TMA4275 LIFETIME ANALYSIS

Slides 5: Censoring and Kaplan-Meier estimator

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NTNU, Spring 2020

CENSORING

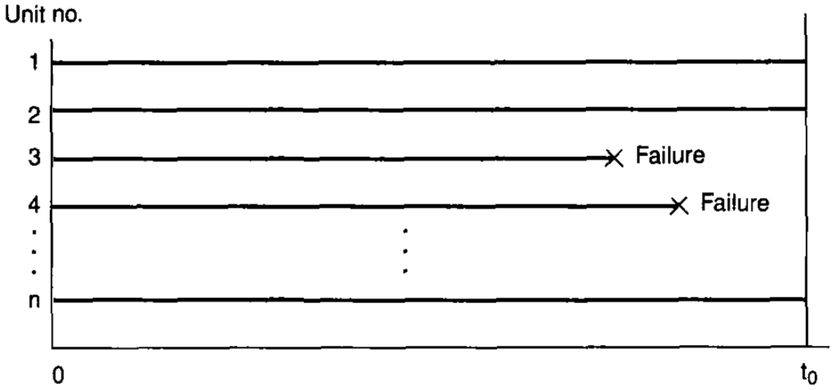
Lifetime data typically include *censored* data, meaning that:

- some lifetimes are known to have occurred only within certain intervals.
- The remaining lifetimes are known exactly.

Categories of censoring:

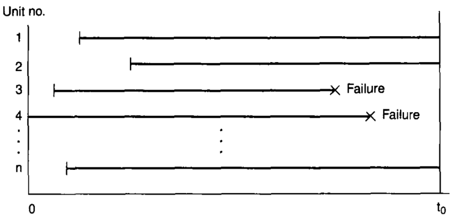
- right censoring
- left censoring
- interval censoring

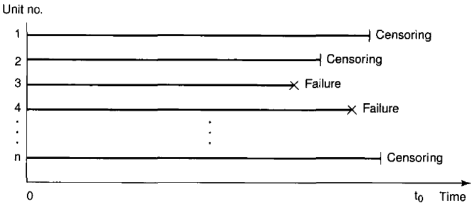
n units put on test at time $t = 0$. Experiment stopped at time $t = t_0$.



GENERALIZED TYPE I CENSORING ("STAGGERED ENTRY")

Individuals enter the study at different times, and the terminal point of the study is predetermined.





n units are put on test at time $t = 0$.

The study continues until r individuals have failed, where r is some predetermined integer ($r < n$).

Advantage: It could take a very long time for all items to fail. Also, the statistical treatment of Type II censored data is simpler because the joint distribution of the order statistics is available.

This is a mix of Type I and Type II censoring. Choose both an end time t_0 as for Type I censoring and an $r < n$ as for Type II censoring. Stop the experiment at time t_0 or at the rth failure, whatever comes first.

RANDOM RIGHT CENSORING (TYPE IV CENSORING)

- For each unit we define
  - T_i to be the potential lifetime
  - C_i to be the potential censoring time

  where
- T_i, C_i are **independent random variables**.
- Then we *observe* the pair (Y_i, δ_i), where

$$\begin{aligned} Y_i &= \min(T_i, C_i) \\ \delta_i &= \begin{cases} 1 & \text{if} \quad T_i \leq C_i \\ 0 & \text{if} \quad T_i > C_i \end{cases} \end{aligned}$$

Example of use: Cancer treatment, with T_i being the time of death due to this cancer; while C_i is the time of death of another cause, or an accident, or migration, etc.

(*Right censoring is the most common way of censoring.*)

Right censoring of Type I, II, III, IV can all be represented as follows:

n units are observed, with potential i.i.d. lifetimes $T_1, T_2, \cdots, T_n$. For each i, we observe a time Y_i which is either the true lifetime T_i, or a censoring time $C_i < T_i$, in which case the true lifetime is "to the right" of the observed time C_i.

The observation from a unit is the pair (Y_i, δ_i) where the *censoring indicator* δ_i is defined by

$$\delta_i = \begin{cases} 1 & \text{if} \quad Y_i = T_i, \text{ in which case we observe the true lifetime } T_i \\ 0 & \text{if} \quad Y_i = C_i, \text{ in which case it is only known that } T_i > Y_i \end{cases}$$

Consider a situation where n individuals are followed from time $t = 0$. The ith individual is followed until $Y_i = \min(T_i, C_i)$, i.e. until either failure (death) or censoring at time C_i.

The ith individual is said to be at risk at time t if $t < Y_i$, i.e. if the individual has not yet been censored and have not failed.

