Two-Sample Tests

- We now consider comparing the survival functions of two groups.
- Suppose one set of patients receives Treatment 1 and another set receives Treatment 2.
- We observe the survival (or censoring) times for each subject in the two samples.
- Our null hypothesis implies no difference between the treatments:

- This could be equivalently stated:

- We again have three possible alternatives:

(1)

- Alternative ① implies: Treatment 1 is _____ effective than Treatment 2.

②

- Alternative ② implies: Treatment 1 is _____ effective than Treatment 2.

③

- This simply tests for some difference between the survival functions of the two treatments.

The Log-rank Test

- The procedure we will use is a distribution-free method called the log-rank test.
- The goal is to test $H_0: S_1(t) = S_2(t)$ for all t against one of the 3 alternatives.

Notation: For each individual, $i=1,\ldots,n$, we observe

where X_i is the observed data value for subject i:

Δ_i is the failure indicator for subject i:

(i.e., $\Delta_i = 0$ if subject i is _____)

and Z_i is the treatment-group indicator for subject i:

Let n_1 = # subjects in treatment group 1
n_2 = # subjects in treatment group 2

- So $n_1 + n_2 = n$.

- Denote the number at risk (not yet died or been censored) at time u from treatment 1 as:

- The number at risk at time u from treatment 2 is:

- Let $n(u) = n_1(u) + n_2(u)$.
- The number of deaths at time u from treatment group 1 is:

- The number of deaths at time u from treatment group 2 is:

- The total number of deaths at time u is:

- At any time u, we can produce the following 2×2 table:

- If $H_0: S_1(t) = S_2(t)$ is true, then the chance of dying at time u does not depend on the treatment.
- Under H_0, dying/surviving is independent of treatment, in which case:

- Now, consider a sequence of such 2×2 tables at every time u at which a death occurs.
- Let's add these differences over this whole sequence of tables:

where $A(u)$ is the set of distinct death times.

- If H_0 is true, then
- If $S_1(t) > S_2(t)$ for all t, then we would expect treatment 1 to have _____ deaths than expected under independence: We expect $d_1(u)$ to be _____.

$\Rightarrow T^*$ should be

- If $S_1(t) < S_2(t)$ for all t, we would expect treatment 1 to have _____ deaths than expected under independence: We expect $d_1(u)$ to be _____.

$\Rightarrow T^*$ should be

- If $S_1(t) \neq S_2(t)$, we will reject H_0 if T^* is

- We can standardize T^* in the following way to obtain a formal test:

- Under H_0, $T_{LR} \dot{\sim} N(0,1)$ for large n (we will justify this later).

H_0 H_a RR

Example 1 (Ovarian cancer): Survival (or censoring) times (in days) were measured for 26 ovarian cancer patients. There were two treatment groups:

Treatment 1 = Cyclophosphamide alone

Treatment 2 = Cyclophosphamide + adriamycin

Is there a difference in the survival functions for the two treatments? Use $\alpha = 0.05$.

Example 2: Time until recurrence of colon cancer (or censoring time) was measured for 614 patients. The two treatments were:

Trt 1 = Levamisol (a low-toxicity compound)

Trt 2 = Levamisol + 5FU (5FU is a stronger but more toxic drug)

Is the survival function better when 5FU is included in the treatment? Use $\alpha = 0.05$.

Sampling Distribution of T_{LR}

- Consider our 2×2 table and assume the marginal counts are fixed:

- Conditional on the marginal counts, the r.v. $d_1(u)$ has a _____ distribution with:

- From our _____ formulas, the conditional mean of $d_1(u)$ is

and its conditional variance is

- It can be shown that T^* is the sum of uncorrelated terms, so that under H_0,

and

and it can be shown that, by a specialized version of the CLT: