MATH 60604A Statistical modelling § 7c - Kaplan-Meier estimator

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Notation

We consider a continuous random variable T and an associated sample of size n.

- Suppose that there are D distinct event times
- Let $0 \le t_1 < t_2 < \cdots < t_D$ denote these ordered D failure times.
- Let r_i denote the number of individuals who are **at risk** at time t_i .
 - That is, these individuals have not had experienced the event (nor been censored) before time t_i.
 - Thus, r_j is the number of known survivors just before time t_j who are "at risk" of experiencing the event at time t_j .
- Let $d_j \in \{0, ..., r_j\}$ denote the number of failures at time t_j (there are d_j deaths at time t_j).

Derivation of Kaplan-Meier estimator

The probability of dying in the time window $(t_j, t_{j+1}]$ given survival until t_j is

$$h_j = \mathsf{P} \left(t_j < T \le t_{j+1} \mid T > t_j
ight) = rac{S(t_j) - S(t_{j+1})}{S(t_j)}.$$

This recursion yields

$$S(t) = \prod_{j:t_i < t} (1 - h_j).$$

The Kaplan-Meier estimator is is non-parametric:

- it does not assume any underlying probability distribution for the variable T_i
- rather, the conditional probabilities $\{h_j\}_{j=1}^D$ are treated as parameters of the model.

Likelihood for the discrete observations

- Each failure at time t_i contributes h_i to the likelihood
 - the probability of failure at t_i given survival in the previous time interval.
- The likelihood contribution of survivors at time t_i is $1 h_i$.
- We may write the log likelihood as

$$\ell(\mathbf{h}) = \sum_{j=1}^{D} \{d_j \ln(h_j) + (r_j - d_j) \ln(1 - h_j)\},$$

the sum of contributions of binomial variables at time t_j .

Optimizing the survival probabilities

- Differentiating $\ell(\boldsymbol{h})$ with respect to h_j , we find $\hat{h}_j = d_j/r_j$.
- The Kaplan-Meier estimator of the survival function is

$$\widehat{S}(t) = \prod_{t_j < t} \left(1 - \frac{d_j}{r_j} \right)$$

• Intuition: d_j/r_j is the sample proportion of death at time t_j relative to the total population still alive at time t_j .

Example

The breastcancer data from Sedmak et al. (1989) contain informations on patients with breast cancer, including the following variables:

- time: time until death, or end of study (in months)
- death: indicator variable for death either 0 for right-censored times or 1 for death
- im: response to immunohistochemical examination, either negative (0) or positive (1)

Descriptive statistics for breastcancer

Analysis Variable : time					
N	Mean	Std Dev	Minimum	Maximum	
45	98.33	51.84	19.00	189.00	

death	Frequency	Percent	
0	21	46.67	
1	24	53.33	

im	Frequency	Percent
0	36	80.00
1	9	20.00

In practice, Kaplan–Meier estimator requires significant number observations to be a reliable approximation of the true survivor curve ($n \gg 1000$).

Keep in mind censored observations contribute less information than observed failure times.

Estimation of the survival function

SAS code to fit the Kaplan-Meier estimator

```
proc lifetest data=statmod.breastcancer method=km plots=(s(cl));
time time*death(0);
run;
```

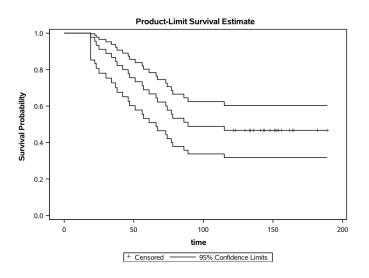
The time argument indicates both the response T_i (time) and the right-censoring indicator δ_i , with the reference in parenthesis for the right-censored observations (death=0)

Estimated survival function

Product-Limit Survival Estimates					
time	Survival	Failure	Survival Standard Error	Number Failed	Number Left
0.000	1.0000	0	0	0	45
19.000	0.9778	0.0222	0.0220	1	44
22.000	0.9556	0.0444	0.0307	2	43
23.000	0.9333	0.0667	0.0372	3	42
25.000	0.9111	0.0889	0.0424	4	41
		:			
165.000	* .			24	2
182.000	* .			24	1
189.000	* .			24	0

Note: The marked survival times are censored observations.

Plot of the survival function



The survival curve is not consistent: $\widehat{S}(t)$ doesn't decrease to zero because the largest observed time is right-censored.

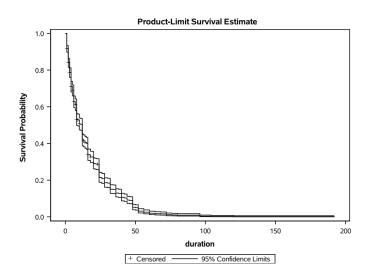
Breastfeeding duration

The breastfeeding data from the National Longitudinal Survey of Youthcontains information on the time until which mothers stop breastfeeding from birth. We focus on the following explanatories:

- duration: duration of breast feeding (in weeks)
- delta: indicator for completed breastfeeding
 - yes (1)
 - right-censored (0)

Summary of the Number of Censored and Uncensored Values				
Total	Failed	Censored	Percent Censored	
927	892	35	3.78	

Survival curve for breastfeeding data



 $\widehat{S}(t)$ reaches zero because the largest survival time is observed, not censored.

Median survival time

The median survival time is the time t_M such that $S(t_m) = 0.5$.

• That is, the median time t_M is such that 50% of people have survived until time t_M .

We can easily find this estimated median time by seeing where the horizontal line $\widehat{S}(t)=0.5$ intersects the survival curve.

Quartile Estimates					
	95% Confidence Interval				
Point					
Percent	Estimate	Transform	Lower	Upper)	
75		LOGLOG			
50	89.000	LOGLOG	66.000	•	
25	51.000	LOGLOG	34.000	67.000	

Mean survival time

For a continuous positive random variable, T>0, it can be shown that

$$\mathsf{E}\left(T\right) = \int_{0}^{\infty} S(t) \mathrm{d}t$$

We can estimate the expected survival time E(T) simply by calculating the area under the survivor curve $\widehat{S}(t)$.

- For example, the mean survival time for the breastfeeding data is 16.89 weeks with standard error 0.614 weeks.
- If the largest recorded survival time is censored, the estimated survival curve $\hat{S}(t)$ will plateau and never reaches 0. The area under the curve is infinite!
- In this case, we can estimate instead the restricted mean survival time: $E\left(\min\{T,\tau\}\right)$ for a chosen τ . It amounts to calculating the average as if the curve dropped to 0 at time τ (rmst option in SAS).