A sensoring scheme is said to satisfy the property of **independent censoring** if, at any time t, the individuals that are *at risk* are representative for the distribution of T in the sense that their probaility of failing in a small time interval $(t, t + h)$ is (in the limit as h tends to 0) is $z(t)h$.

The censoring types we have considered so far all satisfy this independent censoring property.

We are interested in estimating the distribution of the lifetime T of some equipment or the time to some given event in a medical context.

We have indicated how parametric models like exponential and Weibull can be fitted to data.

Now we shall instead see how in particular $R(t)$ can be estimated without making parametric assumptions.

Thus, instead of having to restrict to estimation of one or two parameters, we now have an infinite number of possible functions $R(t)$ to choose from. (Essentially, the only restriction is that it is decreasing, starts in 1 and converges to 0 as $t \to \infty$.)

In this case our observations are the exact failure times $T_1, \ldots, T_n$, assumed to be i.i.d. observations of a lifetime T.

Hence we can estimate $R(t) = P(T > t)$ for a given $t > 0$ by the relative proportion of lifetimes that exceed t:

$$\hat{R}(t) = \frac{\text{number of } T_i > t}{n}$$

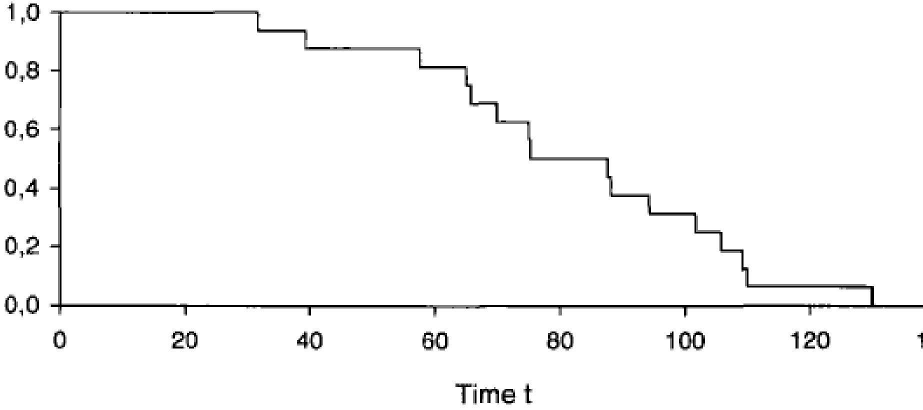
This is called the *empirical survivial function*.

If we order the observations as $T_{(1)} < T_{(2)} < \cdots < T_{(n)}$, then $\hat{R}(t)$ starts at 1 for $t = 0$ and makes a downward jump of $1/n$ at $T_{(1)}$, a new downward jump of $1/n$ at $T_{(2)}$, and so on until it jumps from $1/n$ to 0 at $T_{(n)}$.

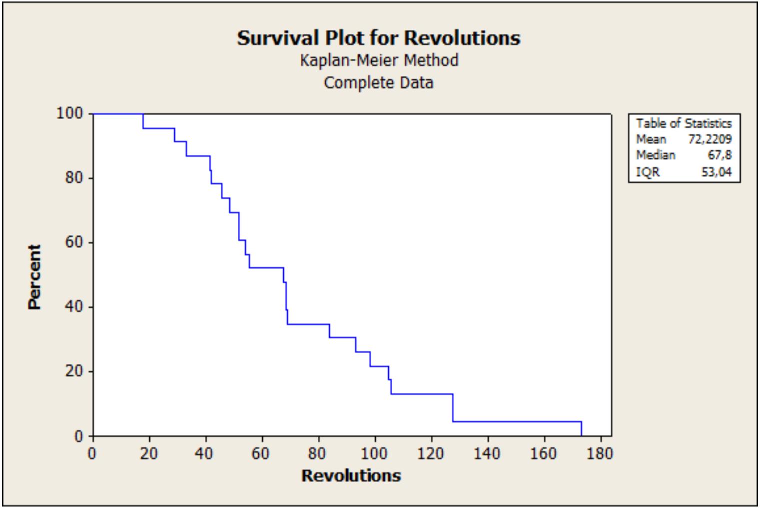
EXAMPLE OF EMPIRICAL SURVIVAL PLOT, $\hat{R}(t)$

$n = 16$ *observed lifetimes:*

31.7, 39.2, 57.5, 65.0, 65.8, 70.0, 75.0, 75.2, 87.7, 88.3, 94.2, 101.7, 105.8, 109.2, 110.0, 130.0



