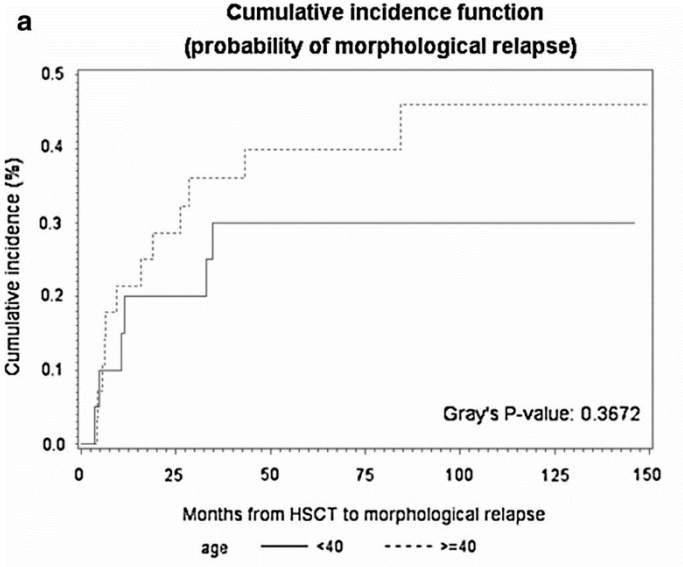
UPPSALA UNIVERSITET

Analysis of Survival Data

Lecture 4 in-class
Summary curves for competing risks
Hypothesis testing



$$H_0 : h_1(t) = h_2(t) \quad \text{for all } t \le \tau$$

$$H_a : h_1(t) \neq h_2(t) \quad \text{for some } t \le \tau$$

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Program L4 in-class

- **Summary curves for competing risks**
- **Hypothesis testing**
  - Online lecture follow-up
  - Review questions
  - Exercises

Review question

Describe the concept of competing risks and describe why this is important to take into consideration. How is e.g. the Kaplan-Meier estimator affected by competing risks?

Exercise 4.10

Using the data reported in section 1.3 for the AML low risk and AML high risk groups, find and interpret the following quantities for each of the two competing risks relapse and death:

a) The estimated cumulative incidence at one year.

b) The confidence intervals of the two estimates in part a.

e) Graphically express the development of relapse and death in remission for these two disease groups.

Section 1.3: Bone marrow transplantation for leukemia

Section 1.3 describes a clinical trial for leukemia (*BMT.txt*).

Group = disease group (ALL, AML low risk, AML high risk)

TDFS = Disease free survival time (time from transplantation to relapse, death, or end of study)

Death = Treatment related death indicator

Relapse = Relapse indicator

(More variables included in the data set)

Review question

How are differences of hazard functions tested?
Describe K samples tests.

Section 1.6: Time to infection for burn patients

In section 1.6 a study is described to evaluate a protocol change in disinfectant practice in a large midwestern university medical center.

Control of infection is the primary concern for the 154 patients entered into the burn unit with varying degrees of burns.

The outcome variable is the time until infection from admission to the unit. Censoring variables are discharge from the hospital without an infection or death without an infection.

84 patients were in a group which had a body-cleansing method (disinfectant: chlorhexidine) and 70 patients received the routine bathing care method (disinfectant: povidone-iodine).

Example: infection in burns

Variables:

Trt = treatment (0=routine bathing, 1=body cleansing)

TimeStaph = Time to staphylococcus infection (days)

Staph = Staphylococcus indicator (1=infection, 0=no inf.)

Exercise 7.3

Consider the data reported in section 1.6 on the times until staphylococcus infection of burn patients.

a) Using the log-rank test, test the hypothesis of no difference in the rate of staphylococcus infection between patients whose burns were cared for with a routine bathing care method versus those whose body cleansing was initially performed using 4% chlorhexidine gluconate.

Exercise 7.3

$$H_0 : S_{routine}(t) = S_{body\_cleans}(t) \quad \text{for all } t \leq \tau$$
$$H_a : S_{routine}(t) \neq S_{body\_cleans}(t) \quad \text{for some } t \leq \tau$$

But what we really test is

$$H_0 : h_{routine}(t) = h_{body\_cleans}(t) \quad \text{for all } t \leq \tau$$
$$H_a : h_{routine}(t) \neq h_{body\_cleans}(t) \quad \text{for some } t \leq \tau$$

τ = largest time at which all of the groups have at least one subject at risk

Exercise 7.3

Significance level?

Wrongly rejecting H_0 in this case means that we would claim that time to infection of burn patients are different for patients given the routine caring method compared to the new body cleansing method, when in fact they are the same.

Consequences?

If there are no serious consequences, the standard 5% is fine to use.

Exercise 7.3

b) Repeat the test using Gehan's weights.

c) Repeat the test using the tarone and Ware weights.

Section 1.3: Bone marrow transplantation for leukemia

Section 1.3 describes a clinical trial for leukemia (*BMT.txt*).

Group = disease group (ALL, AML low risk, AML high risk)

TDFS = Disease free survival time (time to relapse, death, or end of study)

DFS = Disease free survival indicator

TA = Time to acute graft-versus-host disease

A = Acute graft-versus-host disease indicator

(More variables included in the data set)

Exercise 7.8

Use the data reported in section 1.3 again, for bone marrow transplanted leukemia patients and their times to relapse.

Acute graft-versus-host disease is considered to have an antileukemic effect, therefore one would expect lower relapse rates for patients who have developed aGVHD than for those that do not develop aGVHD.

Examine the validity of this finding.

Exercise 7.8

a) Test if the hazard rate for the occurrence of aGVHD is the same for the three disease groups

Exercise 7.8

$$H_0 : h_{ALL}(t) = h_{AML\_low}(t) = h_{AML\_high}(t) \quad \text{for all } t \leq \tau$$

$$H_a : \text{at least one of the } h_j(t)'s \quad \text{different for some } t \leq \tau$$

τ = largest time at which all of the groups have at least one subject at risk

Exercise 7.8

Significance level?

Wrongly rejecting H_0 in this case means that we would claim that the risk of relapse is different for patients in different disease groups, when they in fact are the same.

Consequences?

No serious consequences unless this e.g. implies a change in treatment, and the treatment can have consequences. The standard 5% is most likely fine to use.

Exercise 7.8

Choice of test?

Review question

Describe what a stratified test is and when it should or shouldn't be used. When would it be better to perform different tests in each stratum instead of a stratified test?

Exercise 7.8

b) Test if the hazard rates for relapse is the same in all three disease groups, taking aGVHD into account

Exercise 7.8

$$H_0 : h_{ALL\_s}(t) = h_{AML\_low\_s}(t) = h_{AML\_high\_s}(t),$$

$$\text{for s} = 1,2, \quad t < \tau$$

$$H_a : \text{At least one of the } h_{js}(t)\text{'s different for some } t < \tau$$

τ = largest time at which all of the groups have at least one subject at risk

Home assignment 1

You can now solve the rest of the tasks