Understanding Survival Analysis

The Statistical Study of Time, Risk, and Outcomes

Introduction

Time isn't just ticking it's talking

Start/Follow-up Time -----> **Event** (Failure) [Death, Disease, Relapse, Recovery]

Outcome Variable (Survival Time)

[Years, months, weeks or even days from the beginning of the follow-up of an individual until an event occurs.]

Major Problem - Censoring !

We don't know the exact time when something happened. Only the part of the information is available to us.

Reason for Censoring

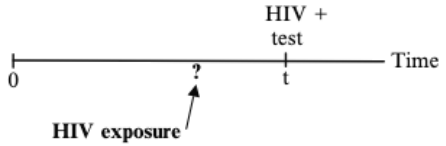
1. Study ends with no events.
   Example: A patient still in remission when the study wraps up.
2. Lost To Follow-up.
   (moved away, dropped out)
3. Withdrawn from the Study.

Right Censoring

We know the event didn't happen until a certain time, but we don't know when it exactly happened.

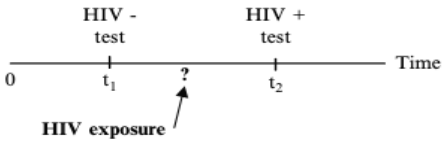
Left Censoring

We know the event already happened, but don't know exactly when.



Interval Censoring

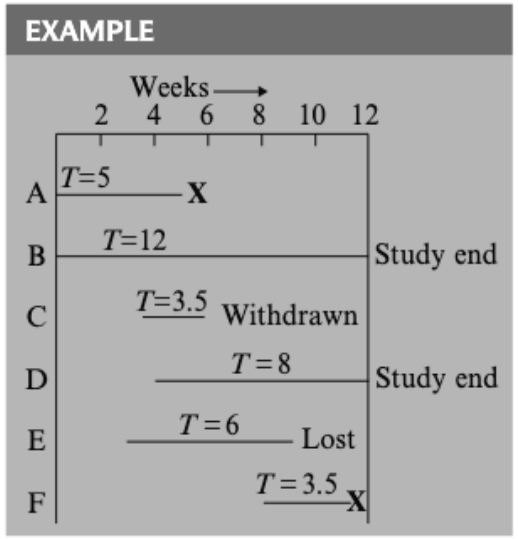
We know the event happened between two times, but not the exact moment.



Examples

1. Leukemia patients/time in remission.
(A study that follows leukemia patients in remission over several weeks to see how long they stay in remission)

2. Elderly Population (60+) /time until death. (13+ years follow-up of an elderly population (60+ years) to see how long remain alive.)



Notation:

T : Random Variable denoting a person's Survival Time.

t : Specific Value of interest of our Random Variable 'T'

d : Dichotomous variable denoting failure or Censoring. 1:Censored, 0:Failure.

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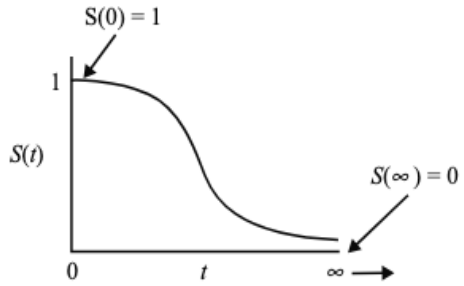
Terminology & Notation

Some Useful Metrics in Survival Analysis

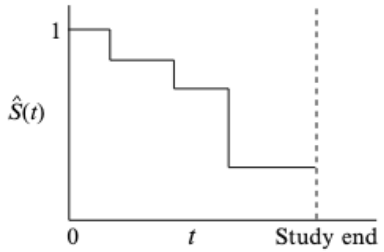
Survival Function

Intuitively, it is the probability that a person survives longer than some specified time 't'.
S(t) = P(T>t)

Theoretical $S(t)$:



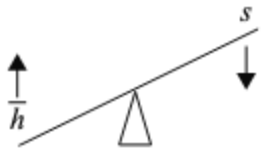
$\hat{S}(t)$ in practice:



Relationship

$$S(t) = \exp\left[-\int_0^t h(u)du\right]$$

$$h(t) = -\left[\frac{d\,S(t)/dt}{S(t)}\right]$$



Properties

1. Survival functions are non-increasing. That is they head downwards as t increases.
2. At time t=0, S(t=0) = 1, i.e. at the beginning of the study, survival rate is the highest.
3. At time t=∞ , S(t=∞) = 0, i.e. if the study period increased without limit, eventually nobody would survive.