EMPIRICAL SURVIVAL PLOT FOR BALL BEARING DATA



CENSORED DATA: KAPLAN-MEIER ESTIMATOR FOR $R(t)$

Consider n individuals, where the ith individual has potential lifetime T_i and potential censoring time C_i. We *observe* the pair (Y_i, δ_i), where

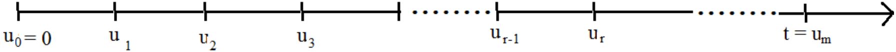
$$\begin{aligned} Y_i &= \min(T_i, C_i) \\ \delta_i &= \begin{cases} 1 & \text{if} \quad Y_i = T_i \\ 0 & \text{if} \quad Y_i = C_i \end{cases} \end{aligned}$$

Assume:

- $T_1, T_2, \cdots, T_n$ are *independent and identically distributed* with common reliability function $R(t)$.
- The censoring mechanism satisfies the property of *independent censoring*.

The estimator is constructed in the following.

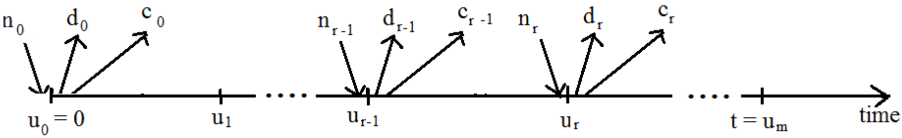
MAIN IDEA OF CONSTRUCTION



Assume first that time is measured on a discrete scale with values $u_0 = 0 \leq u_1 \leq u_2 \leq \cdots$, so that all T_i, C_i, Y_i are among these. Let $t = u_m$. Then

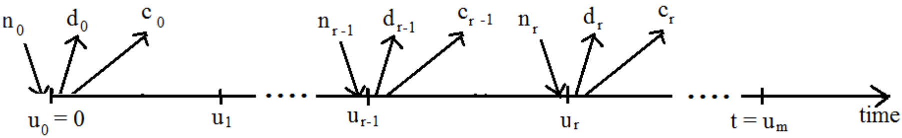
$$\begin{aligned}
R(t) &= P(T > t) = P(T > u_m) \\
&= P(T > u_m \cap T > u_{m-1} \cap \cdots \cap T > u_2 \cap T > u_1 \cap T > u_0) \\
&= P(T > u_0) \cdot P(T > u_1 \mid T > u_0) \cdot P(T > u_2 \mid T > u_1 \cap T > u_0) \\
&\cdots P(T > u_r \mid T > u_{r-1} \cap T > u_{r-2} \cdots \cap T > u_0) \cdots \\
&\cdots P(T > u_m \mid T > u_{m-1} \cap \cdots \cap T > u_0) \\
&= P(T > u_0) \cdot P(T > u_1 \mid T > u_0) \cdot P(T > u_2 \mid T > u_1) \\
&\cdots P(T > u_r \mid T > u_{r-1}) \cdots P(T > u_m \mid T > u_{m-1})
\end{aligned}$$

Idea: Estimate each factor $P(T > u_r \mid T > u_{r-1})$, from data (Y_i, δ_i); $i = 1, \cdots, n$.



Define:

- n_r = number at risk at time u_r; i.e. number that can fail at u_r; counted immediately before u_r.
- d_r = number failing at u_r (those with $Y = u_r$, $\delta = 1$)
- c_r = number censored at u_r (those with $Y = u_r$, $\delta = 0$); assumed to be censored right after u_r, and by convention after all failures at u_r (in practice in the interval following u_r)



Note: The d_i, c_i are found directly from the data, while the n_i are found recursively as:

$$
\begin{aligned}
n_0 &= n \\
n_1 &= n_0 - d_0 - c_0 \\
\dots \\
n_r &= n_{r-1} - d_{r-1} - c_{r-1}
\end{aligned}
$$

Then estimate,

$$P(T > u_r \mid T > u_{r-1}) = 1 - P(T = u_r \mid T > u_{r-1}) \approx 1 - \frac{d_r}{n_r} = \frac{n_r - d_r}{n_r}$$

$$\& \quad P(T > u_0) = 1 - P(T = u_0) \approx 1 - \frac{d_0}{n_0} = \frac{n_0 - d_0}{n_0}$$

It follows that $R(t) = P(T > t)$ can be estimated by

$$\hat{R}(t) = \frac{n_0 - d_0}{n_0} \cdot \frac{n_1 - d_1}{n_1} \cdots \frac{n_r - d_r}{n_r} \cdots \frac{n_m - d_m}{n_m}$$

Note that these factors are 1, whenever $d_r = 0$. Thus

$$\hat{R}(t) = \prod_{\substack{\text{all } u_r \leq t \\ \text{with } d_r \geq 1}} \frac{n_r - d_r}{n_r}$$

In practice we have continous time. But this case can be approximated by making the grid $u_1 < u_2 < \cdots$ finer and finer.

