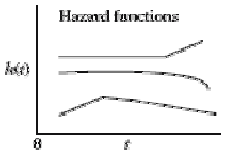
- Theoretical S(t):





Terminology

- h(t):Hazard function
- h(t) is the short-term event rate for subjects who have not yet experienced the outcome event.



- $h(t) \geq 0$
- $h(t)$ has no upper bound

Descriptive measures of survival experience

- **Median Survival Time:** Is the time tj at which 50% of the patients have survived.
- At the median survival time, half the subjects have developed the event and half are still on follow-up.

- Average hazard rate ($\bar{h}$)

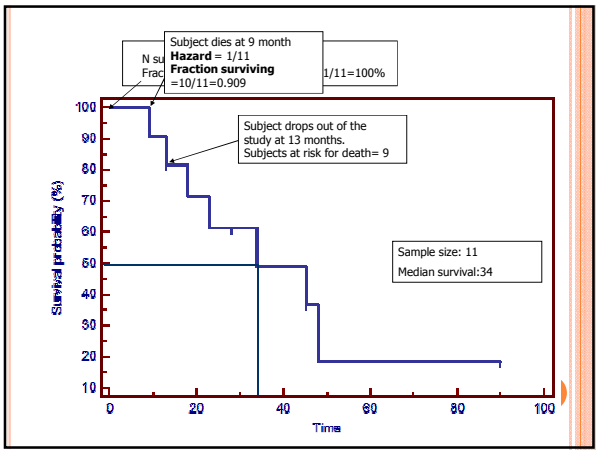
$$\bar{h} = \frac{\#\,\text{failures}}{\sum_{i=1}^{n} t_i}$$

The higher the average hazard rate, the lower is the group's probability of surviving.

Goals of Survival Analysis

Goal 1: Kaplan Meier Estimate: To estimate and interpret survival function from survival data.

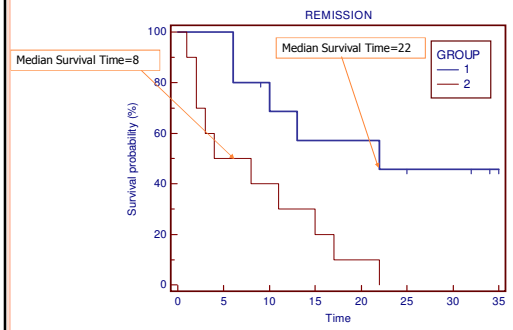
- Non-parametric estimate of the survival function.
- Commonly used to describe survivorship of study population/s.
- Commonly used to compare two study populations.
- Intuitive graphical presentation.



Goal 2: Log rank test: To compare survival functions.

- To evaluate whether or not KM curves for two or more groups are statistically equivalent.
- The most popular testing method is called the log–rank test.
- Null hypothesis is no difference between survival functions of the two groups.

Comparison of survival curves (Logrank test): P=0.0098



Hazard ratio: 3,5799 (95 % CI:1,4174-12,671)

Goal 3: Hazard Regression (Cox Regression): To assess the relationship of explanatory variables to survival time

- Allows for prognostic factors.
- Explore the relationship between survival and explanatory variables.
- Models and compares the hazards for different groups/factors (explanatory variables).
- Under the *proportional hazards assumption* the hazard ratio does not vary with time

Mayo Clinic Primary Biliary Cirrhosis Data

Description: Follow up of 312 with primary biliary cirrhosis, a rare autoimmune liver disease, at Mayo Clinic (Dickson *et al.*, 1989).

Variables:

- Time: Time from diagnose to death (Survival time)
- Age: in years
- Trt: 0-Placebo, 1-D-penicillamine (DPCA)
- alb:serum albumin
- bili:serum bilirunbin
- Status: Censoring status

The variables in the equation table gives summaries of the coefficients' roles in the model.

	B	SE	Wald	df	Sig.	Hazard ratio	95,0% CI for Hazard Ratio	
							Lower	Upper
TRT: DPCA vs Placebo	,021	,184	,013	1	,910	1,021	,712	1,465
AGE	,032	,009	11,906	1	,001	1,033	1,014	1,052
Serum albumin	-1,480	,222	44,312	1	,000	,228	,147	,352
Serum bilirunbin	,138	,014	97,187	1	,000	1,148	1,117	1,180
SEX: Female vs Male	,560	,249	5,064	1	,024	1,751	1,075	2,851

- B is the estimated coefficient, with standard error S.E.
- The ratio of B to S.E., squared, equals the Wald statistic. If the Wald statistic is significant (i.e., less than 0.05) then the variable is useful to the model.

Treatment has no statistical significant effect on mortality rate (p=0,910)

The risk of death increases by a factor of 1.033 as age increases by 1 year

	B	SE	Wald	df	Sig.	Hazard ratio	95,0% CI for Hazard Ratio	
							Lower	Upper
TRT: DPCA vs Placebo	,021	,184	,013	1	,910	1,021	,712	1,465
AGE	,032	,009	11,906	1	,001	1,033	1,014	1,052
Serum albumin	-1,480	,222	44,312	1	,000	,228	,147	,352
Serum bilirunbin	,138	,014	97,187	1	,000	1,148	1,117	1,180
SEX: Female vs Male	,560	,249	5,064	1	,024	1,751	1,075	2,851

The risk of death decreases by a factor of 0.228 as serum albumin increases by 1 year

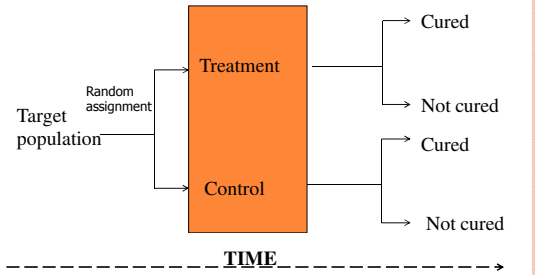
The risk of dying for females is about 2 times higher than males.

Thanks for Your Attention!

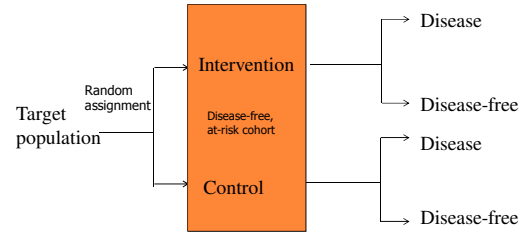
Kind of survival studies

- Randomized clinical trials
- Prospective cohort studies
- Retrospective cohort studies

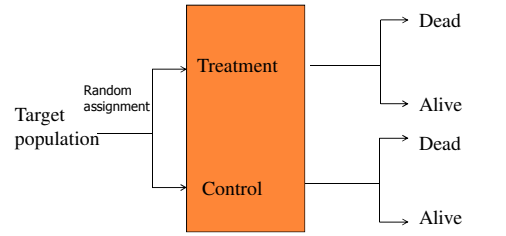
Randomized Clinical Trial (RCT)



Randomized Clinical Trial (RCT)



Randomized Clinical Trial (RCT)



Cohort study (prospective/retrospective)