Hazard Function

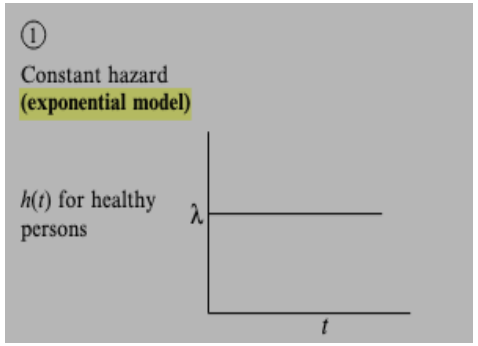
(Conditional Failure Rate)

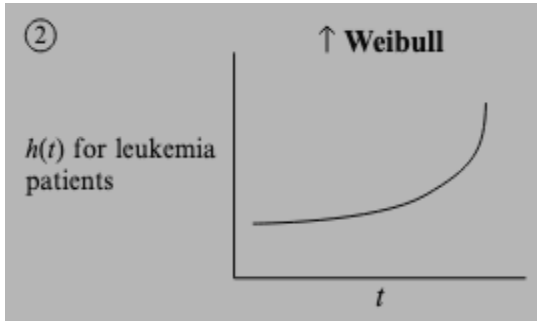
Gives the instantaneous potential per unit time for the event to occur, given that the individual

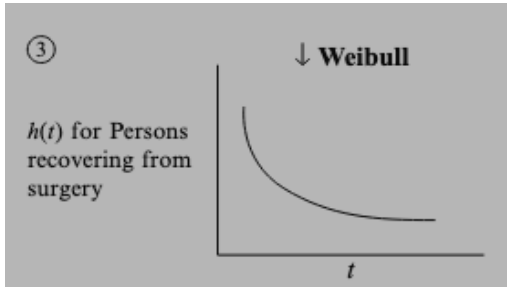
$$h(t) = \lim_{\Delta t \to 0} \frac{P(t \le T < t + \Delta t | T \ge t)}{\Delta t}$$

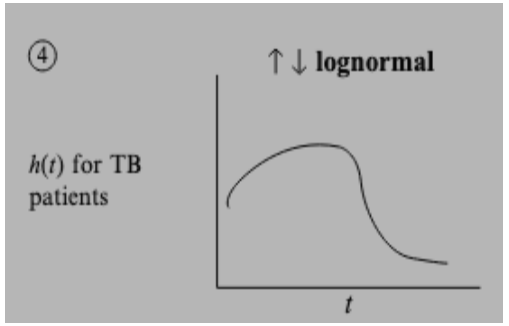
Properties

1. Hazard functions is always non negative.
2. It has No Upper bound.
3. People often think this as a probability, but this is nothing but a rate.









Des. Measures & their Glitches

Some useful Statistic to perform Analysis

Survival Function

leukemia trials conducted by the University of California, Berkeley [Berkson, Dr. David Cox]

Remission times (in weeks) for two groups of leukemia patients

Group 1 (Treatment) $n = 21$	Group 2 (Placebo) $n = 21$
6, 6, 6, 7, 10, 13, 16, 22, 23, 6+, 9+, 10+, 11+, 17+, 19+, 20+, 25+, 32+, 32+, 34+, 35+	1, 1, 2, 2, 3, 4, 4, 5, 5, 8, 8, 8, 8, 11, 11, 12, 12, 15, 17, 22, 23
$\bar{T}_1$ (ignoring + 's) = 17.1	$\bar{T}_2 = 8.6$
$\bar{h}_1 = \frac{9}{359} = .025$	$\bar{h}_2 = \frac{21}{182} = .115$

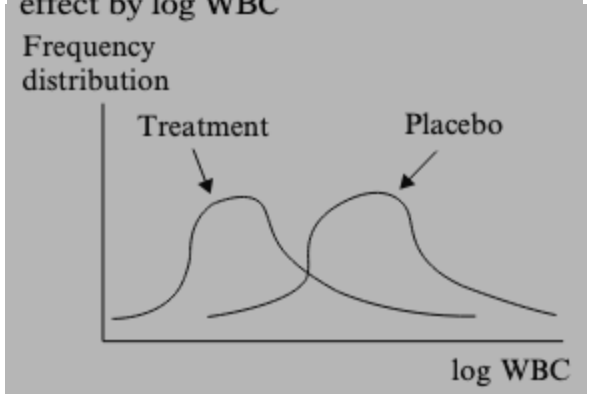
$$\text{Average hazard rate } (\bar{h}) = \frac{\#\text{failures}}{\sum_{i=1}^{n} t_i}$$

Using average hazard rates, we again see that the treatment group appears to be doing better overall than the placebo group; that is, the treatment group is less prone to fail than the placebo group.