Thus in general the KM-estimator is given by:

If $T_{(1)} < T_{(2)} < \cdots$, are the times with at least one failure, and n_i, d_i are, respectively, the number at risk and the number of failures at $T_{(i)}$, then

$$\hat{R}(t) = \prod_{i: T_{(i)} \leq t} \frac{n_i - d_i}{n_i}$$

GREENWOOD'S FORMULA FOR VARIANCE OF THE KM-ESTIMATOR

$$\widehat{Var(\hat{R}(t))} = \left(\hat{R}(t)\right)^2 \cdot \sum_{T_{(i)} \leq t} \frac{d_i}{n_i(n_i - d_i)}$$

It can shown that for large n, $\hat{R}(t)$ is approximately normally distributed,

$$\hat{R}(t) \approx N(R(t), \widehat{SD(\hat{R}(t))})$$

Thus an approximate 95% confidence interval can be obtained for each t by

$$P\left(\hat{R}(t) - 1.96 \cdot \widehat{SD(\hat{R}(t))} \leq R(t) \leq \hat{R}(t) + 1.96 \cdot \widehat{SD(\hat{R}(t))}\right)$$

Recall thet MTTF $= \int_0^\infty R(t)dt$. Hence it seems natural to estimate MTTF by $\widehat{\text{MTTF}} = \int_0^\infty \hat{R}(t)dt$.

But - recall that

$$\hat{R}(t) = \prod_{T_{(i)} \leq t} \frac{n_i - d_i}{n_i}$$

- If *largest observed time is a failure time: the last factor is 0, so* $\int_0^\infty \hat{R}(t)dt$ *is a finite number.*
- *If largest observed time is censored: the last factor is* $\frac{n_i - d_i}{n_i} > 0$. *So the estimate* $\hat{R}(t)$ *is constant and positive from this time on, making* $\int_0^\infty \hat{R}(t)dt = \infty$.

But - MINITAB uses the common convention:

$$\widehat{MTTF} = \int_0^{\text{largest observed time}} \hat{R}(t)dt$$

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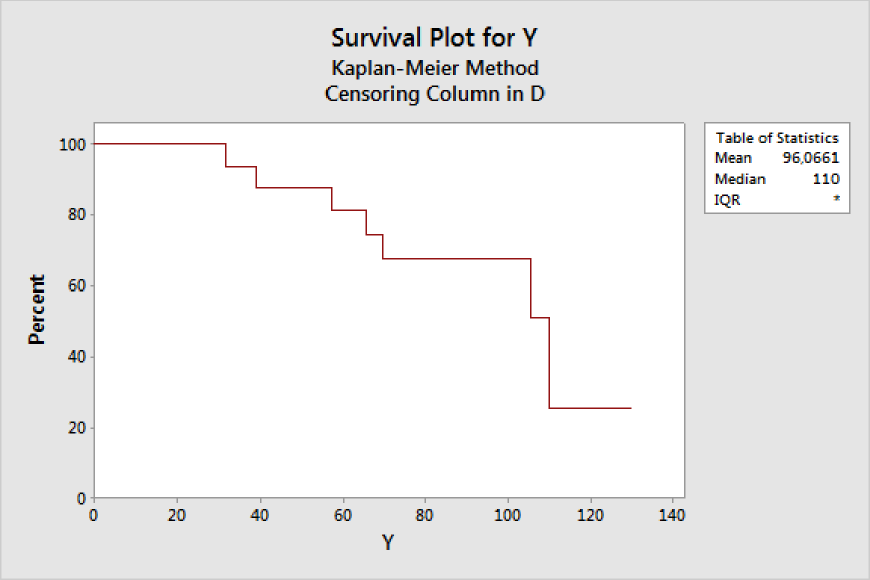
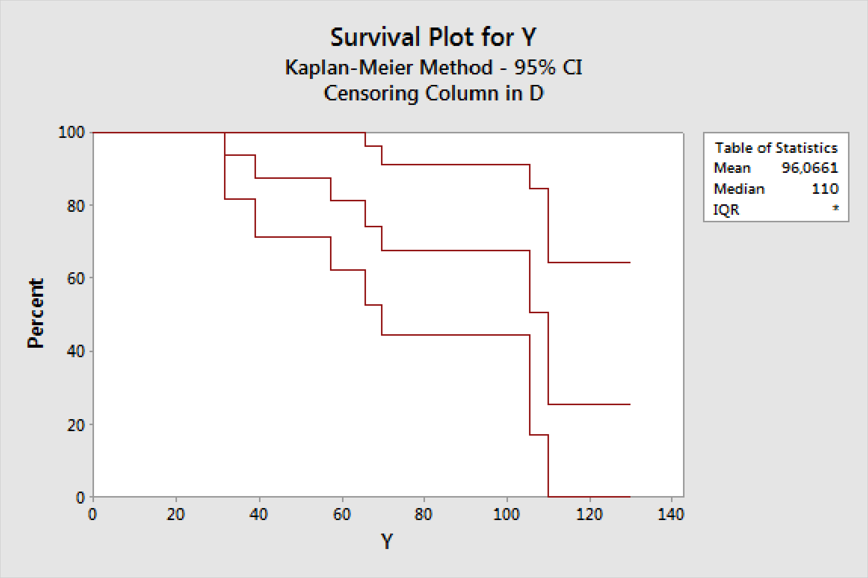
KM-ESTIMATOR FOR CENSORED DATA

Row	Y	D
1	31,7	1
2	39,2	1
3	57,5	1
4	65,0	0
5	65,8	1
6	70,0	1
7	75,0	0
8	75,2	0
9	87,5	0
10	88,3	0
11	94,2	0
12	101,7	0
13	105,8	1
14	109,2	0
15	110,0	1
16	130,0	0

	Number	Number	Survival	Standard	95,0% Normal CI	
Time	at Risk	Failed	Probability	Error	Lower	Upper
31,7000	16	1	0,9375	0,0605	0,8189	1,0000
39,2000	15	1	0,8750	0,0827	0,7130	1,0000
57,5000	14	1	0,8125	0,0976	0,6213	1,0000
65,8000	12	1	0,7448	0,1105	0,5283	0,9613
70,0000	11	1	0,6771	0,1194	0,4431	0,9111
105,8000	4	1	0,5078	0,1718	0,1711	0,8445
110,0000	2	1	0,2539	0,1990	0,0000	0,6440


Survival Plot for Y
Kaplan-Meier Method
Censoring Column in D
Percent
100
80
60
40
20
0
0
20
40
60
80
100
120
140
Y
Table of Statistics
Mean 96,0661
Median 110
IQR *

KM-PLOT WITH CONFIDENCE LIMITS



BREAST CANCER DATA (from Collett's book)

Table 1.2 *Survival times of women with tumours that were negatively or positively stained with HPA.*

Negative staining	Positive staining	
23	5	68
47	8	71
69	10	76*
70*	13	105*
71*	18	107*
100*	24	109*
101*	26	113
148	26	116*
181	31	118
198*	35	143
208*	40	154*
212*	41	162*
224*	48	188*
	50	212*
	59	217*
	61	225*

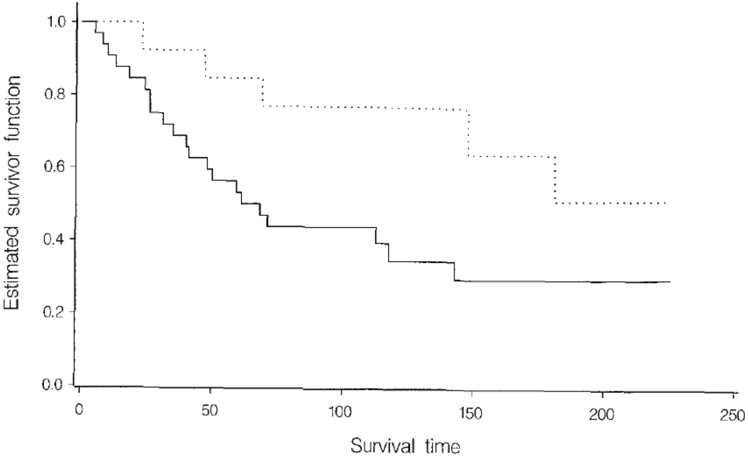


Figure 2.9 *Kaplan-Meier estimate of the survivor functions for women with tumours that were positively stained (—) and negatively stained (···).*

- *Right censoring*
  - Type I-IV censoring
  - General formulation of right censoring
  - Independent censoring
- *Nonparametric estimation of* $R(t)$
  - Empirical survival function
  - The Kaplan-Meier estimator