Group 1		Group 2	
t (weeks)	log WBC	t (weeks)	log WBC
6	2.31	1	2.80
6	4.06	1	5.00
6	3.28	2	4.91
7	4.43	2	4.48
10	2.96	3	4.01
13	2.88	4	4.36
16	3.60	4	2.42
22	2.32	5	3.49
23	2.57	5	3.97
6+	3.20	8	3.52
9+	2.80	8	3.05
10+	2.70	8	2.32
11+	2.60	8	3.26
17+	2.16	11	3.49
19+	2.05	11	2.12
20+	2.01	12	1.50
25+	1.78	12	3.06
32+	2.20	15	2.30
32+	2.53	17	2.95
34+	1.47	22	2.73
35+	1.45	23	1.97

The table at the left gives the remission survival times for the two groups with additional information about white blood cell count for each person studied. In particular, each person's log white blood cell count is given next to that person's survival time.

Treatment group: $\overline{\log \text{WBC}} = 1.8$
Placebo group: $\overline{\log \text{WBC}} = 4.1$
Indicates **confounding** of treatment effect by log WBC



The treatment group may appear to survive longer due to low log WBC, not treatment efficacy — indicating the treatment effect is confounded by log WBC.

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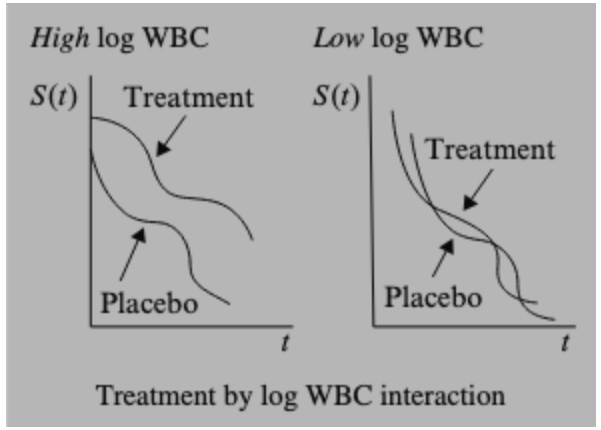
Interaction Effect

Interaction means the treatment's effect varies by log WBC levels. For high log WBC, treatment improves survival over placebo; for low log WBC, there's no difference. This indicates a strong treatment-log WBC interaction - treatment efficacy depends on log WBC.



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	Individual #	t (weeks)	d	X_1 (Group)	X_2 (log WBC)
Group 1	1	6	1	1	2.31
	2	6	1	1	4.06
	3	6	1	1	3.28
	4	7	1	1	4.43
	5	10	1	1	2.96
	6	13	1	1	2.88
	7	16	1	1	3.60
	8	22	1	1	2.32
	9	23	1	1	2.57
	10	6	0	1	3.20
	11	9	0	1	2.80
	12	10	0	1	2.70
	13	11	0	1	2.60
	14	17	0	1	2.16
	15	19	0	1	2.05
	16	20	0	1	2.01
	17	25	0	1	1.78
	18	32	0	1	2.20
	19	32	0	1	2.53
	20	34	0	1	1.47
	21	35	0	1	1.45

Problem

Compare two groups after adjusting for confounding and interaction.

we are now considering two explanatory variables in our extended example, whereas we previously considered a single variable, group status. The data layout for the computer needs to reflect the addition of the second variable, log WBC.

X1 – Primary interest
X2 – Extraneous variable used to get over the Confounding and/or Interaction Effect.

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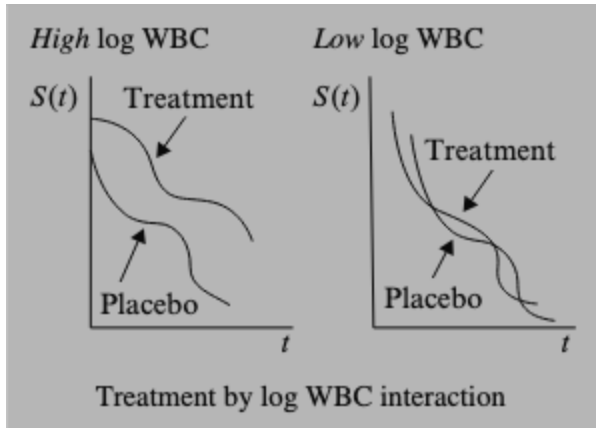

Alt. way of analysis

1. Stratify on log WBC.
2. Use math modelling.
   Ex - proportional hazard model

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